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BOOK OF ABSTRACTS

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This book contains abstracts submitted from Keynote, Seminar, Oral and Poster Presentations for the 16th World Congress on Endometriosis.

- Keynote Presentations are featured at the beginning of the book.
- Oral presentation abstracts appear in the order in which they were presented during the Congress.
- The Top 24 3MT Poster Presentations are also listed in the order in which they were presented during the Congress.
- Poster presentations appear by poster session and within each session, are grouped by theme.
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KEYNOTE PRESENTATIONS

KEYNOTE SESSION 1

EPIDEMIOLOGY AND ENDOMETRIOSIS

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Introduction/Background
Endometriosis affects about 10% of reproductive-age women globally, including an estimated 50 million in India. Despite this high burden, data on its epidemiology, clinical presentation, and risk factors remain limited in India and other low- and middle-income countries (LMICs), highlighting a critical gap in evidence and care.

Materials and Methods
The Endometriosis Clinical and Genetic Research in India (ECGRI) study, a national multi- center case-control study, was conducted from 2020–2024 across 18 sites in 9 Indian states. A total of 1,775 women aged 18–50 with surgically and/or histologically confirmed endometriosis were enrolled, along with 1,775 unrelated controls. Data collection followed a modified version of the World Endometriosis Research Foundation's EPHect Endometriosis Patient Questionnaire (EPQ) and the Standard Surgical Form (SSF).

Results
The ECGRI study revealed geographic variation in endometriosis lesion types among Indian women, with endometrioma being the most common (59%). Advanced-stage endometriosis was more frequently reported in public health facilities (73.1%) than in private ones. The diagnostic delay [mean (SD)] was 6.9 (8.3) years with longer delays observed in Central [10 (8.4)], South [7.5 (9.9)] and North [7.5 (7.2)] zones. Pain (73%) and infertility (46%) were the most common presenting symptoms. Women with endometriosis had a 7.5-fold higher burden of multimorbidity (≥3 comorbidities). A high prevalence of gynecological (50.6%), autoimmune (18.6%), musculoskeletal (13.5%), and psychiatric (11.6%) conditions was reported. The most common comorbidities were fibroid uterus (34.3%), thyroid disease (17.6%), and adenomyosis (10.6%).

Conclusion
The ECGRI study reveals geographic differences in endometriosis presentation across India, with significant diagnostic delays and high rates of advanced disease in public facilities. Multimorbidity, especially gynecological, autoimmune, and psychiatric conditions, was prevalent, highlighting the urgent need for timely diagnosis and integrated, multidisciplinary care In India.

Key words
Endometriosis, multimorbidity, diagnosis delay

KEYNOTE SESSION 2

ENDOMETRIOSIS AND CANCER: OPPORTUNITIES FOR A PRECISION MEDICINE APPROACH TO IMPROVE OUTCOMES

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Country where research was undertaken:
Australia

Introduction/Background
Gynaecological cancers and endometriosis share several similarities. Both have been stigmatised, dismissed, underfunded and subsequently under researched. For a small but important subset of people with endometriosis, their diagnosis signifies an increased risk of developing a gynaecological cancer later in life, yet we have no current way of identifying them.

Materials and Methods
Gynaecological cancer research and treatment has been transformed over the last 15 years by the adoption of personalised medicine and precision oncology. Collaboration between basic scientists and clinical experts, along with meaningful engagement with consumers has led to increased awareness, research investment and improved outcomes for people with ovarian and endometrial cancers.

Results
The genomic revolution, investment in basic research and collaborative initiatives such as linked biobanks, have allowed ovarian and endometrial cancers to be classified into molecular subtypes. Treatment can now be

targeted to specific subtypes of disease, and in some cases de-escalated to ensure each patient is receiving the most appropriate care for their specific disease. Progress has been made in symptom awareness, early detection and monitoring of disease recurrence using liquid biopsy, AI and other modern technologies. Advanced pre-clinical models such as patient derived organoids and co-cultures are helping to unravel disease complexity and heterogeneity and providing opportunities for testing of novel and repurposed drugs.

In this talk, it will be argued that all these approaches can and should be applied to endometriosis research and treatment.

Conclusion
Endometriosis can no longer be treated with a one size fits all approach. A strategic and collaborative precision medicine approach to endometriosis research, treatment and management will improve outcomes for people with endometriosis. Lessons can be learned from the field of oncology and adapted to encompass the complexity of endometriosis and associated conditions.

Key words
Endometriosis, ovarian cancer, endometrial cancer

KEYNOTE SESSION 3

INTEGRATED ANALYSIS OF CANCER-ASSOCIATED GENE ALTERATIONS AND THREE-DIMENSIONAL STRUCTURE OF NORMAL HUMAN UTERINE ENDOMETRIUM: FOR BETTER UNDERSTANDINGS OF ENDOMETRIUM-RELATED DISEASES

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The human endometrium is a highly regenerative tissue and involved in menstruation and implantation of the fertilized egg, giving it a central role in women's reproductive health. However, the regenerative nature of the endometrial glands can lead to the development and progression of "endometrium-related diseases" such as adenomyosis, endometriosis, endometriosis-associated ovarian cancer, endometrial hyperplasia, and endometrial cancer. To clarify the pathogenesis of endometrium-related diseases and develop effective preventative measures and therapeutic strategies, comprehensive understanding of molecular biological linkage between endometrium and endometrium-related diseases is crucially important.

To this end, we focused on genomic alterations of endometrial epithelium which is considered the origin of endometriosis. Intriguingly, several genes recurrently mutated in endometriosis-associated ovarian cancers were frequently mutated in both endometriotic epithelium and normal uterine endometrial glands. Mutation allele frequencies of somatic mutations in uterine endometrial epithelium samples were significantly lower than those in ovarian endometriotic epithelium samples, suggesting the heterogeneous genomic compositions in uterine endometrium. To interpret this genomic heterogeneity in uterine endometrium, we focused on endometrial gland, the minimum functional unit of uterine endometrium, and conducted single endometrial glands sequencing. As a result, we unveiled that each gland carried distinct somatic mutations in cancer-associated genes, such as *PIK3CA, KRAS*, and *PTEN,* with high mutant allele frequencies, suggesting the monoclonality of each gland.

However, our study could not determine the spread of endometrial gland harboring cancer-associated gene mutation because there is a limitation to two-dimensional assessment of the whole shapes of endometrial gland due to its complicatedly winding morphology. Therefore, we tackled with three-dimensional (3D) assessment of human endometrium. To construct a large picture of endometrial gland structure, we performed tissue-clearing-based 3D imaging of full-thickness human uterine endometrial tissue with the use of light-sheet fluorescence microscopy. Our 3D immunohistochemistry discovered some new and unique 3D morphologies of endometrial glands, including plexus network of glands or occluded glands. Notably, computational analysis of 3D layer clarified that the plexus structure of the glands was mainly located in the stratum basalis and expanded along muscular layer horizontally, similar to the so-called "rhizome of grass". Although previous studies have shown the 3D structure of murine endometrial glands, the bottom of these glands forms a crypt but not a rhizome. This can potentially be explained by the existence of menstruation, which is the crucial difference

between the human and murine endometrium. The rhizome structure of endometrial gland in the human endometrium will have a functional advantage over the crypt in terms of the conservation of progenitor/stem cells and regeneration. In addition, some endometrial glands shared the plexus and rose toward the luminal epithelium, suggesting that these glands were the same origin. The rhizome of the endometrium may be a crucial element for understanding the expansion of endometrial glands harboring cancer-associated gene mutations.

Integrated analysis of the naughty gene alterations and the 3D structure in human endometrium will lead to a better understanding of the human endometrium in various fields, including histology, pathology, pathophysiology, reproduction, and oncology.

KEYNOTE SESSION 4

PSYCHOSOCIAL CARE OF PATIENTS WITH CHRONIC PAIN AND DISEASE: INSIGHTS AND LESSONS FROM A GASTROPSYCHOLOGIST

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Chronic pain is a costly and refractory condition that cuts across many disease states. Limited objective measures of pain and inflammation, the opioid crisis, health care inequities and lack of scalable resources make chronic pain particularly challenging in the current, fast paced medical milieu. For the patient, chronic pain is associated with poor outcomes, including depression, anxiety, low quality of life and disability. Furthermore, coordinating care across multiple health professionals and systems carries substantial financial and emotional burden for patients and their families.

This presentation will focus on the application of the biopsychosocial model to chronic pain in a fast-paced clinical setting and the role of the multidisciplinary care team in 1) identifying common risk factors for chronic pain development; 2) assessing and mitigating psychological “influencers” such as depression and anxiety disorders; and 3) delivering varying levels of self- management and behavioral interventions to address cognitive and emotional drivers of pain perception and response (1).

Throughout the presentation, I will share my experiences as a gastropsychologist focused over the past 20 years on the development and implementation of “brain-gut” behavior therapies(2) for chronic, painful disorders of gut-brain interaction (DGBI). I will also share my more recent experiences developing, implementing and scaling the Gaining Resilience through Transitions [GRITT] methodology, a positive psychology(3) based approach to integrated care(4) associated with reductions in unplanned care and opioid use in inflammatory bowel disease(5).

Key words
Integrated care, behavior therapy, positive psychology

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KEYNOTE SESSION 5

AI IN ENDOMETRIOSIS RESEARCH: WHERE WE ARE AT AND WHAT DOES THE FUTURE HOLD

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Country where research was undertaken:
Canada

Introduction/Background
Endometriosis is a widespread and often underdiagnosed condition that impacts millions of women globally. Despite advances in medical research, early detection and effective treatment options remain limited. AI technologies are emerging as promising tools to address these challenges, offering new ways to improve diagnosis, treatment, and patient outcomes.

Materials and Methods
This presentation examines current applications of AI in gynecology with a focus on endometriosis. It considers the role of multi-omics bioinformatics in identifying molecular signatures, image analysis for improving diagnostic accuracy, and natural language processing to extract insights from unstructured clinical data. The potential of computational models to simulate disease progression and predict treatment response is also explored, along with methodological pitfalls and mitigation strategies, including rigorous dataset curation, transparent model reporting, and interdisciplinary collaboration.

Results
AI is advancing gynecologic research through improved diagnostics, prediction, and treatment planning. Machine learning models trained on imaging, clinical records, and patient histories are enhancing diagnostic accuracy by detecting patterns not visible through conventional analysis. Bioinformatics approaches are identifying molecular features for risk stratification and targeted interventions. Natural language processing enables large-scale analysis of unstructured clinical text, supporting case identification and cohort studies. Predictive models are being explored to forecast disease progression, personalize treatments, and monitor therapeutic response. Despite this progress, challenges remain in data availability, model validation, and clinical integration. Close collaboration between clinicians and AI developers is needed to address challenges and leverage the power of technology while ensuring relevance and usability.

Conclusion
AI offers significant promise in advancing the understanding and management of endometriosis, particularly in early detection, personalized treatment, and disease monitoring. However, overcoming existing technical, ethical, and logistical hurdles will be crucial for its widespread adoption in clinical practice.

Key words
Artificial intelligence, endometriosis, diagnosis, treatment response, decision-making

RODOLPHE MAHEUX AWARD PRESENTATIONS

PATIENT REPORTED OUTCOMES AFTER SURGERY FOR RECTAL ENDOMETRIOSIS: A MULTICENTER INTERNATIONAL PROSPECTIVE STUDY

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Countries where research was undertaken:
Belgium and Hungary

Introduction/Background
The ideal surgical technique for rectal endometriosis is still being debated: a radical approach (with segmental resection) versus a more conservative approach aiming at preserving the rectal ampulla (by disc excision). Our aim was to describe the differences in patients reported outcomes (PROMs) after both techniques.

Materials and Methods
Multicenter international prospective study (NCT04204707) assesing functional outcomes after surgery for rectal endometriosis (12/2019 – 03/2023). PROMs were evaluated with standardized questionnaires: endometriosis related pain symptoms (using numerical rating scale), bowel endometriosis syndrome score (BENS) and low anterior resection syndrome (LARS). For changes between baseline and postoperative timepoints a multivariate linear model for longitudinal measures was used.

Presented data are at 12 months postoperatively.

Results
277 patients were included: 118(42.6%) disc-excision and 159(57.4%) segmental resection; 12-month response rate 206/277(74.4%).

Pain scores (chronic pelvic pain, dysmenorrhea, dyspareunia, dyschezia and overall pain) decreased in both groups (all p<.0001) irrespective of surgical technique (p□.0551).

At baseline, BENS was present in 184/277(66.4%). Postoperatively, the score decreased in both groups independent of the surgical technique used (p .5786).

At baseline, LARS was observed in 113/276 (48.2%). When comparing both techniques, postoperatively a significant difference was found in favour of disc-excision (p .0221) where LARS decreased significantly with -3.87 (95% CI: -6.13;1.61; p .0008). In the segmental resection group, no decrease in LARS-score was seen (-0.37; 95%CI: -2.34;1.59, p=.7094). After Bonferroni/Holm correction no significant difference between groups was seen.

Conclusion
Both surgical techniques lead to important pain reduction and improvement of BENS. Concerning LARS-score, a benefit was seen in the conservative group. These data further support the current trend of performing the least harmful procedure (or the most conservative treatment) possible on the rectum.

Key words
Rectal endometriosis, surgical treatment, PROMs

TRANSFORMING THE #ENZIAN CLASSIFICATION INTO A FOUR-STAGE MODEL: A FEASIBILITY ANALYSIS IN COMPARISON WITH THE 2021 AAGL ENDOMETRIOSIS CLASSIFICATION

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Country where research was undertaken:
Austria

Introduction
This study aims to create a model that translates the #Enzian classification into a four-stage system and to evaluate its performance within a retrospective cohort of endometriosis patients.

Materials and Methods
Feasibility study conducted in two parts: first, assigning points for translating the #Enzian classification into a four-stage system; second, comparing the AAGL 2021 stages with the new #Enzian stages in a retrospective cohort of 222 patients undergoing endometriosis surgery.

Results
The translation model's structure was based on point values from the AAGL 2021 classification for various anatomical sites. When direct translation was not feasible, points for #Enzian compartments were determined via a survey of experienced endometriosis surgeons. The four- stage model was compared against the AAGL 2021 classification using a retrospective dataset. Both systems exhibited a similar distribution of endometriosis stages, with comparable patient proportions per stage (stage 1: 43% vs. 44%, stage 2: 20% vs. 24%, stage 3: 11% vs. 9%, stage 4: 27% vs. 21% for #Enzian and AAGL 2021, respectively). There were slight differences in the composition of stages, particularly in stages 2 and 3. Certain deep endometriotic lesions in compartment B and adenomyosis are not fully addressed within the AAGL 2021 classification.

Conclusion
The #Enzian classification can be adapted into a four-stage scoring system, similar to the AAGL 2021 classification. The findings suggest that there is currently no necessity to adopt an alternative classification system beyond the #Enzian. Future research could explore point values based on outcomes like pain, infertility, or surgical complexity.

DETECTION OF ENDOMETRIOSIS (INCLUDING SPE) WITH 99TC-MARACICLATIDE IMAGING

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Country where research was undertaken:
United Kingdom

Introduction/Background
The WES Research Priority Consensus called for imaging advances to be applied to endometriosis. Current imaging methods are limited in detecting the commonest subtype of endometriosis, superficial peritoneal endometriosis (SPE). Therefore, the utility of integrin marker ^{99}Tc-maraciclatide, capable of detecting other inflammatory diseases, was investigated in endometriosis patients.

Materials and Methods
Twenty individuals with suspected or confirmed pelvic or thoracic endometriosis were recruited prior to planned surgery. Typically, 18 (mean) days before the participant's planned surgery, a 10- or 20-minute SPECT-CT was performed with intravenous ^{99}Tc-maraciclatide given 10-30 minutes prior. Regions of interest (ROIs) highlighted by radiologists and endometriosis surgeons were compared. Tissue samples of ROIs were taken during surgery for immunohistochemical staining of angiogenic markers. A post-participation survey explored the acceptability of the scan.

Results
Participants were aged 22-59. Scan acceptability was high as a diagnostic test (mean 97.1 (SD 5.9) VAS 0-100, n=12) and disease monitoring tool (97.5 (7.4), n=12). 17 participants had laparoscopy following pelvic scans, and 2 had thoracoscopic surgery following thoracic scans. The scan agreed with surgical presence or absence of endometriosis in 15/19 cases, with endometriosis imaged in 13/17 surgically positive participants, including the 2 thoracic endometriosis cases. Marker uptake was seen in all endometriosis subtypes, with SPE visualised in 8/12 participants where SPE was seen surgically. Prior imaging with US and/or MRI detected 0/10 SPE cases. In three cases where ^{99}Tc-maraciclatide missed SPE, the disease was located in regions where marker accumulation from the bladder and uterus would mask lesion signals.

Conclusion
DETECT shows reliable visualisation of endometriosis with nuclear imaging is possible. In this phase 2 study, ^{99}Tc-maraciclatide was able to accurately rule-in disease that current imaging modalities could not. If confirmed, these results suggest a novel role for ^{99}Tc- maraciclatide as a diagnostic tool for diagnosing and monitoring endometriosis.

Key words
Diagnostics, SPECT-CT, angiogenesis

SOCIOECONOMIC DETERMINANTS OF CARE-SEEKING BEHAVIOR FOR MENSTRUATION-RELATED PELVIC PAIN

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Country where research was undertaken:
United States of America

Introduction/Background
Pelvic pain, frequently associated with endometriosis, is common and often debilitating among menstruating people[1]. Many with severe or persistent pelvic pain seek out help to improve symptoms; however, disparities hinder access to healthcare[2–5]. How socioeconomic status (SES) impacts healthcare-seeking behaviors for menstruation-related pelvic pain requires more research.

Materials and Methods
The W.O.R.K. Study follows menstruating people who have experienced moderate or severe pelvic pain. Expanded EPHect-compliant assessment included health insurance, household income, and regular primary care access. We conducted a survival analysis to estimate the association between SES and the likelihood of seeing a provider for menstruation-related pelvic pain during follow up, adjusting for confounders including age, race/ethnicity, and pain improvement. Secondary analyses examined persistent pelvic pain during follow up and type of provider seen.

Results
Among 1,068 participants, median age=23 years (range=12-30 years); 76% reported White race, 45% were categorized as middle SES and 8.8% were categorized as low SES;

2.2% were uninsured. At baseline, 38% had never seen a provider for pelvic pain; 17.4% of participants saw a provider new to them during follow up. Preliminary results show that after adjustment, low vs. high SES was insignificantly associated with lower odds of seeing a provider for period-related pain (odds ratio=0.83; 95% confidence interval=0.40-1.65). Regular vs. limited access to primary care was associated with 30% higher odds of seeing a provider for period- related pain during follow-up (odds ratio=1.31; 95% confidence interval=0.87-1.98). Predictive analyses across 18 months of follow up and exploration of non-menstrual pelvic pain are in progress.

Conclusion
Structural determinants of health impact access to care for menstrual conditions and pelvic pain, delaying treatment and biasing clinic populations for research. Identifying barriers, particularly for low or middle SES individuals, can inform targeted policies to maximize access to gynecological healthcare and improve well-being for individuals experiencing menstruation- related pelvic pain.

Key words
Pelvic pain, socioeconomic status, healthcare seeking

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PREDICTION OF PRESENCE OF DEEP ENDOMETRIOSIS WITH EACH ADDITIONAL STEP OF THE IDEA ULTRASOUND METHODOLOGY.

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Country where research was undertaken:
Australia

Introduction/Background
Established guidelines on transvaginal ultrasound (TVS) for 'deep endometriosis' (DE) in the IDEA consensus 2016 and ESHRE 2022 endometriosis guideline establish imaging as 'gold standard' for endometriosis diagnosis. Assessing the ability of each cumulative step of the four- step IDEA TVS methodology for deep endometriosis may provide useful primary screening.

Materials and Methods
This retrospective international multi-centre study used data previously collected to assess diagnostic accuracy of predicting and developing UBESS and validating the IDEA methodology with results published previously. Patients scheduled for laparoscopy underwent DE ultrasound within 12 months of their intended surgery. Each step was analysed in correlation with key features in prediction of DE and endometrioma (OE). As the IDEA methodology does not describe SE, only SE at laparoscopy is recorded as ‘negative finding’.

Results
640 participants were included. Endometriosis confirmed in 557 patients. 354 had DE, 203 had only SE, 83 patients had no endometriosis at laparoscopy. Step 1: endometrioma, ‘ear-sign’ uterus and hydrosalpinx showed sensitivity 0.64, specificity 0.91, positive predictive value (PPV) 0.90, negative

predictive value (NPV) 0.67. Step 2 added 'soft marker' of ovarian imobility, step 3 adds pouch of douglas (POD) negative sliding sign and step 4 assessed compartments of pelvis for DE nodules. Sensitivity increased, specificity decreased, PPV decreased and NPV increased with each additional step. Cumulating to a four step IDEA TVS for having sensitivity 0.92, specificity 0.68, PPV 0.78 and NPV 0.88. Greatest interval increase in sensitivity was 17% with the addition of step 2.

Conclusion
Incorporating all four steps increases the sensitivity of detecting DE to a sensitivity of 0.92 from 0.64 with step 1. The high NPV 0.88 of a four step IDEA TVS indicates negative findings strongly support the absence of deep endometriosis. Addition of ovarian mobility may be useful in endometriosis screening.

Key words
Endometriosis, ultrasound, diagnosis

PAIN SCIENCE EDUCATION CONCEPTS FOR PELVIC PAIN: AN E-DELPHI OF EXPERT CLINICIANS

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Country where research was undertaken:
Australia

Introduction/Background
Pain science education (PSE) involves learning about the biology of pain. However, PSE is yet to be thoroughly investigated for persistent pelvic pain potentially due to the lack of targeted curricula. This study gained consensus on PSE learning concepts important for persistent pelvic pain according to expert clinicians.

Materials and Methods
A three-round e-Delphi survey was conducted to generate and gain consensus on important PSE learning concepts for female persistent pelvic pain among 20 international, multidisciplinary expert clinicians. Learning concepts generated by clinicians were rated by importance using a six-point Likert scale. Concepts were considered important if they had a median rating important >3.0. Consensus on importance rating was considered reached for items with an interquartile range <1.0.

Results
The panel included expert clinicians from seven countries and six healthcare professions. Most clinicians (40%) had 20+ years of experience in pelvic pain. Overall, the expert clinicians generated 125 PSE learning concepts that were considered important for persistent pelvic pain; 92 (73.6%) learning concepts reached consensus on their importance rating. Of the 125 learning concepts, 102 were generated for persistent pelvic pain in general, and were categorised into 13 overarching PSE concepts (e.g., persistent pelvic pain involves changes to the brain and nervous system; many factors influence persistent pelvic pain). Sixteen concepts were generated for specific pelvic pain conditions (e.g., endometriosis) and seven concepts for specific life stages (e.g., adolescence).

Conclusion
This study provides the first list of key PSE concepts for persistent pelvic pain developed by expert clinicians. These concepts share similarities to those valued by consumers.[1] Taken together, they provide a framework for developing and implementing PSE curricula for persistent pelvic pain in research and clinical settings.

Key words
Pain science education, pelvic pain, patient education

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ACCURACY & REPRODUCIBILITY OF OPEN AI-GENERATED RESPONSES ABOUT ENDOMETRIOSIS: AN EVALUATION OF CHATGPT AS AN ENDOMETRIOSIS PATIENT EDUCATION TOOL

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Country where research was undertaken:
Canada

Introduction
Endometriosis is a chronic systemic inflammatory disorder with long diagnostic delays of 5- 12 years, driving many to seek information, support, and validation online. With the recent development of AI tools like ChatGPT, patients increasingly turn to these platforms for medical insights. Given ChatGPT's popularity and novelty, this study aims to assess its accuracy and reliability for endometriosis-related inquiries to determine its ability to affectively support patient knowledge and informed decision-making.

Materials & Methods
To assess ChatGPT's accuracy, frequently asked questions (FAQs) about endometriosis from The American College of Obstetricians and Gynecologists (ACOG) (12 questions) and Mayo Clinic (7 questions) were entered as prompts. Responses were compared for factual accuracy and alignment with guidelines. Additionally, ChatGPT's responses to 14 ACOG clinical considerations (published in 2010 and reaffirmed in 2022) and 109 European Society of Human Reproduction and Embryology (ESHRE) 2022 guideline recommendations (rephrased as questions) were evaluated for adherence to clinical standards in medical advice.

Results
ChatGPT accurately answered FAQs on endometriosis from both The American College of Obstetricians and Gynecologists (ACOG) (12/12) and the Mayo Clinic website (7/7). Additionally, 85.7% (12/14) of ACOG's clinical recommendations were accurately reproduced by ChatGPT. However, reproducibility was lower for the ESHRE guidelines, achieving 71.1% (78/109) overall. Reproducibility across ESHRE guideline sections included: diagnosis of endometriosis (66.7%, 6/9), treatment of endometriosis-associated pain (75.6%, 22/29), treatment of endometriosis-related infertility (80%, 20/25), recurrence (66.7%, 4/6), adolescence (70.6%, 12/17), menopause (50%, 3/6), extra-pelvic endometriosis (100%, 4/4), asymptomatic endometriosis (75%, 3/4), primary prevention (100%, 3/3), and endometriosis and cancer (66.7%, 4/6).

Conclusion
In summary, ChatGPT accurately responded to endometriosis FAQs and reproduced most ACOG guideline recommendations, though it showed a lower reproducibility rate for the ESHRE endometriosis guidelines. Further research and model refinement are needed to address inaccuracies and better understand patients' perspectives and use of ChatGPT.

Key words
ChatGPT, endometriosis, AI

THE IMPORTANCE OF UNMET-NEED SURVEY TOOLS: HELPING YOUNG ADULTS WITH ENDO AND THEIR DOCTORS IDENTIFY WHAT THEY NEED TO THRIVE

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Country where research was undertaken:
Australia

Introduction/Background
As the impact of uncontrolled endometriosis in adolescence is better understood and diagnostic delay decreases, disease management is being initiated at a younger age. Patient experience of endometriosis can be different for younger people, compared to older adults. Therefore, understanding these patients' unmet needs is paramount for providing best care.

Materials and Methods
We recruited a convenience sample of 18-25 year old Australian residents who reported surgically diagnosed endometriosis. An invitation was shared through the social media of Australian endometriosis organisations and the Royal Women's Hospital, Melbourne. Interested parties could participate in an open-ended online survey. Questions were derived from prior research looking at areas of unmet need in healthcare, career and work, financial, information, psychological, social and cultural domains. Surveys were analysed qualitatively through template analysis.

Results
One hundred and thirty-one respondents fit the eligibility criteria. Median age 23 years, most participants were born in Australia (94%), university-educated (54%) and lived in a metropolitan setting (69%). There was a range of unmet needs reported across education, work, healthcare and relationships. Group-specific challenges were identified for these young people: doctors either over- or under-emphasising their future fertility; a disrupted development of sexual and romantic life due to painful sex; a need for increased public awareness for endometriosis and its impacts; increased access to educational resources to help their family and/or romantic partners understand the condition; difficulties managing pain in the classroom and workplace where periods are taboo; and difficulties navigating gynaecological medical spaces while being gender-queer.

Conclusion
This study outlines some practices and services in healthcare that young patients find inadequate. These areas of need should be considered when updating current medical education and practice. This study also highlights the potential utility of unmet needs survey tools for aiding patients and clinicians with treatment and care decisions.

Key words
Adolescent, quality of life, unmet-needs

DAVID HEALY AWARD PRESENTATIONS

HIGH-RESOLUTION SPATIAL TRANSCRIPTOMICS REVEALS STROMAL AND NEUROIMMUNE MICROENVIRONMENTS IN ENDOMETRIOSIS LESIONS

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Country where research was undertaken:
United States of America

Introduction/Background
Current research on endometriotic lesions and pain mechanisms often uses biased methods and murine models, failing to capture human lesion diversity and neuronal types and neurotrophins involved. Using diverse human biospecimens and advanced technologies, we analyzed neurons and neuropeptides to understand endometriosis pain at a subcellular resolution.

Materials and Methods
We obtained endometrium, ovarian lesions and peritoneal lesions from endometriosis patients undergoing surgery. We employed spatial transcriptomics (Visium and VisiumHD) of each tissue type to analyze the spatial distribution of cells surrounding epithelial glands. We validated the transcriptomic signatures identified through targeted spatial proteomics, and developed a 3D complex cellular system to further identify pathways implicated in lesion innervation.

Results
Our findings indicate that the stromal compartment around epithelial glands in lesions can be categorized into two layers, defined by their position and transcriptomic profiles: stroma close to glands with CD10-expressing fibroblasts, and stroma far from glands with OGN-expressing fibroblasts. Each layer, defined spatially through transcriptomics, is enriched with unique subsets of neurotrophic factors, neuronal markers and sensory signaling pathways. The stroma layer close to glands shows a significant enrichment of immune cells and related-pathways, including Natural Killer cell activation and T-cell proliferation. We identified upregulated neural guidance molecules, such as Semaphorins, and neural inflammatory peptides, such as CGRP and RAMP1, in specific stromal layers. This creates a microenvironment conducive to the recruitment of neurons into lesions, leading to the onset of pain.

Conclusion
These advanced technologies facilitate the comprehensive analysis of the spatial lesion landscape and the construction of a whole transcriptome high-resolution map of lesions. Utilizing this unbiased spatial approach, we identify neuropeptides and neuronal markers, as well as their distinct spatial organization within the lesions.

Key words
Spatial transcriptomics, neural-inflammation, pain

GENETIC UNDERPINNINGS OF ENDOMETRIOSIS AND ADENOMYOSIS: A COMPARATIVE ANALYSIS ACROSS EUROPEAN AND EASTERN MEDITERRANEAN POPULATIONS

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Countries where research was undertaken:
United Kingdom, Türkiye, North Cyprus and Finland

Introduction/Background
Endometriosis and adenomyosis are highly comorbid conditions, with adenomyosis largely understudied. Prior genetic research focused on endometriosis in European populations, identifying 42 genetic risk loci. This study aims to explore genetic differences between adenomyosis and endometriosis across European and Eastern Mediterranean (EM) populations to better understand their genetic profiles.

Materials and Methods
EM data included two studies: the COHERE Initiative, a population-based study in North-Cyprus (N=7,646 women) contributing 106 endometriosis and 641 controls, and TROX, a clinical-based study in Türkiye with 239 endometriosis, 259 adenomyosis (88% pathologically confirmed), and 230 controls. All samples were genotyped and imputed together (TOPMed panel). Genome-wide association study (GWAS) was conducted via SNPTEST. Meta-analysis of European ancestry data from UK BioBank, All of Us, and FinnGen was performed for comparative analyses.

Results
Adenomyosis GWAS in EM data yielded 24 nominally significant ($p<5x10^{-5}$) independent loci. None of them overlapped with 42 endometriosis established loci. One of the top two SNPs ($p<5x10^{-7}$) rs2745309 is an eQTLs for novel transcript antisense to PAX7 which regulates muscle stem cell proliferation and differentiation. The other one is rs116908616 which is an eQTL for novel transcript RP11-666E17.1 expressed in both male and female genital tract including uterus and vagina. These results will be compared to European ancestry data, which yielded 25 nominally significant ($p<5x10^{-5}$) independent loci for adenomyosis, one of the top two SNPs (rs10093042) overlapped with an endometriosis locus (GDAP1/8q21.11). Additionally, the results of the first endometriosis GWAS conducted in EM populations will be presented in comparison to established European data.

Conclusion
Preliminary findings show nominally significant loci for adenomyosis, with only one shared locus with endometriosis, indicating distinct genetic profiles. Further analysis in EM populations will assess if these variants persist across diverse groups and whether genetic distinctions between endometriosis and adenomyosis hold in broader ethnic ancestries.

Key words
Endometriosis, adenomyosis, genome-wide association study

RRX-001, A SPECIFIC MACROPHAGE-TARGETED IMMUNOTHERAPEUTIC, ORCHESTRATES A CD45+ ANTI-ENDOMETRIOSIS IMPACT

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Country where research was undertaken:
United Kingdom

Introduction/background
We previously demonstrated that RRx-001 (erythrophagoimmunotherapeutic with intrinsic hypoxic region targeting), reduces lesion growth, pain-like behaviour, and modifies peritoneal macrophages in a preclinical endometriosis mouse model. Here, we aimed to confirm specificity to disease-modified macrophages and determine the immune interactions in blood and peritoneal fluid that coordinate the anti-endometriosis impact.

Materials and Methods
We evaluated $Cd45^+$ cells isolated from a 'menses' mouse model of endometriosis using 10x scRNA-seq, to assess i) the specificity of RRx-001 by analysing immune populations in distal tissues (endometrium, liver, lungs and spleen) and ii) the impact of RRx-001 on immune populations and cell-cell interactions in peritoneal fluid and blood using communication inference. Experimental groups were: endometriosis mice treated with RRx-001 (i.v 2x weekly, 10mg/kg, n = 4) and vehicle (DMA-PEG400, n = 4).

Results
Single cell analyses using Seurat revealed 14,670 high-quality cells and all expected immune populations. RRx-001 treatment did not induce any pronounced off-target impacts on distal intra-organ immune composition. Specifically in the endometrium, RRx-001 did not modify NK, B cell or monocyte/ macrophage proportions, and we observed no impact to endometrial macrophage gene expression, with <10 significant DEGs detected. Conversely, immune cell composition and macrophage populations were specifically modified within the peritoneal fluid (PF), with >3000 significant DEGs, and gene set enrichment analysis of gene ontology revealing enhanced establishment of lymphocyte polarity. We also detected corresponding changes to the peripheral blood immune composition including enhanced $Ly6c^+$ monocyte abundance and transcriptional modification (>200 significant DEGs). CellChat revealed RRx- 001 modified $Cd45^+$ cell-cell communication only in the blood and PF.

Conclusion
Preclinically, RRx-001 exhibits specificity to disease-modified macrophages, orchestrates a macrophage-led anti-endometriosis immunological impact in PF and enhances circulating monocyte abundance. RRx-001 minimally impacts the endometrium, supporting our previous findings of unaffected fertility. Taken together, RRx-001 represents a promising new therapy for endometriosis and is soon to enter a clinical trial.

Key words
Therapeutic, transcriptomics, immunology

SCREENING OF TRACE ELEMENT STATUS AND MUCIN O-GLYCOME IN ENDOMETRIOSIS

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Country where research was undertaken:
Germany

Introduction/Background
Research indicates that essential trace elements, like zinc, play a key role in endometriosis progression, linked to an altered zinc homeostasis, altered mucin expression, and *O*- glycosylation. However, zinc's specific impact on the mucin O-glycome in endometriosis remains unclear. We analyzed trace element status and mucin O-glycome in endometriosis lesions.

Materials and Methods
The study examined 38 endometriosis patients (peritoneal, ovarian, and deep infiltrating) and 66 non-endometriosis participants. Trace element status in serum and peritoneal fluid were analyzed using inductively coupled plasma tandem mass spectrometry and fluorescence assay for free zinc. Mucin (MUC1, MUC2, MUC5AC, MUC6, and MUC16) expression was evaluated using immunohistochemistry. The EndometDB Turku (https://endometdb.utu.fi/) enables comparison of mucin gene expression and phenotypical

data from endometriosis and non-endometriosis patients. MUC16 (CA-125) was evaluated in peritoneal fluid.

Results
Altered levels of free zinc, manganese, and selenium were observed in serum and peritoneal fluid of patients with endometriosis compared to those without the condition, with notably elevated selenium-to-copper ratios. MUC1 was significantly higher in all endometriosis groups, each compared to the control group. Furthermore, MUC5AC was overexpressed in peritoneal endometriosis (pEM) compared to the control group. Database analysis confirmed differential mucin mRNA expression: MUC1 varied between control endometrium and deep infiltrating endometriosis (DIE) as well as ovarian endometriosis (OEM), in addition to differences seen between control peritoneum and pEM. MUC5AC and MUC16 varied between pEM and DIE, as well as OEM. MUC16 also differed between control peritoneum and pEM. However, MUC16 levels in peritoneal fluid showed no significant difference between endometriosis and control groups.

Conclusion
This study presents evidence of abnormal levels of free zinc, manganese, and selenium in patients with endometriosis. It also indicates increased mucin expression in both pEM and DIE. Furthermore, the study offers the first insights into the relationship between endometriosis, altered trace element status, and the mucin O-glycome.

Key words
Trace elements, mucins, O-glycome

ORAL MICROBIOME ALTERATIONS IN ADOLESCENTS AND YOUNG ADULTS WITH ENDOMETRIOSIS

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Country where research was undertaken:
United States of America

Introduction/Background
While immune dysregulation is postulated to contribute to endometriosis and other chronic inflammatory diseases have been linked with oral flora dysbiosis, the association between endometriosis oral microbiome and endometriosis is unclear. Thus, the objective of this study was to identify endometriosis-associated oral microbiota that could lead to a non-invasive diagnostic.

Materials and Methods
We performed whole genome sequencing(target:40 million reads/sample) on salivary DNA from 89 laparoscopically-confirmed endometriosis (>90% rASRM stage I/II) patients and 101 frequency-matched controls who participated in the WERF EPHect compliant Women's Health Study: From Adolescence to Adulthood. To determine the oral microbiome profiles associated with endometriosis, we used general linear models and examined the differences in oral microbiome diversity and composition between endometriosis patients and controls. False discovery rate(FDR) was used for multiple testing correction.

Results
Median age was 21 years (IQR=17-27 years) for endometriosis cases and 23 years (IQR=20- 27 years) for controls. Endometriosis case-control status was significantly associated with the beta diversity or the overall oral microbial composition (p=0.006) accounting for 1.3% of variation between groups. Among individual species, *Veillonella parvula* (□=1.16, FDR=0.04) was more abundant in endometriosis cases compared to controls, while *Alloprevotella* (□=- 2.00, FDR=0.049), was less abundant in endometriosis cases compared to controls. *Prevotella loescheii* (□=0.99, FDR=0.07) and *Prevotella oulorum* (□=0.81, FDR=0.14) were suggestively more prevalent in endometriosis cases compared to controls, while *Prevotella intermedia*(□=- 1.26,FDR=0.04), *Eubacterium sulci* (□=-1.46,FDR=0.049), *Prevotellaceae* (□=-1.22, FDR=0.10), and *Catonella massiliensis* (□=-1.27, FDR=0.10) were less prevalent. Among endometriosis cases, *Provetella salivae* abundance was associated with having life-impacting pain(□=1.25, FDR=0.11).

Conclusion
We identified multiple endometriosis-associated oral microbes which have been linked with autoimmune disorders/systemic inflammation, providing biological insight into

systemic immune dysregulation in endometriosis. With validation in larger independent cohorts, our results could lead to novel non-invasive biomarkers for earlier diagnosis of endometriosis that could be applied to a younger population.

Key words
Endometriosis, oral microbiome, non-invasive biomarker

PARSING PROGESTIN RESPONSES IN A VASCULARIZED MICROFLUIDIC MODEL OF THE ENDOMETRIOTIC LESION MICROENVIRONMENT

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Country where research was undertaken:
United States of America

Introduction/Background
In vitro models of endometriosis have potential to yield valuable insights into disease pathogenesis. We engineered a microphysiological system that fosters interactions between a 3D microvascular bed and lesion mimics comprising patient-derived epithelia and stroma. We investigated influence of disease state on lesion phenotype, including angiogenesis and response to hormones.

Materials and Methods
Endothelial cells and supporting fibroblasts were mixed in fibrin, where they form perfusable microvascular networks within PDMS-based microfluidic devices. Patient biopsy-derived endometrial stromal cells (ESCs) from multiple donors were screened for level of progesterone responsiveness before loading into the vascularized devices as spheroids, along with donor- matched endometrial epithelial organoids (EEOs). Confocal imaging, label-free nonlinear multiphoton microscopy, and ELISAs were used to assess angiogenesis, vascular permeability, collagen deposition, and cytokine profiles in response to progesterone stimulation.

Results
ESCs isolated from 10+ donors with and without endometriosis exhibited a wide range of progesterone responsiveness (measured by prolactin secretion) that did not separate cleanly by disease status, highlighting the importance of using primary cells for proper recapitulation of disease heterogeneity. In vascularized devices, ESC spheroids induced angiogenic sprouting from the surrounding vascular bed, with progesterone stimulation leading to different extents of sprouting for a “low-response” vs. “high-response” donor. When EEOs were incorporated into the ESC spheroids, they self-organized to recapitulate the “cystic” glandular architecture seen in tissue-cleared lesions. Within vascularized devices, the epithelial-stromal cell spheroids also induced changes in the permeability of the nearby vasculature. Label-free imaging additionally revealed differences in collagen deposition and metabolic activity across donors and hormone treatment conditions.

Conclusion
We engineered a vascularized microphysiological system that allows us to probe endometrial cell and vascular responses to stimulation with progestins and related therapeutics. By using primary cells and permitting spatiotemporal measurements of disease-relevant phenotypes, this platform enables more physiologically relevant, patient-specific studies of cell-cell interactions in the endometriotic lesion microenvironment.

Key words
Microfluidics, organoids, vascularization

MOLECULAR PROFILING OF OVARIAN ENDOMETRIOSIS: TOWARDS A PERSONALIZED MANAGEMENT

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Introduction/Background
Endometriosis' high heterogeneity in clinical presentation and lesion characteristics, combined with its unclear pathophysiology, complicates the development of targeted therapies and limits treatment to symptom relief through hormonal or surgical approaches. However, 5-year postoperative recurrence rates can reach 50%, with no reliable strategy or biomarker to predict prognosis.

Materials and Methods
We obtained the proteomic and phospho-proteomic complete profiles of 134 formalin-fixed paraffin-embedded (FFPE) ovarian endometriosis (OMA) tissues from 68 patients using non- targeted mass spectrometry (MS) in a data-independent acquisition (DIA) method. Patients were classified as non-recurrent (n=38) or recurrent (n=30) after a 5-year follow-up to identify prognostic biomarkers and potential therapeutic targets for postoperative recurrence, that were subsequently validated in an independent cohort (n=26, 18 non-recurrent vs. 8 recurrent) by DIA-MS.

Results
Unsupervised hierarchical clustering of the sample proteome profiles revealed three main molecular subtypes of endometrioma with distinct molecular signatures, differing in stromal and immune content but apparently similar regarding prognosis. Functional analysis of phospho-proteomic data identified important kinases differentially activated in the subtype characterized by a metabolic profile and low immune activation. Several proteins were identified as potential markers for OMA recurrence, globally and in each subtype, with one candidate validated in both cohorts with an Area Under the Curve (AUC) = 0.74 rising to 0.81 when constructing a predictive model with two relevant clinical traits identified using logistic regression analysis. Enrichment and functional analysis highlighted altered pathways and potential therapeutic targets, shedding light on the underlying molecular mechanisms of ovarian endometriosis recurrence.

Conclusion
Our investigation addresses research gaps in endometriosis by identifying three molecular subtypes of OMA with unique molecular signatures and potential therapeutic targets, providing new insights into OMA pathogenesis. We propose a predictive model for endometrioma recurrence incorporating two clinical factors and a validated proteomic marker to improve prognosis strategies.

Key words
Ovarian endometriosis, molecular heterogeneity, recurrence

EXPANDING THE GENETIC LANDSCAPE OF ENDOMETRIOSIS: INTEGRATING MULTI-OMICS WITH A GENOME-WIDE META-ANALYSIS OF OVER 900,000 GENETICALLY DIVERSE WOMEN

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Country where research was undertaken:
United States of America

Introduction/Background
Endometriosis is a complex heritable disorder requiring comprehensive genomic investigation across diverse populations. Previous studies have been somewhat limited by European-centric data. The Global Biobank Meta-Analysis Initiative (GBMI) enables large-scale genomic analysis across multiple genetic ancestry groups, complemented by computational multi-omic and single cell

analyses to understand disease mechanisms.

Materials and Methods
We performed a Genome-Wide Association Study (GWAS) meta-analysis across 14 biobanks worldwide, with 31% non-European samples. Multiple endometriosis phenotype definitions were analyzed, including broad and surgically-confirmed cases. Post-GWAS analyses included ancestry-stratified heritability estimation and fine-mapping. We conducted Transcriptome- wide and Proteome-wide association analyses, followed by single-cell analyses of implicated genes. Integration of multi-omic data through Mergeomics analysis enabled comprehensive pathway enrichment assessment.

Results
The GWAS (N=928,413 : 44,125 cases) identified 45 significant loci using a broad phenotype definition, including seven previously-unreported signals and the first genome-wide significant locus (*POLR2M*) in African ancestry. Narrow phenotypes and surgically confirmed cases replicated known loci near *CDC42* and *SYNE1*. Observed heritability was consistent (10-12%) across ancestral groups. Cross-ancestry fine-mapping revealed putative causal variants in 38 loci. Multi-omic imputed association analyses identified 11 significantly-associated gene transcripts (two previously unknown: *DTD1* and *CCDC88B*), two intronic splicing events (within *PGR* and *NSRP1*), and one protein, RSPO3. *In silico* single-cell analyses prioritized 18 disease-relevant cell types including venous cells and macrophages. The results of these analyses specified key players in enriched molecular pathways involving immunopathogenesis, angiogenesis, Wnt signaling, and balance between proliferation, differentiation, and migration of endometrial cells as major hallmarks in genomics of endometriosis.

Conclusion
This diverse GWAS combined with transcriptomic, splice-omic, proteomic, and single-cell analyses revealed novel genetic associations and molecular mechanisms in endometriosis. The identification of ancestry-specific variants and pathway interactions provides multiple targets for developing precise therapeutic interventions across diverse populations.

Key words
Genome wide association analyses, multi-omic data integration, diverse populations

SEMINAR SESSION 1: EMERGING THEORIES IN ENDOMETRIOSIS

DECIPHERING PATHOLOGICAL IMMUNE TOLERANCE IN ENDOMETRIOSIS

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Country where research was undertaken:
United Kingdom

Introduction/Background
Retrograde menstruation disseminates endometrial tissue into the peritoneal cavity; mechanisms that prevent most menstruating people from developing endometriosis are unknown. We hypothesize that menstrual tissue is intrinsically immunogenic, leading to recognition and clearance of refluxed tissue. However, if immunogenicity is attenuated or tolerated, ectopic tissue persists, resulting in lesion formation.

Materials and Methods
Published and our own unpublished single-cell RNA-seq (scRNA-seq) datasets of human proliferative, secretory and menstrual endometrium were bioinformatically interrogated. scRNA-seq data from a mouse model of endometriosis (endometrium, lesions and peritoneal fluid (PF)), was also explored. We investigated the impact of decidualization and progesterone withdrawal (menses) and drug-induced immunogenicity in donor endometrium and on the formation of lesions in recipient mice. Mouse endometrial cells were sorted for sequencing and PF collected for full spectrum immune profiling.

Results
Type I interferon (IFN) signaling is typically immunostimulatory; playing a vital role in promoting disposal of damaged or infected cells and may contribute to removal of refluxed tissue. Paradoxically, it can also induce immune tolerance through several mechanisms. In donor mice, induced menses lead to enrichment of Gene Ontology (GO) immune response terms verses naïve endometrium. Formation of lesions using menses endometrium triggered enhanced Type I IFN signaling in peritoneal immune cells, particularly dendritic cells, compared to lesion formation with ‘naïve’ endometrial tissue. This aligns with faster regression of lesions formed from menses versus naïve tissue and is consistent with menstrual tissue exhibiting an immunogenic phenotype. Conversely, in

people with endometriosis, Type I IFN signaling was elevated in menstrual effluent (ME) compared to those without.

Conclusion
Our data support the concept that menses tissue is immunogenic, promoting ectopic tissue clearance. In women with endometriosis, attenuated decidualization could dampen intrinsic immunogenicity. Elevated Type I IFN in ME of endometriosis patients may represent the pathway's paradoxical role in inducing immune tolerance via impacts on several immune cell types.

Key words
Tolerance, immunogenic, aetiology

BLOCKING CGRP-MEDIATED NEUROIMMUNE COMMUNICATION REDUCES PAIN AND LESION SIZE IN A VALIDATED MOUSE MODEL OF ENDOMETRIOSIS.

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Country where research was undertaken:
United States of America

Introduction/Background
Endometriosis is characterized by a dysfunctional local immune/inflammatory environment. Nociceptors (pain-sensing neurons) release neuropeptides such as calcitonin gene-related peptide (CGRP), that are known to shape immunity through neuroimmune communication. In addition, there is substantial comorbidity between endometriosis and migraine, with the latter being effectively treated with CGPR pathway antagonists.

Materials and Methods
We stained human surgical specimens and used a validated mouse model to test the hypothesis that CGRP-mediated neuroimmune communication drives pain and lesion growth in endometriosis. In mice, we used genetic and chemical ablation of nociceptors, chemical blockade of nociceptor signaling, and CGRP pathway antagonists to measure the effect of nociceptor-derived CGRP signaling on lesion size and spontaneous and evoked pain. We used scRNAseq and coculture to elucidate the cellular mechanism underlying CGRP action.

Results
Human and mouse lesions contain both CGRP and its co-receptor, receptor activity modifying protein 1 (RAMP1). Addition of factors released by lesions such as PlGF (placental growth factor) and VEGF (vascular endothelial growth factor) increased the release of CGRP from cultured dorsal root ganglion neuron cell bodies. In mice, nociceptor ablation or signaling blockade reduced both spontaneous and evoked pain, as well as lesion size. Similarly, treatment of lesion-bearing mice with FDA-approved drugs that block CGRP-RAMP1 signaling reduced mechanical hyperalgesia, spontaneous pain, and lesion size, suggesting that nociceptor activation and neuropeptide release contribute to endometriosis lesion growth and pain. Mechanistically, CGRP-treated macrophages exhibited impaired efferocytosis and the release of factors that increased endometrial cell growth in a RAMP1-dependent manner, resulting in a pro-endometriosis phenotype.

Conclusion
Our data demonstrate that key mediators of neuroimmune communication are present in endometriosis lesions. Furthermore, CGRP release resulting from nociceptor activation can reprogram peritoneal macrophages to a pro-endometriosis phenotype. This suggests that treatment with FDA-approved, non-hormonal, non-opioid drugs that block CGRP/RAMP1 signaling may benefit endometriosis patients.

Key words
RAMP1, candidate therapeutics

PRO-ENDOMETRIOSIS MACROPHAGE RELEASE OF IL-33 IS KEY FOR ENDOMETRIOSIS PAIN AND LESION FORMATION

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Country where research was undertaken:
United States of America

Introduction/Background
Endometriosis is a painful disease affecting ~10% of females. Current treatments are ineffective for a substantial proportion of patients, underscoring the need for additional therapies. Nociceptors release neuropeptides such as calcitonin gene-related peptide (CGRP), that shape immunity through neuroimmune communication. We therefore sought evidence for neuroimmune communication during endometriosis.

Materials and Methods
A validated non-surgical mouse model of endometriosis was used to study the effect of anti- IL-33 therapy in endometriosis. Bulk RNAseq of a macrophage/endometrial epithelial cell co- culture was performed to identify factors released by macrophages upon CGRP stimulation. Mouse lesions were stained for IL-33 and its receptor ST2. Chemical and genetic ablation of macrophages and nociceptors was used to assess IL-33 production in the lesion. Behavioral assays were performed to measure the efficacy of anti-IL-33 therapy.

Results
Our co-culture assay showed macrophages support endometrial epithelial (endo-epi) cell growth. Bulk RNAseq of CGRP-stimulated macrophages revealed that IL-33 is significantly upregulated. CellPhoneDB was used to determine cell-cell communication, and we found that ST2 is highly expressed by endo-epi cells as per our bulk RNAseq and staining of mouse lesions. In vitro, we confirmed that recombinant IL-33 induces cell proliferation and in lesions, ST2 colocalized with $Ki67^{+}$ cells, indicating macrophage-derived IL-33 promotes cell growth/proliferation. To establish that IL-33/ST2 signaling is required for lesion formation, we induced endometriosis using uterine tissue from mice lacking ST2. We found a reduced number of lesions and size when ST2-KO uterus was used as donor tissue. Importantly, treatment with α-IL-33 reduced both evoked and spontaneous pain, and lesion size.

Conclusion
We demonstrated that neuroimmune-communication-driven activation of macrophages leads to IL-33 production in the lesions. Blocking IL-33/ST2 signaling using an anti-IL-33 antibody reduces both pain and lesion size. Moreover, we found that IL-33 induces cell proliferation in an ST2-dependent manner as treatment with soluble ST2 reduces endo-epi cell proliferation.

Key words
Neuroimmune communication, IL-33

EPITHELIAL TO MESENCHYMAL TRANSITION IN ENDOMETRIAL CYCLING – IMPLICATIONS FOR ENDOMETRIOSIS

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Countries where research was undertaken:
United Kingdom, Brazil

Introduction/Background
The epithelial to mesenchymal transition [EMT] and its reverse process [MET] plays a key role in the molecular and phenotypic changes observed in the endometrial regular cycling. Endometriosis pathophysiology can be related to disruptions of EMT/MET regulation across the menstrual cycle.

Materials and Methods
We aimed to identify differences in the expression of EMT/MET related genes in eutopic endometrial tissues. A list of 70 genes encoding for proteins related to EMT/MET process were selected from literature. Differential expression of 65 selected genes was evaluated in 180 eutopic endometrium samples from surgically diagnosed endometriosis 68 rASRM I/II, 53 rASRM III/IV vs. 59 surgical controls accounting for menstrual cycle phases (18 menstrual, 58 proliferative and 104 secretory).

Results
EMT was favored in the menstrual phase of the controls reflected by the increased expression of pro-inflammatory (*IL1B* and *CXCL8*), pro-angiogenic (*VEGF-A*), motility and invasion genes (*SNAIL1*, *TWIST1* and *WNT2*) and decrease of epithelial cell adhesion molecule (*CDH1*) expression in comparison to both proliferative and secretory phases. MET was favored in the secretory phase by the increased expression of *DKK1* and *ESR2* in comparison to proliferative phase. On the other hand, endometriosis cases showed increased expression of pro- inflammatory (IL1B, CXCL8) and matrix degradation (LCN2)

genes in the secretory phase in comparison to proliferative phase. rASRM III/IV cases compared to rASRM I/II and controls, on secretory phase, had EMT enhanced by the increased expression of pro-inflammatory (CXCL8) and migration, invasion and fibrosis (ACTA-2) related genes.

Conclusion
The EMT/MET process is related to regular endometrial cycling. The increased expression of genes involved in extra-cellular matrix stiffness, cell migration and invasion, and pro-inflammatory status suggests a possible role of aberrant EMT/MET in the eutopic endometrium underlying endometriosis.

Key words
Epithelial to mesenchymal transition, endometrial cycling, gene expression

STEROID METABOLOME PROFILING IDENTIFIES A UNIQUE HORMONE SIGNATURE ASSOCIATED WITH ENDOMETRIOSIS

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Country where research was undertaken:
United Kingdom

Introduction/Background
Endometriosis is a chronic, hormone-dependent inflammatory condition. There are no validated biomarkers for endometriosis and this delays diagnosis and treatment. Steroid metabolomics has emerged as a powerful tool in aiding diagnosis of hormone-dependent disorders but has not been investigated in the context of endometriosis.

Materials and Methods
Serum samples from patients with diagnosis of endometriosis confirmed by laparoscopy (n=157) and healthy controls matched by age and BMI (n=61) were profiled using an LC-MS/MS assay to simultaneously measure 21 steroid hormones/metabolites. Analysis controlled for menstrual cycle phase and endometriosis subtype, participants were not receiving hormone treatment. Additionally, urine samples from patients with suspected endometriosis (n=50) and healthy controls (n=40) were profiled by GC/MS to quantify urinary steroid metabolites (37 analytes).

Results
The hormone signature in patients with endometriosis was distinct from healthy controls consistent with a disease-specific hormone profile. This was characterized by increased serum concentrations of androgens including dehydroepiandrosterone (DHEA; elevated 2-fold $p<0.0001$), testosterone (T; elevated 1.8-fold, $p<0.0001$) and dihydrotestosterone (DHT; elevated 1.3-fold, $p<0.05$). Consistent with elevated serum androgens, urinary androgen metabolites, androsterone (elevated 2-fold, $p<0.0001$) and etiocholanolone (elevated 2.6-fold, $p<0.0001$), were significantly elevated in endometriosis patients compared to healthy controls.

Metabolomic data were used as input variables and multiple logistic regression analysis was performed to generate a statistical model to predict diagnostic outcome. ROC curve analysis of the multiple logistic regression analysis demonstrated robust discrimination between healthy controls and endometriosis patients (AUC=0.998; $p<0.0001$) with 98.08% positive predictive power and 94.55% negative predictive power.

Conclusion
We have discovered a disease-specific hormone signature that identifies endometriosis with high specificity and sensitivity. These data present a unique opportunity to develop a non- surgical approach for endometriosis diagnosis.

Key words
Diagnosis, metabolomics, hormones

EVALUATION OF C-JUN N-TERMINAL KINASE (JNK) INHIBITORS IN A VASCULARIZED MICROPHYSIOLOGICAL MODEL OF ENDOMETRIOSIS

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Country where research was undertaken:
United States of America

Introduction/Background
Endometriosis is characterized by the growth of vascularized lesions rich with macrophages. C-Jun N-terminal kinase inhibitor (JNKi) bentamapimod has demonstrated lesion regression *in vivo* but lacks potency required for clinical translation. To evaluate novel JNKi, we have developed a microfluidic lesion model using a synthetic hydrogel.

Materials and Methods
Synthetic hydrogels are polyethylene glycol-based with a cell degradable crosslinker and adhesive peptides. Primary endometrial epithelial organoids (EEOs) and stromal cells (ESCs), uterine endothelial cells (HUTMVEC), and macrophages from CD14+ human monocyte were combined in a gel precursor and injected into a custom microfluidic device used in static or continuous culture and exposed to media containing JNKi. Vessel morphology and organoid growth assessed via imaging. JNKi impact on the macrophage secretome assessed via ELISA.

Results
We show formation of perfusable microvasculature with adenomyosis-relevant source cells, using HUTMVEC-ESC co culture and can incorporate EEOs to form lesion–like structures in microfluidic devices. Next, we established conditions to achieve microvascular network formation with macrophages at a ratio comparable to that found in endometriosis lesions *in vivo* and demonstrated macrophage functionality via IL-6 and MMP-9 secretion. Novel JNKi with over 100X the potency of bentamapimod enhanced the ability of ESCs to decidualize, quantified through prolactin secretion over 6 days. Moreover, in co-cultures with macrophages treated with inflammatory cytokine IL1B, bentamapimod *increased* TNFa detected in spent media while the novel JNKi dampened TNFa. We are currently translating these readouts to device cultures, where we can simultaneously evaluate vascularization of the lesion microenvironment.

Conclusion
Here we describe our efforts to systematically evaluate the effects of highly selective JNKi in a microphysiological hydrogel platform that recapitulates critical aspects of the endometriosis microenvironment. This microfluidic culture model has potential for impacts on a better scientific understanding of endometriosis and new drug development.

Key words
Microphysiological system, inflammation, vascularization

SEMINAR SESSION 2: HEALTH (IN)EQUITY AND ENDOMETRIOSIS

ENDOMETRIOSIS IN AN INDIGENOUS AUSTRALIAN POPULATION: FINDINGS FROM THE NATIONAL ENDOMETRIOSIS CLINICAL AND SCIENTIFIC TRIALS (NECST) REGISTRY

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Country where research was undertaken:
Australia

Introduction/Background
Limited to no data on endometriosis and how this is managed exist for Indigenous Australians, as previous large population studies have focused on those from White backgrounds[1]. This study aims to describe the endometriosis-associated clinical and pathological characteristics of Indigenous Australians captured in the NECST Registry.

Materials and Methods
Clinical and health data were sourced from the NECST Registry and assessed for completeness between 2020-2024. Women and people over 18 years, diagnosed or experiencing endometriosis-related symptoms were recruited from hospitals, private clinics or social media across Australia. Demographics, presenting and medical history using a shortened Endometriosis Phenome and Biobanking Harmonisation Project (EPHect)

patient questionnaire (EPQ), and surgical and medical data were collected and analysed.

Results
Data on 1693 participants were analysed; n=36/1693 (2.2%) identified as Indigenous. Endometriosis was diagnosed in n=34 (2.0%) in the Indigenous population, primarily surgically (n=30/34, 88.2%); by symptoms (n=8/34, 23.5%), or imaging (n=7/34, 20.6%), with a median diagnostic delay of 14-years. The majority resided in metropolitan areas (n=22/34, 64.7%), with n=5/34 (14.7%) residing in regional and rural areas respectively. The most common symptom was dysmenorrhoea (n=18/34, 52.9%), followed by pelvic pain (n=5/34, 14.7%). Independent samples T-test showed that Indigenous vs non-Indigenous Australians were significantly younger when symptoms started, reported greater overall symptom burden, and symptom distress. Management also included analgesics (n=22/34, 64.7%), other medications (n=14/34, 41.2%), hormones (n=13/34, 38.2%) and allied health/complementary therapies (n=10/34, 29.4%), not mutually exclusive.

Conclusion
Endometriosis prevalence in the Indigenous Australian population was low in this cohort. With a median diagnostic delay of 14-years, it is important to better understand, the limitations of Indigenous Australian's access to appropriate and timely healthcare for endometriosis, especially those who reside in rural and/or remote areas.

Key words
Endometriosis, Indigenous Australians, global challenges

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DIVERSITY IN ENDOMETRIOSIS: LEVERAGING THE POWER OF AN AFRICAN-EUROPEAN ADMIXED DATASET FOR GENETIC ANALYSIS

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Countries where research was undertaken:
United States of America and United Kingdom

Introduction/Background
Genetic research of endometriosis reflects trends seen in clinical and scientific studies, where knowledge is predominantly based on studies of participants from high-income countries. Published genome-wide association studies (GWAS) predominantly include European- ancestry individuals, leaving African-ancestry populations – despite their rich genetic diversity and potential to reveal novel genetic insights – largely unrepresented.

Materials and Methods
Using All-of-Us Research Program data – a US Biobank which includes over 100,000 females from non-European ancestry groups – we identified an ethnically diverse set of endometriosis cases using medical records and self-reported data. We first confirmed reliability of known genetic signals in medically-confirmed, self-reported, and combined subsets. We then investigated the degree of admixture in non-European cases and performed admixture-aware GWAS on African-European admixed participants using dedicated software (TRACTOR) to localise associated signals closer to causal variants.

Results
Within the All of Us dataset, we identified a total of 7,605 endometriosis cases and 134,322 suitable female controls with whole genome sequence data. We confirmed that most known endometriosis-associated variants had similar effect sizes to published data in a subset GWAS of 5,018 cases and 58,829 controls of European genetic ancestry. Principal component and ADMIXTURE analysis of the remaining non-European-ancestry cases against a 1000 Genomes Project reference panel identified 1,016 cases with varying degrees of African- European admixture. These are set to undergo admixture-aware GWAS with 35,131 similarly admixed controls to produce ancestry-stratified genetic association results. Combining these in multi-ancestry meta-analysis and fine-mapping will improve power for variant discovery and localising potential causal variants, with results to be presented at the meeting.

Conclusion
Diverse, accessible genetic data with robust supporting phenotypic data is crucial to ensure genetic findings and future precision medicine tools are reliable and globally applicable. By investigating the genetics of endometriosis in an admixed cohort, we hope to contribute to and improve the understanding of endometriosis in different global populations.

Key words
Genetics, admixture, multi-ancestry

UTILISATION OF A NURSE-LED TELEHEALTH SERVICE FOR MANAGING ENDOMETRIOSIS IN REGIONAL, RURAL AND REMOTE PATIENTS

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Country where research was undertaken:
Australia

Introduction/Background
A nurse-led telehealth clinic was established in early 2022 to support patients with known or suspected endometriosis navigate care. The aim of the nurse-led model was to increase accessibility through a self-referral pathway and enhance access to specialist endometriosis care for patients.

Materials and Methods
Retrospective audit of patient postcode data was performed for the first 2 years of the nursing service (March 2022 – February 2024). Patient postcodes were classified according to the Modified Monash Model, a framework that categorises geographic areas as metropolitan (MM1), regional (MM2), rural (MM3-5), or remote (MM6-7). A radius was applied to our Endometriosis Centre in metropolitan Melbourne to determine the number of patients from outside a 50km radius.

Results
400 patients utilised the nurse-led clinic between March 2022 and February 2024. 825 episodes of care were provided. 78% (n=310) of patients were from MM1 (metropolitan) areas. The next highest proportion of patients (12%, n=46) were from small rural towns (MM5). The remaining 10% of patients were from MM2 (6%), MM3 (3%) and MM4 (2%). No patients from remote areas were seen. 4% of patients were from interstate. Patients from regional and small rural towns in New South Wales comprised the largest subgroup in this cohort (n=7).

Using the radius model, 23% of patients lived beyond a 50 km radius of our Centre; thus would need to travel over one hour if they were to attend face to face.

Conclusion
Our Centre demonstrates a telehealth delivery of care method that enhances access to specialist endometriosis nursing care for patients with suspected or confirmed endometriosis. While we predominantly see patients from metropolitan areas, we facilitate access for regional and rural patients, particularly those from MM5 areas - who incidentally have the lowest access to General Practitioners (AIHW, 2021).

Key words
Telehealth, nursing, care-coordination

References
Australian Institute of Health and Welfare. (2021). *Figure 8: Employed health professionals, clinical full-time equivalent (FTE) rate, by Modified Monash (MM) category: General Practitioners, 2021.* https://www.aihw.gov.au/reports/rural-remote-australians/rural-and- remote-health

DISPARITIES IN DIAGNOSTIC DELAYS FOR ENDOMETRIOSIS IN INDIA: EVIDENCE FROM THE ENDOMETRIOSIS CLINICAL & GENETIC RESEARCH (ECGRI) STUDY

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Country where research was undertaken:
India

Introduction/Background
Endometriosis is a chronic condition affecting about 10% of reproductive-aged women, with

an estimated 50 million cases in India. Diagnostic delay remains a significant concern, as it exacerbates disease progression and worsens clinical outcomes. This study investigates differences in diagnostic delay among women with surgically confirmed endometriosis across India.

Materials and Methods
Endometriosis Clinical & Genetic Research in India (ECGRI) is prospective case-control study conducted from 2020 to 2024 across five geographic zones in India. A total of 1775 women aged 18-50 years with laparoscopically and/or histologically confirmed endometriosis were enrolled. Data were collected using modified World Endometriosis Research Foundation Endometriosis Phenome and Biobanking Harmonisation Project (WERF EPHect) tools. Diagnostic delay was defined as the interval between initial symptom onset and surgically confirmed diagnosis.

Results
The mean diagnostic delay was 6.7 years (Standard Deviation, SD 8.2) with significant regional differences ($p < 0.001$). The longest delay occurred in the central zone (9.7 years, SD 8.3), followed by the south (7.4 years, SD 9.8), north (7.1 years, SD 7.1), west (4.7 years, SD 7.7), and northeast/east (3.6 years, SD 5.5). Those receiving public care faced longer delays than those using private facilities (7.7 vs. 5.3 years, $p < 0.001$). Deep infiltrating endometriosis had the longest delay (7.8 years), followed by superficial peritoneal endometriosis (6.5 years) and ovarian endometrioma (6.3 years) ($p < 0.001$). Significantly longer delays were also observed among women with Dravidian ethnicity, lower education levels, unemployment, widow/divorce status, passive smoking exposure, and body mass index ≥25.

Conclusion
ECGRI is the first national study demonstrating substantial delays in diagnosis of endometriosis in India with significant disparities. To accelerate diagnostic timelines for optimizing clinical outcomes and improving quality of life of affected individuals, it is essential to mobilize resources to strengthen diagnostics and expand access to healthcare services.

Key words
Delay in diagnosis, endometriosis, India

INCREASING DIVERSITY IN ENDOMETRIOSIS RESEARCH: INITIATION OF TWO STUDIES TO CHARACTERISE ENDOMETRIOSIS IN AFRICAN POPULATIONS

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Countries where research was undertaken:
South Africa, Kenya, Ghana, United Kingdom

Introduction/Background
The current understanding and management of endometriosis is based on evidence that largely excludes women in Africa, despite evidence of similar impact and prevalence. Understanding phenotypic and genetic manifestations of endometriosis will improve our understanding of the disease as well as help build effective pathways for diagnosis and treatment.

Materials and Methods
We initiated two collaborative studies investigating endometriosis in Africa. In the first, we are conducting the first multi-country (Ghana, Kenya, South Africa) case-control study of endometriosis in African women, through collection of WERF-EPHect-standardised phenotypic information and saliva samples for genetic analysis. In the second questionnaire- based study, ENDURE (Endometriosis in South Africa: Understanding the Patient Experience), we investigate the endometriosis care-seeking and patient experience of diagnosed patients and those still seeking a diagnosis in South Africa.

Results
Eight centres across the three countries joined the multi-country study. We adapted and translated WERF-EPHect questionnaires to be appropriate for use in the different settings. Through prospective and retrospective methods we are recruiting 1,500 women (500 per country), with the aims of (i) providing a comprehensive phenotypic characterisation of the manifestation and impact of endometriosis, and (ii) capturing regional genetic diversity through an African-ancestry genome-wide association study. For ENDURE we developed a short questionnaire that aims to collect information from >350 women on care-seeking and diagnostic delays, care-seeking triggers, symptomatology, awareness of endometriosis, satisfaction with overall endometriosis healthcare, and research priorities in the South African setting. Data will be presented at the meeting.

Conclusions
These studies aim to make headway in improving the global understanding of endometriosis manifestations and pathogenesis. They will provide the first genome-wide endometriosis data from the African subcontinent, raise awareness of endometriosis in African women through characterisation of the disease presentation, and provide data for improving the current care- seeking and diagnostic journey.

Key words
Genetics, Africa, diversity

A PHOTOVOICE EXPLORATION OF EAST, SOUTH AND SOUTHEAST ASIAN WOMEN'S EXPERIENCES OF ENDOMETRIOSIS DURING COVID-19.

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[1]University of British Columbia, Vancouver, Canada
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Country where research was undertaken:
Canada

Introduction/Background
What we know about endometriosis typically represents the experiences of White women of reproductive age, but this may not encompass the experiences of all people. We sought to explore the experiences of East, South and Southeast Asian people with endometriosis during the COVID-19 pandemic – a time of global unrest.

Materials and Methods
Through a novel arts-based methodology called photovoice, we invited 22 Asian women with endometriosis to photograph what the world around them looked like while navigating endometriosis during the COVID-19 pandemic. Each participant submitted 8-10 photographs accompanied by brief captions, which guided a 1-hour, one-to-one online interview to explore the meaning behind each photograph. Interview data was then coded thematically by 3 qualitative researchers and analyzed according to qualitative thematic analysis to uncover shared themes.

Results
We found that the COVID-19 pandemic exacerbated the already present disruptions that Asian women with endometriosis experience, including isolation, lack of control, guilt, and grief. However, we also noted that the pandemic provided an opportunity to re-evaluate social supports, where participants expressed that the additional time during the pandemic allowed them to re-focus their energy on relationships that felt supportive. We also found that Asian women with endometriosis took empowering actions over their situations, building resiliency and experiencing benefits from increased adaptability and community understanding. Taking empowering action was expressed through the sentiment that: *sometimes you have to be your own light or ray of hope to keep on going.*

Conclusion
Although COVID-19 disruptions affected the mental health and social support of people in this study, East, South and Southeast Asian people with endometriosis demonstrated resiliency and built coping and management strategies that would extend beyond the COVID-19 pandemic.

Key words
Photovoice, endometriosis, ethnicity

FREE- COMMUNICATION SESSION 1

SESSION 1A: ADVANCES IN MOLECULAR CHARACTERISATION

DIFFERENTIAL GENE EXPRESSION IN SUPERFICIAL PERITONEAL LESIONS BY PAIN SYMPTOMS

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Country where research was undertaken:
United States of America

Introduction/Background
Superficial peritoneal endometriosis (SPE) lesions are the most common type among those with endometriosis, often presenting with pain. To identify clinically relevant SPE subtypes and elucidate underlying mechanisms contributing to pain, we assessed differences in gene expression between those with and without specific pain symptoms.

Materials and Methods
Using hybrid exome capture, we RNA-sequenced 425 SPE samples in the Women's Health Study: From Adolescence to Adulthood(A2A) and Endometriosis in Oxford University(ENDOX) WERF-EPHect-compliant cohorts. We identified differentially expressed genes with DESeq2 by pelvic pain symptoms adjusted for site, sample type, age at surgery, and menstrual phase. The Benjamini Hochberg method was used for false-discovery rate corrected p-values. We used gene set enrichment analyses to identify altered MSigDB hallmark pathways and calculate normalized enrichment scores(NES).

Results
Among 342 participants on hormones at surgery, 228(67%) reported acyclic pelvic pain and 272(80%) reported extra-pelvic pain. Among 83 not on hormones, 56(67%) reported dysmenorrhea, 51(61%) acyclic pelvic pain, and 55(66%) extra-pelvic pain. Acyclic pelvic pain was associated with downregulated inflammation and proliferation(e.g.MTORC1,NES=- 1.86 on hormones, -2.07 not on hormones) pathways compared to those without, regardless of

hormone usage. Dysmenorrhea was associated with upregulated inflammatory(e.g.TNFA,NES=3.00) and immune pathways(e.g.allograft rejection,NES=2.89) among participants not on hormones. Extra-pelvic pain, compared to only pelvic pain, featured upregulated inflammatory and immune pathways(e.g.allograft rejection,NES=2.78 on hormones, 2.11 not on hormones), regardless of hormone use. Among hormone non-users, the luteal-phase was associated with increased estrogen response and decreased cellular proliferation while peri-ovulatory phase immune and proliferative pathways were down- regulated compared to follicular phase.

Conclusion
Among 425 superficial peritoneal endometriosis lesions from 425 individuals, gene expression pathways were significantly associated with pelvic pain symptoms and menstrual cycle phase, providing insights into biological pathways contributing to pain symptom development or presentation. Analyses of other pain phenotypes are currently underway.

Key words
Pain, gene expression, superficial

CENTRAL FATIGUE IS ASSOCIATED WITH SPECIFIC STOOL METABOLITE SIGNATURE IN WOMEN WITH CHRONIC PELVIC PAIN

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Country where research was undertaken:
Scotland

Introduction/Background
Central fatigue is a common symptom of chronic pelvic pain (CPP) and endometriosis. A role has emerged for the microbiota-gut-brain axis and associated metabolites in endometriosis, but their impact on central fatigue has not been considered. We aimed to identify associations between the gut microbiome/metabolome and fatigue symptoms in CPP.

Materials and Methods
Stool samples were provided by women (n=45) awaiting a diagnostic laparoscopy. Patients completed the Brief Fatigue Inventory. Bacterial taxa were analysed by 16S-rRNA V3-V4 amplicon sequencing and profiled using an established functional-module framework. Stool metabolites were profiled with liquid-chromatography mass spectrometry (LC-MS). Each taxon, functional module, and LC-MS ion was modelled using multivariate linear regression and partial correlations with fatigue scores, including age and BMI as covariates, and with Benjamini-Hochberg false discovery rate (FDR) correction.

Results
Higher fatigue scores were associated with lower abundance of *Prevotellaceae Prevotella 9* (p=0.00157), as well as changes in 19 gut-brain functional modules, including short-chain fatty acid production and numerous pathways involving neurotransmitters, e.g. the kynurenine pathway, GABA/glutamate metabolism, and dopamine synthesis. These findings were further supported by identification of a signature of 12 LC-MS features (metabolites) associated with higher fatigue scores (p<0.001). Once p-values had been adjusted using FDR corrections, one metabolite (X) was found to be significantly less abundant in those with higher fatigue scores (FDR=0.08). When metabolite 'X' was correlated against fatigue scores, with age and BMI as covariates, this gave a correlation coefficient of -0.76 (p<0.00001). These findings were independent of a laparoscopic diagnosis of endometriosis.

Conclusion
This study has highlighted the potential role of the gut microbiome and derived metabolites in the experience of central fatigue associated with chronic pelvic pain. Further analysis is underway to identify stool metabolite 'X' and evaluate its potential use as a novel therapeutic target to treat this debilitating symptom.

Key words
Gut bacteria-derived metabolites, fatigue, therapeutic target

OPTIMISATION OF MULTI-OMIC SPATIAL ANALYSES OF FORMALIN-FIXED PARAFFIN-EMBEDDED (FFPE) ENDOMETRIOSIS LESIONS USING MASS SPECTROMETRY IMAGING (MSI)

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Country where research was undertaken:
Australia

Introduction/Background
The origins and pathogenesis of endometriosis remains to be poorly understood. Mass Spectrometry Imaging (MSI) is an omics (metabolomics, proteomics, glycomics) technique that permits spatial biomolecule identification within tissue sections. Utilising MSI, we aimed to investigate endometriotic lesions, to uncover disease mechanisms and potential diagnostic biomarkers.

Materials and Methods
We optimised published MSI methods for analysing 'omic profiles (proteomics and glycomics) of endometrium (tissue array) and endometriosis lesions (n=10 patients) using FFPE sections. Digestive enzymes (trypsin/PNGaseF) and matrix-assisted laser desorption/ionization (MALDI) matrices (cyano-4-hydroxycinnamic acid, 2,5-dihydroxybenzoic acid, 9- aminoacridine) were utilised for slide preparation. Tissue sections were analysed using Bruker SolariX 2XR MALDI fourier transform ion cyclotron resonance mass spectrometry (MALDI- FT-ICR MS), processed using SCiLS Lab (2024), receiver operating characteristic curves and linear discriminant analysis.

Results
Preliminary data suggests that protein peptides and N-glycans are capable of discriminating between tissues of interest. Fifteen peptides distinguished endometrial cycle phases on the endometrial array; elevated during the secretory phase. Eight peptides within endometriotic lesions, hold promise as potential lesion-specific biomarkers.

Our N-glycome analysis identified 15 differential N-glycans across endometrial cycle phases, also with increased levels during the secretory phase. This increase, compared to proliferative phase, was mimicked in endometriotic lesions. Four N-glycans were found exclusively in lesions, and not in the endometrium tissue array.

Lesion classification modelling, using significant lesion-specific peptides and N-glycans, showed successful prediction in a small sample cohort.

Conclusion
These findings reiterate a similarity between lesions and endometrial profiles, particularly during the secretory phase, warranting further analysis. While continued investigation of the peptides and N-glycans are needed, combined with annotation and validation using orthogonal tandem mass spectrometry (currently underway), they hold promise of becoming tools in understanding endometriosis.

Key words
Mass spectrometry imaging, lesions, biomolecules

GENETIC RISK AND MECHANISTIC STRATIFICATION FACTORS AND DRUG REPURPOSING TARGETS FOR ENDOMETRIOSIS IDENTIFIED USING COMBINATORIAL ANALYSIS

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Country where research was undertaken:
United Kingdom

Introduction/Background
Endometriosis is a complex chronic disease that impacts about 10% of reproductive-age women. In the UK, the average time to diagnosis from symptom onset is almost 9 years and this is confirmed using invasive, painful, and costly laparoscopic surgery, which fails to detect lesions in up to 30% of surgeries.

Materials and Methods
We used combinatorial analysis to identify combinations of single nucleotide polymorphisms (SNPs) that were significantly associated with endometriosis and examined the biological mechanisms underpinning endometriosis-associated fertility and disease stage. We compared two disjoint endometriosis populations from Oxegene and UK Biobank cohorts. We demonstrated supporting evidence for novel disease mechanisms identified from single cell and literature sources, including a recent meta-GWAS study.

Results
Combinatorial analysis identified 360 disease signatures (combinations of 1-5 SNPs) that were significantly associated with endometriosis in Oxegene and which could be reproduced in the disjoint UK Biobank endometriosis population. These signatures contained 403 unique SNPs, mapping to 175 genes. Of these genes, 18 have a prior association with endometriosis and a further 21 have a female reproductive system phenotype in mouse models.

We clustered the genetic signatures based on the endometriosis patients in which they co-occur. We identified seven patient subgroups in Oxegene, mapping to 16 genes, that were significantly enriched with endometriosis stage or fertility status. We annotated these genes to understand their biological relevance to the endometriosis phenotypes. We identified 27 drug repurposing candidate genes targeted by drugs in clinical development.

Conclusion
This study demonstrates the utility of combinatorial analytics in stratifying heterogeneous populations. These results build on the genetic findings from previous GWAS in endometriosis and we expect access to additional larger patient datasets will improve these disease insights and accelerate development of novel diagnostic tools and treatment options in endometriosis.

Key words
Precision medicine, genetics, drug repurposing

TRANSCRIPTOMIC PROFILING OF ADENOMYOSIS HIGHLIGHTS THE ROLE OF EXTRACELLULAR MATRIX REMODELING, TETRASPANINS AND CELL CYCLE REGULATION.

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Country where research was undertaken:
Poland

Introduction/Background
Little is known about mechanisms underlying adenomyosis. There is a limited number of genomic studies and the sample size in those is small. Using a meta-analysis to combine various datasets, we aimed to understand the main molecular events contributing to adenomyosis and to highlight genes with a biomarker potential.

Materials and Methods
Gene Expression Omnibus was searched for expression data on unprocessed endometrium from adenomyosis patients and respective controls according to predefined inclusion criteria. Data-specific preprocessing and normalization steps were applied to raw data and differential gene expression analysis followed. Meta-analysis was performed on five datasets containing endometrium samples from women with adenomyosis (n=26) and healthy controls (n=41). Enrichment, gene ontology and functional clustering was done in DAVID and gProfiler. Computational pharmacogenomics was done in cMap.

Results
MMP7 was the most upregulated gene in adenomyosis ($p<0.05$ logFC=1.7). Both *MMP11* and *MMP16* also showed a strong increase in expression compared to healthy tissue ($p<0.05$ logFC=1). *GLIPR1*, recently found to correlate with recurrent implantation failure[1], was also higher in adenomyosis ($p<0.05$ logFC=1.5). *SCGB1D4* and *ADAMTS8* showed the lowest expression ($p<0.05$ logFC=1.5, logFC=1.4 respectively). It was shown before that the downregulation of *SCGB1D4* correlated with fibrosis[2] and that serum levels of *ADAMTS8* decreased in endometrial cancer[3].

Pathways that showed highest enrichment in adenomyosis were: extracellular matrix remodeling, tetraspanins[4] (enrichment score of 7.22 and 4.22) followed by cell adhesion, inflammation and cell cycle (enrichment score above 2). Gene ontology analysis highlighted the importance of lipid metabolism while drug repurposing investigation suggested CDK inhibitors.

Conclusion
Our analysis revealed, for the first time, the importance of tetraspanins in adenomyosis. Extracellular matrix remodelling and cell cycle deregulation play a key role. Adenomyosis-driving genes also associate with implantation failure, fibrosis and cancer. Our data has a potential to inform endometrial biopsy and suggest the best diagnostic targets.

Key words
Adenomyosis, extracellular matrix remodelling, tetraspanins

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SPATIALLY RESOLVED CELL ATLAS OF THE ENDOMETRIUM AND ENDOMETRIOTIC LESIONS

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Country where research was undertaken:
Australia

Introduction/Background
Endometrial cellular composition is characterized through single-cell RNA sequencing. However, this technique lacks spatial resolution, missing critical details of cellular location, microenvironment, and interactions. These factors are crucial for distinguishing differences in the endometrium of women with and without endometriosis.

Materials and Methods
Endometrial biopsies from women with (n=12) and without endometriosis (n=12), and matching lesions (n=10) were multiplexed onto 10X Visium slides. Haematoxylin and Eosin staining was performed for cellular orientation. Barcoded cellular spots were sequenced, and data mapped to tissue locations using 10X Genomics Loupe browser. Cell annotation and deconvolution were performed with Cell2locate programs. Comparisons across the menstrual cycle, endometriosis cases and controls.

Results
We recorded an average sequencing depth of 45,986 reads per spot for eutopic and 26,933 for ectopic samples. The stratification of the single-cell dataset enabled accurate cell annotation, identifying epithelial, fibroblast, macrophage, and T-cell markers. Fibroblasts were most abundant in eutopic endometrium, with variations across the menstrual cycle. A significant increase in immune cells was observed during the secretory phase. The spatial data allowed us to accurately map the menstrual phases, which single-cell data alone could not achieve. We observed distinct stromal cell differentiation across phases, further confirming the phase- specific tissue composition. Endometriosis patients showed greater epithelial/stromal ratio variations, particularly in epithelial cells with reduced SA100A6 and increased Indian Hedgehog (IHH).

Conclusion
We mapped significant changes in endometrial cellular composition across the menstrual cycle, highlighting variations between women with and without endometriosis. Notably, epithelial progenitor cells were localized to highly glandular regions in endometriosis. This spatial data provides insights into cellular heterogeneity and immune infiltration in lesion subtypes, advancing our understanding of endometriosis microenvironments.

Key words
Endometriosis, single-cell, spatial transcriptomics

MULTI-OMICS DATA INTEGRATION REVEALS METABOLOME AS TOP PREDICTOR OF ADENOMYOSIS

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Country where research was undertaken:
United States of America

Introduction/Background
Adenomyosis is a painful gynecological condition with a prevalence ranging from 20-35% in symptomatic patients. Currently, detection methods, such as ultrasonography or magnetic resonance, are suboptimal and definitive diagnosis relies on hysterectomy, prompting more research for less invasive diagnostic tests, the aim of this study.

Materials and Methods
We enrolled 108 women undergoing hysterectomy for benign gynecological conditions. Cervicovaginal lavage (CVL) and vaginal swab samples were collected at time of hysterectomy. Based on histopathology, 46 women were diagnosed with adenomyosis and 62 with other benign conditions. Global metabolic analysis was performed on CVLs (yielding >900 metabolites), as well as immunoproteomic profiling (yielding 90 immune proteins). Vaginal swabs were used for microbiome analysis, yielding 399 microbial features. Multi- omics data integration was performed using Metaboanalyst.

Results
No significant differences were found in body mass index, menopausal status, co-occurring conditions, and parity between patient groups. Using least absolute shrinkage and selection operator (LASSO) for biomarker selection, multivariate receiver operating characteristic (ROC) analysis revealed that a model based on metabolomics dataset had area under the curve (AUC) of 0.852, predictive accuracy (PA) of 77%, and Youden's Index (J) of 0.607. As compared to immunoproteomics or microbiome models with PA of 68.8% and 66.5% respectively. Combining metabolomics and immunoproteomic we observed PA of 74.8%. Combining metabolomics and microbiome we observed PA of 74.3%. Multi-omics integration in a multivariate model resulted in an AUC of 0.859, PA of 77.4%, and J of 0.624, with metabolites being the top predictive features in the model.

Conclusion
Global metabolome is the best predictor of adenomyosis. Multi-omics integration increases performance metrics. Incorporating risk factors, parity and age of menarche, did not improve our multi--omics model. Overall, this study identified key immunometabolic biomarkers for diagnostic development and assessment and pathophysiological mechanisms in future studies.

Key words
Adenomyosis, multi-omics, biomarker

SESSION 1B: PREDICTORS OF DISEASE, PROGRESSION AND CLINICAL MANAGEMENT

GENETIC EVALUATION OF A COHORT COMPRISING PATHOLOGICALLY CONFIRMED SPORADIC ADENOMYOSIS CASES: A SYMPTOM-BASED ANALYSIS OF WHOLE EXOME SEQUENCE DATA

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Country where research was undertaken:
Türkiye

Introduction/Background
Adenomyosis is a benign gynecological condition, where endometrial-like tissue grows within the myometrium, causing symptoms like menorrhagia, dysmenorrhea, and irregular menstruation. Its pathogenesis remains unclear. We aimed to identify novel and/or rare genetic variants utilizing whole exome sequencing (WES) on a cohort of pathologically confirmed, sporadic adenomyosis cases.

Materials and Methods
Adenomyosis was diagnosed via histopathological examination following hysterectomy. World Endometriosis Research Foundation–The Endometriosis Phenome Harmonisation Project (WERF-EPHect) standard operating protocols were adapted. WES was performed on genomic DNA utilizing Illumina NovaSeq 6000. Bioinformatic analysis, subsequent filtering for MAF<1% and adenomyosis-related symptoms were conducted on Pairend NGS Cloud platform. Variants were prioritized based on functional relevance, classification under American College of Medical Genetics (ACMG) guidelines, and predicted impact on protein function using *in silico* tools.

Results
A total of 33 women diagnosed with adenomyosis were recruited. Adenomyosis-related symptoms were evaluated through WERF-EPHect questionnaire revealing that 15 (45%) had menorrhagia, 15 (45%) had metrorrhagia, 3 (10%) had infertility, 8 (24%) had dyspareunia, 15 (45%) experienced dysmenorrhea, and 6 (18%) had irregular menstruation prior to hysterectomy. WES revealed 55 novel variants along with rare variants in *VPS13B, SYNE1, MIB1* and *ADRB2,* as genes previously identified in studies involving endometriosis and adenomyosis. Among novel variants, the ones in *ATRX* and *CCDC141* were likely pathogenic and pathogenic, respectively, where these are linked to irregular menstruation according to Human Phenotype Ontology (HPO). The remaining 53 novel variants were reported as variant of uncertain significance (VUS). Some cases, having the same symptoms, shared genes harboring different variants.

Conclusion
This is the first study to highlight the link between adenomyosis pathogenesis and symptoms through WES. The cases did not exhibit shared genetic variants, suggesting a polygenic influence on adenomyosis. Future studies will expand the cohort and investigate the potential pathways through which the candidate genes may interact.

Key words
Adenomyosis, whole exome sequencing, genetic variants

MACHINE LEARNING FOR THE DETECTION OF ENDOMETRIOSIS FROM ELECTRONIC HEALTH RECORDS

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[2]University of Cincinnati Medical Center, Cincinnati, United States Machine Learning for the Detection of Endometriosis from Electronic Health Records

Country where research was undertaken:
United States of America

Introduction/Background
Endometriosis affects 10-15% of reproductive-aged women, and the average diagnostic delay ranges from six to twelve years. Electronic health record (EHR) data can be used to identify predictors of endometriosis. Our goal was to develop ML-based algorithms using EHR data to detect endometriosis.

Materials and Methods
This retrospective study included all adult patients with at least one visit at UCMC between 2011-20. Endometriosis diagnosis was defined by ICD9 or ICD10 code (N80). Demographics, visit data, diagnoses, comorbidities, and medications were extracted. Machine learning was used to predict diagnosis of endometriosis, including logistic regression, Support Vector Machines (SVMs), and decision trees. Data were randomly split into 80% training and 20% testing. Outcomes included: accuracy, sensitivity, specificity, precision, recall, and AUC.

Results
There were 13,231 patients with visits at UCMC clinic between 2011-2020; 1,332 unique patients were included in the study. Demographics (see table) included an average age of 42 years, with 74.1% white and 20% black. Patients diagnosed with endometriosis were significantly different in age ($p<0.05$) than those without an endometriosis diagnosis. The model with the highest performance was logistic regression, followed by the decision tree. From electronic health record data, we were able to successfully predict endometriosis. The accuracy from logistic regression, random forest, and decision tree were 0.895, 0.902, and 0.865 respectively. These models had AUC values of 0.912, 0.783 and 0.891.

Conclusion
Using machine learning, we predicted cases of endometriosis from electronic health record data. We used feature analysis to reduce dimensionality and protect against overfitting. This retrospective study provides the foundation for future prospective clinical investigations.

Key words
Machine learning, medical informatics, diagnosis

EXAMINING THE VAGINAL MICROBIOME IN WOMEN WITH SEVERE ENDOMETRIOSIS: A CASE-CONTROL STUDY

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Country where research was undertaken:
Denmark

Introduction/Background
The underlying pathophysiology of endometriosis remains unclear (1). The potential role of the vaginal microbiome in the development of endometriosis is debated with existing studies providing conflicting results (2,3). This study aimed to compare the vaginal microbiota between cases and controls and its association with intraoperative findings.

Materials and Methods
In this case-control study, samples and data were collected from endometriosis patients undergoing surgery at a tertiary endometriosis center and unaffected controls at smear test. Participants provided self-reported questionnaire data close to the time of sampling. Surgical findings were documented by the surgeon postoperatively. All microbiome data were analyzed using a metagenomic sequencing approach. Alpha- and beta-diversity were assessed, and differential abundances examined. The intraoperative findings were associated with the microbiome using hierarchical clustering.

Results
Of the 125 cases, 23.2 % were classified as stage III and 66.4% as stage IV disease according to the rASRM score. A total of 77.6% had endometriomas and 84.0% had deep endometriosis in the pelvic area. Three-hundred-and-fifty women participated as unaffected controls. The alpha-diversity differed between cases and controls, with cases having a more diverse vaginal microbiome. There were no differences in the beta-diversity. A total of five genera and 11 species were differentially abundant, however, we found no clustering of disease phenotypes associated with vaginal bacterial clusters. Cases had lower abundances of *L. crispatus*, *L. iners*, and *L. jensenii*, but no differences were identified when comparing the CST classification of cases and controls.

Conclusion
We found alterations in the vaginal microbiome between endometriosis cases and unaffected controls at both genus and species level. However, these changes were not associated with endometriosis-specific symptoms or clinical findings. Our findings do not support a significant role of the vaginal microbiome in the pathogenesis of endometriosis.

Key words
Endometriosis, microbiome, metagonomics

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PREDICTING ENDOMETRIOSIS WITH MACHINE LEARNING: ANALYZING SELF-REPORTED DATA FROM THE LUCY MOBILE APP

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Country where research was undertaken:
Hungary

Introduction/Background
Limited funding and research have stalled medical innovation in endometriosis, contributing to diagnostic delays of 4-11 years. Mobile healthcare tools can improve chronic disease management, symptom assessment, and prediction, but their application in endometriosis remains scarce. This study tests predictive machine learning (ML) models on Lucy app self- reported data.

Materials and Methods
Lucy app collects self-reported data from individuals with endometriosis and healthy controls. After filtering, the preliminary analysis was performed on 520,000 user records, utilizing correlation methods and visual tools to explore associations between symptoms and endometriosis. An XGBoost and Random Forest methods were implemented to identify key symptom patterns and predict endometriosis, training on the subset of 4812 users (n = 1212 control, n = 3600 endometriosis). This study is registered at ClinicalTrials.gov (Identifier: NCT06147687).

Results
The first step involved data filtering to address issues like nonrealistic dates and inconsistencies typical in real-world datasets. Strong associations between known endometriosis-associated symptoms—including pelvic pain, pelvic cramps, dysmenorrhea, and lower back pain—were shown by records from patients diagnosed with endometriosis but not yet treated. Our Random Forest model achieved an overall accuracy of 0.84, with an F1-score of 0.78 for endometriosis and 0.87 for negative cases, indicating effective discrimination between endometriosis and control cases. These metrics were obtained as mean values from 5-fold cross-validation, supporting the robustness of the model. Using Feature Importance analysis, dysmenorrhea and pelvic pain were identified as the most impactful symptoms on classification decisions.

Conclusion
Our preliminary analysis demonstrated that real-world, self-reported data are reliable and consistent with known endometriosis-associated symptoms, suggesting that the use of mobile apps like Lucy for endometriosis monitoring is a promising strategy. These findings may pave the way to transforming disease management and early detection of endometriosis.

Key words
Machine learning, self-reported data, prediction

BIRTH FACTORS RELATED TO ENDOMETRIOSIS LATER IN LIFE IN THE LIGHT OF NEONATAL UTERINE BLEEDING (NUB)

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Countries where research was undertaken:
Denmark, Netherlands

Introduction/Background
Sampson's retrograde menstruation theory is probably an important origin of endometriosis. Endometriosis occurring around puberty might be explained by neonatal uterine bleeding (NUB), possibly the first retrograde menstrual bleeding, occurring around the 7th day postpartum. NUB is more often seen in neonates born postterm or after hypertension induced complicated pregnancies

Materials and Methods
data were extracted from the Danish Health Register (update 2023) and the Medical Birth Register (Danish new-borns from 1977-1999). Women with and without endometriosis will be compared. Using cross-sectional and longitudinal models we compared the prevalence of the following parameters in both cases and controls: gestational age, birth

weight, hypertensive disorders diagnosed in the pregnancy of the mother i.e. pregnancy induced hypertension, preeclampsia, HELLP.

Results
681970 daughters were evaluated divided in two groups: no endometriosis (n=667524) and with endometriosis (n=14446). A significant negative correlation was seen for the parameter post term. Less daughters with endometriosis were born after the gestational age of 41 weeks. RR=0.93 (95% CI 0.90-0.96, p<0.001). The prevalence of daughters with and without endometriosis, born after a pregnancy with all hypertensive disorders combined was similar. RR=1,00 (95% CI 0.92-1.08, p NS). However, in the group with only hypertension or pre- eclampsia a slightly higher prevalence of daughters with endometriosis was seen. RR=1.07 (95% CI 1.00-1.15, p=0.0495), even more clear in the group with hypertension or pre- eclampsia and born postterm. RR = 1.19 (95% CI 1.02-1.39, p=0.03). These are preliminary results, a full evaluation is in progress.

Conclusion
preliminary results evaluating whether gestational age and/or a complicated pregnancy, due to hypertensive disorders, are predisposing factors for the development of endometriosis, do not directly support the theory of NUB as an origin of endometriosis later in life. Hypertension and preeclampsia might have an association with endometriosis.

Key words
Neonatal, pathophysiology, endometriosis

FRAGPIPE REANALYSIS OF PERITONEAL FLUID-DERIVED SMALL EXTRACELLULAR VESICLE PROTEINS AS POTENTIAL BIOMARKERS FOR ENDOMETRIOSIS

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Country where research was undertaken:
United Kingdom

Introduction/Background
Small extracellular vesicles **(**sEVs), produced by virtually every cell[1], have been implicated in diseases such as cancer[2], diabetes[3], and pre-eclampsia[2], and could similarly serve as biomarkers for endometriosis. Using an updated proteomics methodology, the peritoneal fluid (PF) sEVs were reanalysed to uncover proteins as potential biomarkers for endometriosis.

Materials and Methods
sEVs were isolated from peritoneal fluid (PF) of 63 women and analysed according to rASRM disease stage and menstrual cycle phase. sEVs were purified via size exclusion chromatography and analysed with nanoparticle tracking, immunoblotting, and mass spectrometry. FragPipe was used for protein identification instead of MaxQuant. Unlike MaxQuant, FragPipe leaves undetected or zero-value peptides as missing data rather than removing them, allowing for more accurate downstream analysis for limited amounts of PF.

Results
PF particles from women with endometriosis were positive for sEV marker proteins ALIX, CD9, and syntenin. The mode size of PF particles was 130 ± 8.7 nm in endometriosis and 134 ± 2.12 nm in control samples. Elevated sEV concentrations were found in endometriosis compared to control samples (paired t-test, p = 0.0136), with the highest concentrations in stage III-IV endometriosis, followed by stage I-II, and then control samples (one-way ANOVA, p = 0.0139). In stage III-IV endometriosis, sEV concentrations exhibited a gradual decrease during the transition from proliferative to secretory phases, whereas stage I-II endometriosis samples showed an increase. Proteomic analysis revealed distinct protein distribution patterns in endometriosis-derived sEVs, identifying 14-3-3 protein epsilon as a unique marker for the endometriosis population.

Conclusion
PF-derived sEVs differ between endometriosis and control patients, with concentrations varying independently of cycle phase and disease stage. This variation is also evident in the proteomic analysis.

Key words
Peritoneal fluid, endometriosis, small extracellular vesicles

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SESSION 1C: EMERGING THEORIES OF AETIOLOGY AND THEIR APPLICATION TO BIOMARKERS

CERVICOVAGINAL FLUID PROTEINS AND EXTRACELLULAR VESICLES AS NOVEL ENDOMETRIOSIS BIOMARKERS

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Country where research was undertaken:
New Zealand

Introduction/Background
Decades of global efforts to identify diagnostic endometriosis biomarkers have yielded limited success; novel sample types and innovative approaches may be required to make progress. This study investigated cervicovaginal fluid proteins and extracellular vesicles (EVs) from non- invasive vaginal swabs as biomarkers of endometriosis in surgically confirmed cases and controls.

Materials and Methods
Study participants had surgery for suspected endometriosis in Wellington, New Zealand. Samples of low vaginal swabs in phosphate buffered saline collected prior to surgery were processed for proteomics profiling. Proteins were quantified by data independent Sequential Windows Acquisition of all Theoretical Fragment Ion Spectra – Mass Spectrometry (SWATH- MS). Pathway and multivariate analysis were performed on differentially regulated proteins. Selected candidate markers were investigated by enzyme linked immunosorbent assay (ELISA) and EV spectral flow cytometry.

Results
SWATH-MS was performed on 39 samples (n=20 endometriosis, n=19 no endometriosis). Of the 1,741 proteins quantified, 76 were differentially regulated. Functional protein association network analysis and pathway enrichment analysis identified complement activation and the innate immune response as potential modules enriched in the differentially regulated proteins. Ingenuity pathway analysis (IPA) predicted the S100 family, ferroptosis and complement cascade signalling pathways as most likely to be affected by the observed changes in protein abundance.

EVs carrying immune regulatory proteins ($CCR2^+$, $CD55^+$, $CD59^+$ and $CD82^+$ EVs) were detectable in cervicovaginal fluid. Univariate analysis did not detect differences in the proportions or median fluorescence intensity (MFI) of antigen positive EVs between groups. Multivariate analysis of ELISA and flow cytometry data provided the greatest ability to discriminate between groups.

Conclusion
Using samples of non-invasive vaginal swabs, this study identified cervicovaginal proteins differentially regulated between people with endometriosis and symptomatic controls. Multivariate analysis of protein and EV markers most effectively discriminated cases from controls. Functional analysis underscores the biological relevance of these findings, warranting further investigation in a larger cohort.

Key words
Cervicovaginal fluid, proteomics, extracellular vesicles

A CRISPR VEZT KNOCK-IN MOUSE MODEL OF ENDOMETRIOSIS INCREASES LESION AND ADHESION FORMATION REFLECTIVE OF STAGE IV DISEASE

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Country where research was undertaken:
Australia

Introduction/Background
Endometriosis is an estrogen dependent gynaecological disease where endometrial-like tissue implants in locations ectopic to the uterus. *VEZT*, an adherens junction protein coding gene, is an endometrial risk gene of unknown function. In this study we characterised peritoneal lesion and adhesion formation and impacts on fertility in a CRISPR *VEZT* knock-in mouse model of endometriosis.

Materials and Methods
VEZT-Cre mice induced with tamoxifen daily (5x75mg/kg). Reproductive and liver tissue was collected at 4 and 12 weeks to verify global expression (N=6). Endometriosis was established with the intraperitoneal injection of minced donor uterine tissue (40 mg) into *VEZT*-Cre and C57/BL6 wildtype (WT) recipient mice (N=6 each). Adhesions were established through the injection of 17β-estradiol valerate weekly (4x10 ug/ml). Fertility was observed with crossing induced male and female *VEZT*-Cre mice (N=7).

Results
Tamoxifen induced *VEZT*-Cre mice overexpressed *VEZT* in liver, uterus and testis by 12 weeks. Large cystic, highly proliferative, inflamed and vascularised lesions were identified in all grafted *VEZT*-Cre mice from 4-8 weeks in liver, pancreas, ovary, bowel, peritoneum and inguinal fat pads surrounded by fibrosis and adhesions. WT mice failed to produce lesions beyond 4 weeks. *VEZT*-Cre uteri significantly upregulated TGFβ, TNFα (inflammation) and CTGF (fibrosis) mRNA expression in eutopic endometrium compared to WT mice. When *VEZT*-Cre mice (but not WT mice) were treated with 17β-estradiol-valerate to mimic the endometriotic environment, adhesions formed throughout the peritoneal cavity binding organs along with inguinal fat pad adipogenesis and cystic ovaries. When *VEZT*-Cre mice were mated, they were successfully impregnated with live birth rates and maternal morbidity pending.

Conclusion
This is the first endometriosis mouse model to demonstrate a significant role for *VEZT* in the development, adhesiveness and invasiveness of endometriotic lesions and in the presence of estradiol, the development of significant peritoneal adhesions. These findings identify *VEZT* is a potential therapeutic target or biomarker in the future.

Key words
Endometriosis, mouse, model

SINGLE-CELL TRANSCRIPTOMIC ANALYSIS HIGHLIGHTS THE SIGNIFICANT ROLE OF INFLAMMATORY LYVE1+ MACROPHAGES IN OVARIAN ENDOMETRIOMA

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Country where research was undertaken:
Singapore

Introduction/Background
Macrophages are a group of diverse and plastic immune cells which have critical roles in modulating immune responses, angiogenesis, and extracellular matrix remodelling. While macrophages are implicated in the pathogenesis of endometriosis, macrophage heterogeneity in human endometriosis remains poorly understood.

Materials and Methods
Single-cell suspensions of ectopic ovarian endometrioma tissues and the matched eutopic endometrial tissues were acquired from four patients with stage IV endometriosis based on the revised American Society of Reproductive Medicine score. CD45+ immune cells and CD45- non-immune cells were sorted out separately and then subjected to 10X single-cell RNAseq. The data was processed and analyzed by Seurat package in R. Macrophages were subclustered for in-depth investigation. Cellular interactions were predicted by CellChat package.

Results
We profiled 25143 $CD45^+$ immune cell transcriptomes (Ectopic n=14223, Eutopic n=10920) and 26109 $CD45^-$ non-immune cell transcriptomes (Ectopic n=12529, Eutopic n=13580). Unbiased subclustering of 1938 macrophages (Ectopic n=1058, Eutopic n=880) in our datasets identified five macrophage clusters. Two macrophage clusters associated with eutopic endometrium corresponded to the two major tissue-resident macrophage populations which can be discriminated by their expression of a hyaluronic acid receptor LYVE1. The three endometrioma-associated macrophage clusters also express LYVE1 at high levels. They are also featured by their high expression of genes related to inflammatory responses (S100 genes, TREM1), angiogenesis (THBS1, VEGFA, HBEGF), and extracellular matrix remodelling (TIMP1). Cellular interaction analysis predicted that inflammatory $LYVE1^+$ macrophages actively interact with vasculatures, thus promoting inflammation and angiogenesis in ovarian endometrioma.

Conclusion
Inflammatory $LYVE1^+$ macrophages are a critical macrophage population regulating immune responses, extracellular matrix remodelling and angiogenesis in ovarian endometrioma. It represents a promising therapeutic target for future endometriosis treatment. Macrophage populations in eutopic endometrium corresponded to the two major tissue-resident macrophage populations which have been reported cross tissues.

Key words
Macrophage, LYVE1, inflammation

EXTRACELLULAR VESICLES AS BLOODBORNE BIOMARKERS OF PERITONEAL ENDOMETRIOSIS

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Country where research was undertaken:
Australia

Introduction/Background
Endometriosis is a systemic, gynaecological disorder that affects >10% of AFAB people of reproductive age (1). Laparoscopic surgery is the gold standard diagnostic method for peritoneal endometriosis, with delay from symptom onset extending up to 12 years (2, 3). Currently, no diagnostic biomarkers of endometriosis have reached clinical validity (4).

Materials and Methods
Peripheral blood (PB) and peritoneal fluid (PF) were obtained from patients undergoing laparoscopies at two hospital locations and banked (n=142). sEVs were pelleted using differential ultracentrifugation. Downstream purification was trialed on PB using SEC (n=2) and centrifugal filter units (n=2). sEVs were validated using Western blotting, nanoparticle tracking analysis (NTA) and transmission electron microscopy (TEM). Treated MeT-5A mesothelial cells were analysed using qRT-PCR (n=2), immunofluorescent microscopy (n=1), and trans-endothelial electrical resistance (n=3) for mesothelial-to-mesenchymal transition.

Results
Filter unit isolated sEVs from PB had a median diameter of 137.95 nm (n=2). Automated capillary and traditional western blotting were used to detect syntenin as a marker of EVs (n=4, n=36) and biomarker candidate 2 (n=2, n=36). Traditional western blotting detected candidate 2 in syntenin-positive PB samples (sensitivity 56%, specificity 68%). The treatment of MeT- 5A mesothelium with endometriosis derived sEVs saw upregulation of vimentin, elongation of cell morphology and a decrease in cell monolayer resistance compared to sEVs from symptomatic controls. However, due to the limited sample size, these results were non- significant.

Conclusion
sEVs remain prominent biomarker candidates for diagnosing endometriosis. Candidate 2 requires further refinement to reach the recommended sensitivity of 94% and specificity of 79% for a clinically useful blood test (4). Patient sample validation requires balancing sEV purification with yield. sEV treatment caused mesothelial changes modelling lesion implantation.

Key words
Extracellular vesicles, biomarkers, pathophysiology

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THE CREATION OF CLINICALLY-INFORMED TISSUE MICROARRAYS OF ENDOMETRIOSIS TO ENABLE TRANSLATIONAL BIOMARKER RESEARCH

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Country where research was undertaken:
Australia

Introduction/Background
Tissue microarrays (TMAs) are a high-throughput research resource that enable simultaneous analysis of multiple tissue samples on a single slide. They efficiently facilitate spatial screening of biomarkers and gene expression to accelerate therapeutic development. To date, incomplete clinical and patient-reported data linked to endometriosis TMAs have limited their utility.

Materials and Methods
Participants of the Australian National Endometriosis Clinical and Scientific Trials (NECST) Registry with archived surgical tissue were invited to participate. Donor formalin-fixed paraffin-embedded blocks were reviewed by a pathologist for endometriosis content. Triplicate 1mm diameter cores from indicated areas were embedded in TMA blocks. Patient-reported measures and medical history were captured at baseline, 6 months, 12 months and annually thereafter. Hormone receptors expression and proliferative index were investigated by immunohistochemistry.

Results
Eight TMA blocks, grouped by phenotype, consisting of 610 cores from 53 patients, representing 202 distinct anatomical locations were created. Patients with superficial endometriosis were more likely to have a co-diagnosis with an idiopathic condition (e.g., fibromyalgia), while those with deep infiltrating endometriosis were more likely to present with a concurrent autoimmune disease. Progesterone Receptor (PR) and Ki67 expression both demonstrated heterogenous intrapatient expression, while expression of Estrogen Receptor-α (ERα) was consistently

high. Endometriomas were more proliferative than other phenotypes (p<0.0005). Neither disease stage, hormone treatment, nor a co-diagnosis with an inflammatory or autoimmune disease were associated with a change in endometriosis proliferation.

Conclusion
TMAs represent a valuable tool for biomarker discovery in endometriosis, particularly with matched clinical and patient-reported data. The current pipeline will be applied to a larger cohort of patients (n=130) including rarer subtypes of endometriosis. Ongoing annual patient- reported data will facilitate deeper analysis of molecular and clinical phenotypes of endometriosis.

Key words
Biomarker, immunohistochemistry, tissue microarray

INVESTIGATING MAIT CELLS IN EUTOPIC AND ECTOPIC ENDOMETRIUM: IMMUNE MODULATION WITH DIAGNOSTIC AND THERAPEUTIC IMPLICATIONS IN ENDOMETRIOSIS

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Country where research was undertaken:
United Kingdom

Introduction/Background
Endometrial mucosa contains immune cells, which may influence endometriosis and related subfertility. Mucosal-Associated Invariant T (MAIT) cells, abundant in mucosa, play a key role in microbial defense and modulate immune responses in various inflammatory conditions. We explored MAIT populations in both eutopic and ectopic endometrial tissue of patients with endometriosis.

Materials and Methods
A 35-parameter panel for full-spectrum flow cytometry (Cytek® Aurora) enabled deep immune phenotyping of 28 eutopic and 3 ectopic endometrial samples from 20 patients with surgically confirmed endometriosis and 8 non-endometriosis control samples. A MAIT-specific 13-marker panel was then utilised on 8 eutopic and 2 ectopic samples from endometriosis patients. Additionally, three full-thickness uterine biopsies underwent multiplex immune imaging (ZellScannerONE®) to examine MAIT spatial organization across menstrual cycle phases.

Results
Through deep immune phenotyping of immune cells from matched eutopic and ectopic endometrial samples, we identified elevated levels of MAIT-like CD8+ T cells (CD161+CD8+CD3+) in endometriosis patients compared to controls (p. adj. < 0.05). In the following pilot study, 49,360 MAIT cells (CD161+Va7.2+CD3+) were detected in the eutopic endometrium. They peaked during ovulation and the window of implantation (WOI) compared to earlier menstrual phases (p. adj. < 0.05), indicating a potential role in fertility. MAIT cells constituted 4.03% of T cells in the eutopic endometrium but were <1% in the lesions, likely due to the predominance of fibrotic rather than mucosal tissue. Histological analysis further examined MAIT and MAIT-like cell distributions across the menstrual cycle and between patients and controls in the endometrium and myometrium.

Conclusion
Our findings reveal significant alterations in MAIT-like CD8+ T population within the eutopic endometrium of endometriosis patients and an increase in MAIT cells during ovulation and WOI. This suggests that MAIT cell dysregulation may contribute to endometriosis-associated subfertility, providing a basis for future diagnostic and therapeutic research.

Key words
MAIT, endometrial immunity, deep immune phenotyping

SESSION 1D: THE BURDEN AND SOCIETAL IMPACTS OF ENDOMETRIOSIS

MOMMY THIS HURTS!: UNCOVERING HIGH RATES OF MENSTRUAL PAIN AND DISTRESS IN ADOLESCENTS THROUGH EXPRESSIVE ART

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Country where research was undertaken:
United States of America

Introduction/Background
After showing high prevalence of severe dysmenorrhea and menstrual distress in a cohort of ~1000 Hispanic adolescents living in Puerto Rico, we sought to assess at a deeper level the experiences, feelings, and perceptions regarding menstruation, the menstrual cycle, and menstrual health among this understudied population.

Materials and Methods
A qualitative study was conducted to explore the experiences, emotions, and perceptions regarding the menstrual cycle among Puerto Rican adolescents during activity-oriented focus groups. Participants (14 to 18 y/o students from Middle and High School) were prompted to create artistic mosaics and to describe with narratives their personal menstrual cycle experiences and feelings. Quantitative content analysis and qualitative thematic analysis were conducted with NVivo software using a descriptive and interpretative approach to the data.

Results
90 students representing five regions of the Department of Education participated in the focus groups. Three major themes were uncovered by content analysis of each mosaic and the narratives. The most common codes identified were categorized in "emotions/feelings", "physical symptoms", and "strategies/actions". The depicted and narrated experiences, feelings, and perceptions of the menstrual cycle expressed a high prevalence of emotional distress, anger, pain, sleep disturbances, and references to menstrual blood. Self-care strategies included indulging in snacks, bed rest, exercise and receiving emotional support from their pets. Some identified this as a natural process in their development, while others asked "Why girls?", "Why so young?". Word frequency analysis identified "pain", "school", "emotions" and "help" as commonly used words to describe their experiences.

Conclusion
We showed substantial physical and emotional detriments to health and well-being in adolescents who used artistic expressions to document predominantly negative experiences with their "enemigo" ["my enemy"] and their "worse time of the month". These data will inform the development of curricula to increase awareness of menstrual dysregulations and distress.

Key words
Menstrual health, menstrual distress, adolescents

PATIENT PERSPECTIVES ON THE MISSED OPPORTUNITIES AND BARRIERS DURING THE DIAGNOSTIC JOURNEY FOR ENDOMETRIOSIS IN AUSTRALIA

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Country where research was undertaken:
Australia

Introduction/Background
Endometriosis is a chronic inflammatory condition that can significantly impact physical and psychological well-being, and quality of life (1). Diagnostic delays of up to nine years (2) are marked with significant challenges and missed opportunities. This exploratory mixed-methods research explores these barriers and missed opportunities from the patient's perspective.

Materials and Methods
Quantitative and qualitative data were collected via an online survey. Participants were included if they resided in Australia, were aged 18 years or older, and had their diagnosis confirmed through laparoscopic surgery. Quantitative data were collected using three broad categories: demographics, information regarding diagnosis, and care team. Qualitative findings were derived from free-text boxes. Deductive and inductive analyses were used to derive key themes regarding missed opportunities and barriers in the period to diagnosis.

Results
Ninety-five participants completed the survey. The quantitative data uncovered potential missed opportunities for earlier disease management through multidisciplinary care. After diagnosis, there was an increase in the number of participants seeing pelvic health physiotherapists (21.1%), psychologists (7.4%), pain specialists (7.4%) and naturopaths (3.1%), compared to before diagnosis. The qualitative analysis uncovered four key themes; i) patient invalidation, ii) poor

understanding about endometriosis from healthcare professionals and the community, iii) missed opportunities for holistic early action in symptom management, and iv) the requirement for self-advocacy.

Conclusion
Our study provides a deeper understanding around high value patient-centred care for those on their endometriosis diagnostic journey. Creating awareness of insights presented in this study may help to enhance communication, with health professionals less likely to dismiss, minimise, or misunderstand the patients' symptoms, enabling earlier referrals and symptom management.

Key words
Diagnosis, barriers, validation

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THE 2025 LIVING AUSTRALIAN GUIDELINES FOR THE MANAGEMENT OF ENDOMETRIOSIS

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Introduction/Background
Australian data indicates 1 in 7 women are diagnosed with endometriosis by age 44–49 (AIHW, 2023). RANZCOG developed the first Australian clinical practice guideline for the diagnosis and management of endometriosis in 2021. These 2025 living guidelines incorporate new research to provide evidence-based recommendations for people with suspected or confirmed endometriosis.

Materials and Methods
Searches were completed for 22 clinical questions and evidence summaries prepared by the RANZCOG Research and Policy team with external support. The new evidence was appraised using GRADE methodology. Formalised representation of stakeholders to ensure relevance to the Australian setting. The GDG developed the final recommendations after considering the evidence. For the purpose of living evidence searches of prioritised clinical questions will be repeated every three months.

Results
There are 80 recommendations: 8 strong recommendations, 31 conditional recommendations and 41 practice points.

New evidence was reported for 16 clinical questions including signs and symptoms, the role of imaging to diagnose deep endometriosis, hormonal treatments following surgery, surgery for cyst management, surgery for people where fertility is a priority. Finally, there are recommendations for non-pharmacological and not nonsurgical treatments including physical therapy, psychological interventions and acupuncture. For primary care there is guidance about diagnosis by transvaginal ultrasound, and treatments with 1st line options and when to refer. There are also recommendations about organisation of care and interdisciplinary care.

There was no new evidence about the benefits and harms of laparoscopic excision or ablation with either surgical technique.

Conclusion
There is growing recognition of the need for improved awareness, education, diagnosis, treatment and research into endometriosis. This guideline provides evidence-based recommendations that will go some way towards better care for people with endometriosis. However, more well-designed research is required across most of the endometriosis topics in this guideline.

Key words
Living Evidence Guidelines

AIHW. (2023, 11 15). Retrieved from Australian Institute of health and Welfare: https://www.aihw.gov.au/reports/chronic-disease/endometriosis-in-australia/contents/about

COMPLEX INTERPLAY OF PELVIC SPASM AND WIDESPREAD PAIN: INSIGHTS FROM PHASE 2 TRIAL OF BOTULINUM TOXIN FOR ENDOMETRIOSIS-ASSOCIATED PELVIC PAIN

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Country where research was undertaken:
United States of America

Introduction/Background
Pelvic muscle spasm and widespread sensitization likely contribute to pain persisting despite surgical and hormonal lesion management in women with endometriosis-associated chronic pelvic pain (endo-CPP). We evaluated the association between pelvic and widespread pain over time following botulinum toxin (BoNT) injection into pelvic floor muscles with spasm in endo- CPP.

Materials and Methods
Twenty-nine women (18–50 years) with endo-CPP (surgically-diagnosed, optimized hormonal treatment) in a randomized, placebo-controlled, double-masked trial received 100U onabotulinumtoxinA or placebo into pelvic muscles spasm (NCT01553201). Pain distribution was assessed over 1-year following masked +/- optional open BoNT (given at 1-12 months on request). Pelvic outcomes included muscle spasm and tenderness. Widespread pain outcomes included patient-reported painful bladder syndrome (PBS), irritable bowel syndrome (IBS) and painful body regions. Analyses included correlations and mixed-effects models.

Results
Across the cohort, comparisons between baseline and 1-year showed significant reduction in pelvic and body pain measures (p=0.003–0.04). All pelvic pain measures were interrelated and positively correlated with body pain at study end (r_s 0.41–0.69, p=0.0001–0.03). Longitudinal analysis (5-6 visits per patient) of pelvic floor muscle spasm and painful body regions showed greater reduction over time in those receiving 2 BoNT injections (p=0.002), especially when the second injection was requested after 1 month (p<0.001). Receiving 2 injections also reduced the likelihood of meeting criteria for IBS and/or PBS at study end (p=0.01) and predicted ongoing benefit (p=0.006). Baseline systemic and regional non-pelvic chronic overlapping pain conditions were associated with an increased risk of widespread body pain over time (p=0.001).

Conclusion
Women with endo-CPP have pelvic and widespread body pain, reflecting chronic overlapping pain conditions. BoNT, a targeted, mechanism-based treatment, showed a consistent, progressive reduction in pelvic and body pain over time. This is the first study to describe an approach to assessing neuroplastic changes with effective treatment for endo-CPP.

Key words
Endometriosis-associated chronic pelvic pain, widespread pain, overlapping pain conditions

THE COST OF ENDOMETRIOSIS AND CHRONIC PELVIC PAIN BURDEN IN NEW ZEALAND (AOTEAROA): RESULTS FROM A NATIONWIDE SURVEY

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Country where research was undertaken:
New Zealand

Introduction/Background
Endometriosis and chronic pelvic pain (CPP) impacts negatively on quality of life causing a significant cost of illness burden[1–5]. Direct and indirect costs impact significantly on this burden, with significant cost arising from productivity[3,6]. New Zealand has limited data pertaining to health economics for endometriosis which this study contributes[5,7].

Materials and Methods
A 99 question online survey (hosted via REDCap) was developed using the validated WERF EndoCost tool for direct comparison to international datasets[8,9]. This questionnaire data was collected over 10 weeks in 2021. Inclusion criteria included women aged over 18 with self- reported endometriosis or CPP. Data was used to inform the analysis to obtain health economics data on direct (healthcare-related) and indirect (productivity and carer) costs, which were assumed based on New Zealand population census data[10].

Results
688 participants completed the questionnaire. Figures are yet to be finalised but preliminary analysis reports the total annual economic burden is estimated to be up to $17billion (assumed prevalence rate of 14%) to the New Zealand (NZ) health system and society (direct and indirect costs combined). Per-capita costs differed amongst endometriosis and CPP participants ($98k, $190k respectively), which were significant regardless of diagnosis. Direct costs made up a larger proportion of total cost for endometriosis (58%) compared with CPP (35%). Age and pain severity were associated with increasing cost. Compared to Australia, this represents an increased cost of illness burden which estimated $6.5billion in 2017[3]. NZ Prevalence data is limited, suggesting that prevalence could be underestimated leading to an underestimate of this cost burden figure[11].

Conclusion
This study is the first to report analysis for cost of illness demonstrating a high burden relating to endometriosis and CPP in New Zealand. A significant proportion of this burden arises from productivity estimates, and calls to action investment for improving services and reducing impact of symptoms on affected individuals.

Key words
Endometriosis, health-economics, pelvic-pain

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THE USEFULNESS OF RAISING AWARENESS TOOL FOR ENDOMETRIOSIS (RATE) AMONGST PRIMARY HEALTHCARE PROVIDERS AND CONSUMERS

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Country where research was undertaken:
Australia

Introduction/Background
The Raising Awareness Tool for Endometriosis (RATE) was developed by a multidisciplinary team in Australia and New Zealand to assist those experiencing endometriosis-associated symptoms see their health providers for assessment and discussion.

Objectives
To explore the usability of RATE amongst general practitioners and consumers

Materials and methods
A mixed-methods study was undertaken using a combination of quantitative and qualitative data amongst a sample of general practices in Western Australia from April 2021 to March 2022.

Quantitative data were extracted from 1354 women using the online RATE tool from January 2022 – September 2023. Alongside RATE responses, a 1-10 visual analogue scale (from least to most) was used to assess ease of use, helpfulness and if the tool would encourage them to discuss findings with their doctor.

Results
Interviews from GPs confirmed that RATE was not only acceptable but was most useful if completed prior to consultation and when a problem was identified and presented for discussion.

User feedback reported the online RATE tool was easy to use, (*n*=1029), helpful (*n*=1017), and likely to result in consultation to discuss issues identified in RATE (*n*= 974) with 92% of those completing RATE had pain symptoms requiring over the counter medications.

Conclusion
This study indicates RATE is easy to use and assists consumer-clinician open discussion about endometriosis-associated symptoms.

Key words
Endometriosis, pelvic pain, dysmenorrhoea

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SEMINAR SESSION 3: WHOLE PERSON CARE

IMPROVING THE PERCEPTION OF ENDOMETRIOSIS-RELATED CHRONIC PAIN: THE COGENS TRIAL

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Country where research was undertaken:
The Netherlands

Introduction/Background
Endometriosis surgery can improve chronic pain and Health Related Quality of Life (HRQoL)[1,2]. However, altered pain processing can decrease the effectiveness of the surgery[3,4]. The aim of this study was to combine endometriosis surgery with cognitive behavioral therapy (CBT) to decrease chronic pain and improve HRQoL.

Materials and Methods
In this randomized controlled multicenter trial, 100 patients were included undergoing surgery for endometriosis related chronic pain[5]. Participants were equally randomized between endometriosis surgery or endometriosis surgery and CBT. Questionnaires evaluated HRQoL, pain intensity, catastrophizing, anxiety, fatigue and stress at baseline, 16 and 32weeks post- surgery. Cortisol levels in scalp hair were analyzed as another measure for chronic stress. Group difference was evaluated with linear mixed models (LMM) and a mediation analysis was performed.

Results
Final analysis included all 100 patients, 50 in each group. LMM analysis showed that the CBT group experienced improvement on HRQoL measured by the Endometriosis Health Profile (EHP)-30 modular part (*p=.021*) and the Short Form (SF)-36 physical component scale (*p=.008*) when compared to the surgery only group. In addition, pain catastrophizing and pain anxiety decreased, while cortisol levels increased (*p=.019; p=.047 and p=.022* respectively). Pain intensity, fatigue and stress did not show an overall significant group difference. Although pain intensity did not differ between groups, the improvement in HRQoL in the CBT group was partly mediated by pain intensity with an indirect effect of -2.5. Important other mediators were pain catastrophizing and anxiety with indirect effects of -2.1 and -1.2 respectively.

Conclusion
CBT is effective to improve HRQoL following endometriosis surgery. The effect of CBT on HRQoL is mediated by pain catastrophizing, anxiety and intensity. We conclude that CBT is effective because it improves pain coping which enables patients to deal with their pain, resulting in better HRQoL.

Key words
Cognitive behavioral therapy, health related quality of life, chronic pain

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LONGITUDINAL MONITORING OF POST-OPERATIVE SYMPTOM CHANGES IN ENDOMETRIOSIS USING SMARTWATCHES

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Country where research was undertaken:
Scotland

Introduction/Background
Clinical trials in endometriosis typically assess symptoms using patient-reported outcome measures (PROMs), which may result in

missing data or bias. Wearable technology can complement PROMs by capturing objective data on physical activity and sleep, providing unbiased responses. In this study, we investigated use of smartwatches to assess response to surgery.

Materials and Methods
Patients with deep endometriosis scheduled for excision of lesions, with or without hysterectomy/oophorectomy, wore smartwatches (measuring acceleration, temperature, ambient light) continuously over three 4–6-week cycles. They submitted pain scores and completed the Brief Fatigue Inventory (BFI). Three sets of data were collected: 1) baseline cycle before surgery, 2) period immediately after surgery, 3) 4-6 months after surgery. The smartwatch data was processed to extract information on physical activity, sleep, and diurnal rhythms.

Results
22 patients were recruited, 16 underwent surgery (5 excision only, 11 concurrent hysterectomy): 13 completed 2 cycles (12 completed 3 cycles). In the 10 days following surgery, 11/13 reported elevated pain scores and 12/13 had increased fatigue scores compared to baseline. All (n=13) had decreased physical activity and sleep regularity, and 11/13 had increased sleep disturbance. Recorded physical activity typically increased over the 30 days following surgery as symptom severity decreased (repeated-measures correlation of -0.53 with pain and -0.62 with fatigue). At 4-6 months, pain and fatigue scores were decreased compared to baseline in all but one of the participants. 9/12 participants had an increase in sleep regularity but only 5/12 had an increase in physical activity.

Conclusion
This pilot study demonstrates the potential of smartwatches to assess symptoms after surgery for endometriosis. Our findings suggest that smartwatch data can provide insights into recovery times and outcomes following surgery and highlight the merit of capturing longitudinal objective data to gain a deeper insight into activity and sleep rhythms.

Key words
Fatigue, wearable technology, research inclusivity

TRANSFORMATIVE PERSPECTIVES ON ENDOMETRIOSIS RESEARCH, POLICY, AND PRACTICE: INSIGHTS FROM MULTIDISCIPLINARY FOCUS GROUPS

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Country where research was undertaken:
Switzerland

Introduction/Background
Transgender and gender diverse (TGD) people with endometriosis have unique health needs, that remain largely unmet by current health research, policy, and clinical practice. This study aims to set an agenda for future research, and to make recommendations for policy and practice through participatory research methods.

Materials and Methods
Twenty community members and professionals gathered for a two-day event at the Brocher Foundation, Switzerland. The group was heterogeneous in terms of gender, age, race, ability status, professional background, and seniority in research. Three focus groups and two plenary sessions were facilitated. Two researchers analyzed the data. Thirteen themes were identified and grouped into three categories: research, policy, and practice. Member checks were conducted at several stages of the study implementation.

Results
Future studies should re-center the experiences of TGD people embodying different intersecting identities through transdisciplinary and participatory research methods. The effects of gender-affirming therapies on endometriosis and the adequacy of endometriosis treatments for TGD people need to be further investigated. Subsequent education of healthcare providers is crucial to improve clinical practice, as well as a shift in health policy beyond cisheteronormativity.

Conclusion
TGD people are disproportionately affected by social and health disparities across different countries. TGD people with endometriosis

have unique health needs that need to be met by multidisciplinary teams. Health research, policy and practice should be inclusive of this community to mitigate health disparities.

Key words
Transgender, health disparity, multidisciplinary health research

#ENDOFLARE – WHAT ARE FLARES IN ENDOMETRIOSIS, WHAT IMPACT DO THEY HAVE, AND WHAT HELPS?

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Country where research was undertaken:
United Kingdom

Introduction/Background
People with endometriosis-associated pain often report experiencing flares in their symptoms, which until recently have not been researched. In this study we explore the characteristics of flares in endometriosis, the impact flares have on individuals, how predictable flares are and strategies/ treatments that have been used to help flares.

Materials and Methods
The Flares Questionnaire used was adapted from previous studies in chronic pelvic pain [1,2]. In this adaptation specifically questions were asked to understand flares' predictability, treatments/strategies that are used to prevent/treat flares and where knowledge of flares has come from (e.g. clinicians/social media). Data was collected using Jisc online surveys v3, and was hosted/distributed by charities (e.g. Endometriosis.org, Endometriosis UK & Endometriosis Association of Ireland) and social media. Statistical analysis was performed using SPSS.

Results
235 people with an endometriosis diagnosis responded to our survey. 98.4% experienced a flare of short, medium and/or long length, with all flare lengths having pain and non-pain symptoms. Flares were unpredictable (median of 1 for short and medium, 2 for long; rated on a 6-point scale (0=not at all to 5=entirely predictable)). Participants reported low confidence coping with daily activities despite flares (median of 2 for short and medium, 1 for long; scale 0=not at all to 5=completely confident). Medication was used by 25.8% to prevent flares and by 71% to relieve them, with variable benefit. Only 35.3% reported receiving advice about flares from healthcare-providers, whilst 42.7% reported receiving advice on support groups/social media. Advice from support groups/social media was reported as more helpful.

Conclusion
Symptom flares in endometriosis-associated-pain are very common. Our findings suggest they are unpredictable and impact on individuals' confidence managing their day-to-day lives. There's a clear need for successful strategies to both prevent and treat flares (medical and other) and healthcare providers should be encouraged to discuss these with their patients.

Key words
Endometriosis-associated pain, flares, impact

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EFFECTIVENESS OF EXERCISE AND PELVIC FLOOR MUSCLE TRAINING IN ALLEVIATING PELVIC/GENITAL PAIN IN WOMEN WITH ENDOMETRIOSIS: A RANDOMIZED CONTROLLED TRIAL

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Country where research was undertaken:
Norway

Introduction/Background
Treatments often fail to address the complexity of endometriosis [1,2]. International guidelines recommend research on pain management and exercise training [3,4]. We aim to investigate whether exercise training, including pelvic floor muscle training (PFMT) combined with pain management, reduces pelvic/genital pain more than pain management alone in women with endometriosis.

Materials and Methods
All participants attended a pain management course. The exercise group (n=41) followed weekly supervised general exercise training, including PFMT and home training, 2-3 times/week for four months. The control group (n=40) received no further intervention. The primary outcomes were change in worst pelvic/genital pain over one month and current pelvic/genital pain measured on a numeric rating scale at baseline, 4 months postintervention and 12 months follow-up. The secondary outcome was the participant's experience managing symptoms.

Results
81 women aged 18-45 years with laparoscopic-confirmed endometriosis and experiencing pelvic/genital pain participated in this two-armed, parallel-group randomized controlled trial. The intervention did not improve worst pelvic/genital pain. A significant change in current pelvic/genital pain at post-intervention [mean difference [1.2 (95%CI 0.2–2.4)] and follow-up [mean difference [1.3(95%CI 0.1-2.4)] was found. Participants' experience on managing symptoms was significantly improved [RR=1.613 (95%CI:1.059–2.456)] at postintervention. No other effects from the intervention were found.

Conclusion
Pain management and supervised group- and individual exercise training, including PFMT, did not improve worst pelvic/genital pain but may improve current pelvic/genital pain and help women manage their symptoms. No adverse effects or worsening of symptoms were reported. Exercise training can be recommended due to its general health benefits.

Key words
Pelvic/genital pain, exercise training, pelvic floor muscle training

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ONLINE MULTIMODAL CARE FOR ENDOMETRIOSIS AND PELVIC PAIN

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Country where research was undertaken:
Australia

Introduction/Background
Endometriosis and persistent pelvic pain are associated with impaired quality of life (QoL). International guidelines recommend interdisciplinary management to improve QoL. There is need for an online, interdisciplinary self-management tool to reduce access barriers to treatment. We describe the development and prototype of such a tool, Co-Designing, Evaluating, and Implementing Supportive Care for Endometriosis (*CoDeEndo).*

Methods
Nine intervention modules were co-created by teams consisting of endometriosis clinicians and researchers, consumers living with endometriosis and consumer representatives. The modules were designed through iterative processes drawing on evidence, lived experience, and the clinical expertise of the research and clinical team, ensuring that the interventions were developed with expert knowledge and care.

Results
CodeEndo is an 8-week online program that consists of 9 therapeutic modalities: psychoeducation, cognitive behavior therapy (CBT), acceptance commitment therapy (ACT), hypnotherapy, mindfulness, yoga, relaxation training, dietary education, and physiotherapy information. Each intervention is comprised of sub-modules that consist of a mix of video, audio, and written resources – as well as homework practices. Participants will have access to all modules and will be able to spend as little or as much time accessing CodeEndo. The specific goals of the intervention will vary for each person, depending on their individual symptoms, severity of disease, expectations, motivations, life experience, and what they want to achieve from the intervention.

Conclusion
This world-first initiative will allow for the online delivery of interdisciplinary, supportive care that targets whole person wellbeing. CodeEndo will be delivered online via a dedicated study website, allowing access for people in rural and remote communities, and will be self-directed by participants through pre-recorded intervention modules.

Key words
Psychology, lifestyle, digital

DIGITAL STORYTELLING AS A PSYCHOSOCIAL INTERVENTION FOR ENDOMETRIOSIS

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Country where research was undertaken:
Canada

Introduction/Background
Endometriosis can be a socially isolating and acutely distressing disease. Many individuals suffer in silence in the absence of a supportive community. Collaborative Digital Storytelling (DST) may provide a safe and therapeutic environment for people with endometriosis to benefit from social connection and validation.

Materials and Methods
Virtual DST workshops were completed by 40 English-speaking people with endometriosis of diverse backgrounds and experiences across Canada. Throughout the 7-week workshop, data was collected through four sources: 1) researchers' workshop observations, 2) participants' psychosocial pre- and post-workshop questionnaires, 3) participants' reflective journals, and 4) one-on-one semi-structured interviews following completion of the workshop. Using a patient- oriented research approach, we completed quantitative data distributions and thematic qualitative data analysis.

Results
Participants reflected on the therapeutic effect of the workshop, including how it facilitated emotional processing and social connection with others. Feeling validated, empowered, and supported was a common sentiment among participants of different ages, ethnicities, genders, sexual orientations, and endometriosis stages. Participants shared how impactful the experience of being heard and connected to a shared community was, especially if they did not have other people with endometriosis in their lives. Joining weekly group meetings, sharing and receiving feedback, and working on the stories outside of the sessions facilitated deep levels of connectedness both within the groups and outside (with family members, partners, and friends), respectively. Themes of endometriosis-associated identity erosion, intergenerational impact, and interactions with healthcare commonly surfaced in storytellers' narratives.

Conclusion
All participants reflected on the workshop's therapeutic potential, commonly attributing it to the validation and connectedness they experienced throughout the sessions. Preliminary findings on the benefits of the DST workshops may inform future clinical practices and randomized clinical trials for those experiencing endometriosis.

Key words
Digital storytelling, endometriosis, psychosocial intervention

SEMINAR SESSION 4: APPROACHING SURGERY AND SURGICAL APPROACHES

LONG-TERM OUTCOMES OF SURGICAL EXCISION OF DEEP ENDOMETRIOSIS OF THE RECTUM. TEN-YEAR- FOLLOW-UP OF A RANDOMIZED TRIAL

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Country where research was undertaken:
France

Introduction/Background
Data concerning long term outcomes of excision of deep endometriosis infiltrating the rectum (DIER) are scarce in terms of recurrences, rectal function or fertility. To provide new information in this field, we report 10-year-outcomes of patients enrolled in ENDORE randomized controlled trial (ERCT) (NCT01291576).

Materials and Methods
Patients with symptomatic DIER with more than 2 cm area and surgically managed at Rouen University Hospital were enrolled in ERCT from March 2011 to October 2013. They were randomized between conservative vs. radical surgery (respectively CS and RS). Main endpoint was a combined variable assessing the digestive and urinary function, and secondary endpoints were fertility outcomes, recurrences rate, and scores of quality of life, gastrointestinal and urinary function. Follow-up was 10 years.

Results
There were enrolled 27 women in the CS arm (15 disc excisions, 10 shavings and 2 conversions to rectal resections) and 28 in the RS arm receiving rectal resections. One patient asked to be deleted from the study after 2 year, 1 changed the gender, and 3 were lost of follow up after respectively 6, 8 and 9 years (9.1% of loss of follow up at 10 years).

Rectal recurrences occurred in 3 women (5.5%). Postoperative pregnancy rate was 85.3%, with 64.4% of natural conceptions. No significant differences of endpoints were observed between CS and RS. The improvement of gastrointestinal and urinary scores has been constant for 10 years. Reoperation rate for pain relapse was 10.9% and routinely included hysterectomy for adenomyosis.

Conclusion
Both CS and RS are efficient in the management of DIER, and the improvement is constant during the 10 years after the surgery. Pregnancy rate is excellent, with high rate of natural conceptions. Rectal recurrences are rare. Surgery may be reasonably proposed with good outcomes in the long run.

Key words
Rectal endometriosis, surgery, randomized trial.

EXPLORING THE TRAINING NEEDS OF HEALTHCARE PROFESSIONALS LEARNING TO PERFORM TRANSVAGINAL ULTRASOUND FOR ENDOMETRIOSIS: CAN ARTIFICIAL INTELLIGENCE HELP?

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Country where research was undertaken:
Australia

Introduction/Background
Competency in undertaking transvaginal ultrasound (TVUS) to detect endometriosis (eTVUS) comes with a significant learning curve, however, artificial intelligence (AI) holds potential to teach eTVUS skills. We aimed to investigate current training being undertaken for eTVUS, identify barriers/ enablers to performing eTVUS, and understand how AI tools could assist learning.

Materials and Methods
An online cross-sectional survey was disseminated globally to health care professionals who perform TVUS. A combination of multiple choice and free-text questions were asked regarding demographics information, experience performing eTVUS, training undertaken for eTVUS, experience with AI in ultrasound and how end-users

believed AI could help with learning and performing eTVUS. Statistical and thematic analyses were performed.

Results
A total of 407 response, from 33 countries were included. *Online self-directed learning* (53.3%) was the most undertaken training method. *Working with a skilled mentor* was rated as the most helpful training method (mean 4.49 [range, 3-5]) and the most desired, yet most difficult to access training method reported (42.3%). *Inadequate training/ education in the eTVUS technique* (37.1%) and *lack of confidence in recognising the appearance of endometriosis on ultrasound* (37.1%) were the most common barriers. Overwhelmingly, training/ education in the eTVUS technique was the strongest facilitator (58.7%).

If available, 64.3% stated they would use an AI tool to assist with learning eTVUS. Overwhelmingly, respondents wanted a teaching tool to help recognize disease (68.3%), which would ideally be built into an ultrasound machine (56.6%).

Conclusion
Most training and education undertaken by healthcare professional to perform eTVUS is self- directed online learning, with access to skilled mentors challenging, presenting a significant barrier to eTVUS implementation. Unsurprisingly, eTVUS education can facilitate successful implementation into clinical practice. Most health professionals would use AI tools for learning if available.

Key words
Endometriosis, transvaginal ultrasound, education

EXTERNAL VALIDATION STUDY OF PRE-OPERATIVE ULTRASOUND BASED AAGL STAGING SYSTEM (AAGL-US) IN PREDICTION OF AAGL SURGICAL STAGE AND COMPLEXITY

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Country where research was undertaken:
Australia

Introduction/Background
This study aims to externally validate the AAGL-US in prediction of AAGL laparoscopic stage (AAGL-LPS) and in prediction of surgical complexity level following previously published data in 2022.

Materials and Methods
This retrospective multi-centre study conducted from August 2018-November 2019 recruited patients with possible endometriosis with data presented previously in separate analysis. Patients underwent a deep endometriosis ultrasound conducted in accordance with the IDEA consensus prior to surgical assessment and management. AAGL-US stage (1-4) was documented retrospectively while AAGL-LPS (1-4) and surgical complexity (A-D) was assessed based on findings at time of surgery.

Results
236 patients were included for analysis. Weighted kappa (WK) for AAGL-US in predicting AAGL-LPS was 0.52. WK score of 0.38 for AAGL-US predicting surgical complexity A-D. Intraclass correlation (ICC) has 'good' reliability for right and left ovaries, bladder and rectum, ICC scores 0.83, 0.84, 0.80 and 0.76. Pouch of Douglas obliteration demonstrated moderate reliability 0.53. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for stage 1 predicting level A was 87%, 81%, 47% and 97%, stage 2 predicting B was 32%, 88 %, 64% and 65%, stage 3 predicting C was 22%, 85%, 26% and 81%, stage 4 predicting D was 61%, 75%, 43% and 86%. Diagnostic accuracy of AAGL-US predicting endometriosis presence gave sensitivity 0.56, specificity 0.60, PPV 0.97, NPV 0.23.

Conclusion
There is moderate agreement between AAGL-US and AALG-SS with weighted kappa 0.52 lower than the previously reported 0.76. While there was fair agreement (weighted kappa 0.38) between AAGL-US and surgical complexity. ICC was similar in assessment of ovaries, bladder and rectal disease to previously reported data.

Key words
Endometriosis, surgery, ultrasound

GASTRONITESTINAL FUNCTION AFTER COLORECTAL RESECTION FOR THE TREATMENT OF BOWEL ENDOMETRIOSIS

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Countries where research was undertaken:
Hungary, Austria

Introduction/Background
Patients who have undergone colorectal surgery for symptomatic deep endometriosis (DE) may still encounter persistent or worsening digestive complaints. The aim of the present work was to analyze gastrointestinal function (GI) outcomes after radical and conservative colorectal surgery to further elucidate the effect of surgery on postoperative bowel function.

Materials and Methods
PubMed, EMBASE, Web of Science, Clinical Trials.gov and the Cochrane Database databases were searched through January 1, 2010 until April 1, 2024. The quality of included studies was assessed by the Downs and Black quality checklist. Studies including patients with colorectal endometriosis who either underwent segmental resection (SR) or conservative approaches and reported data on bowel function were included.

Results
From the initial pool of 55 studies, 14 reported patient reported outcome measures (PROMs) eligible to be pooled in the meta-analysis. Patients in the conservative surgery group reported higher postoperative GIQLI when compared to SR (p=0.01). When comparing changes between pre- and postsurgical PROMs within the respective groups, none of the intervention groups showed significant changes between pre and postsurgical GIQLI, KESS and Wexner scores (p=0.28, p= 0.94 and p=0.78, respectively).

Conclusion
SR appears to be associated with increased post-operative constipation rates, increased number of daily stool and lower GIQLI scores when compared to conservative surgery. However, when presurgical PROMs are taken into account and compared to postsurgical values, SR and conservative surgery yield similar GI function outcomes.

Key words
Deep endometriosis (DE), gastrointestinal (GI) function, segmental resection (SR), conservative surgery

LAPAROSCOPIC SCLEROTHERAPY FOR ENDOMETRIOMA DURING SURGERY FOR ENDOMETRIOSIS: OUTCOMES IN 134 CONSECUTIVE PATIENTS

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Country where research was undertaken:
France

Introduction/Background
Ethanol sclerotherapy has been proposed as an alternative to cystectomy for endometrioma to preserve the ovarian function. The objective of this study was to evaluate postoperative fertility outcomes and recurrence rates in patients undergoing laparoscopic ethanol sclerotherapy for endometrioma with concurrent resection of deep endometriosis lesions.

Materials and Methods
We conducted a retrospective study of 134 patients who underwent laparoscopic surgical resection of deep endometriosis lesions and 96% ethanol sclerotherapy, from October 2019 to September 2023. In our center, sclerotherapy was used in patients managed for endometriosis surgery with an endometrioma over 40 mm, and presenting fertility issues. After surgery, postoperative fertility outcomes, recurrences of endometriomas, changes in anti mullerian hormone (AMH) levels, and postoperative complications were collected.

Results
Mean patient age was 31.8 ± 4.6 years, with 29% experiencing infertility. Preoperative AMH levels averaged 2.96 ± 2.02 ng/mL. Postoperatively, AMH levels decreased significantly (mean difference: 1.1 ng/mL, p = 10^-8). Severe postoperative complications occurred in 4.5% of patients, none related to ethanol sclerotherapy. Of the 78 patients wishing to conceive, 45 (57%) conceived, with a mean time to pregnancy of 13 ± 9 months; 42% of these pregnancies were spontaneous. Cumulative pregnancy rate was 55.5% at 24 months and 78.8% at 36 months. Preoperative AMH levels and history of abdominal surgery were significant predictors of pregnancy

(HR=1.35, p=0.005 and HR=0.32, p=0.01, respectively). Recurrence of endometriomas was observed in 16.5% of patients, with a median follow-up of 23 months.

Conclusion
Laparoscopic ethanol sclerotherapy during resection surgery for deep endometriosis is a safe procedure, with satisfactory pregnancy rates and recurrence rates comparable to other ablative techniques.

Key words
Ethanol sclerotherapy, endometrioma, laparoscopic surgery

INVESTIGATING IMMEDIATE PAIN AND POST-SURGICAL RECOVERY FOLLOWING LAPAROSCOPIC SURGERY FOR DIAGNOSIS OR TREATMENT OF ENDOMETRIOSIS: A PROSPECTIVE COHORT STUDY

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Country where research was undertaken:
Australia

Introduction/Background
Long term patient related outcomes following surgery for endometriosis are extensively documented, however there are no published data assessing immediate postoperative recovery following surgery for endometriosis. The aim is to report immediate recovery following laparoscopic surgery for endometriosis and to provide an evidence-based summary for women undergoing future surgery.

Materials and Methods
Participants were asked to rate, using a visual analogue scale (VAS), their dysmenorrhoea, non- menstrual pelvic pain, dyspareunia, dyschezia and backpain. Validated tools assessing quality- of-life (QoL), bladder and bowel function, using Endometriosis Health Profile (EHP-30), EQ- 5D-5L, Colorectal Functional Outcome Questionnaire, International Consultation on Incontinence Questionnaire Female Lower Urinary Tract Symptoms Modules and International Consultation on Incontinence Questionnaire Lower Urinary Tract Symptoms Quality of Life Module, respectively, were collected at baseline, one-, two- and three-months postoperatively.

Results
Preliminary analyses from 209 participants (mean age 32.9-years +/- 6.2), reported pelvic pain as the most frequently reported primary symptom. Paired samples t-test was used to assess improvements in QoL, determined by EHP-30, in relation to pain and function compared to baseline and demonstrated benefit at one, two and three months postoperatively (62.3, 44.8, 33.4 and 31.7 respectively). Additionally, progressive improvements were demonstrated at one (62.3 vs 44.8, $p<0.05$), two (44.8 vs 33.4, $p<0.05$) and three (33.4 vs 31.7, $p=0.02$) months, respectively. Improvements in general health assessed by the EQ-5D-5L VAS are also demonstrated at one (62.8 vs 69.0, $p=0.01$) and two (69.0 vs 74.8, $p=0.01$) months with no further improvements observed at three-months following surgery (74.8 vs 74.4, $p=0.48$).

Conclusion
Preliminary analyses confirm progressive improvements in QoL in the immediate recovery period following surgery for endometriosis, with the greatest improvement demonstrated in the first two months after surgery. Further analyses of patient related outcome measures are underway and will facilitate accurate preoperative patient counselling and informed surgical consent.

Key words
Endometriosis surgery, quality of life, postoperative

MEDICAL VERSUS SURGICAL MANAGEMENT OF RECTAL ENDOMETRIOSIS AND DIGESTIVE FUNCTIONAL OUTCOMES: A RANDOMIZED CONTROLLED TRIAL (MESURE)

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Country where research was undertaken:
France

Introduction/Background
Deep endometriosis infiltrating the rectum (DEIR) may be managed by medical treatment or surgical excision. Comparative data concerning functional outcomes of these wo approaches are scarce in terms of improvement of rectal function. To provide new information in this field, we report the results of a randomized controlled trial (RCT) comparing the two approaches (NCT01973816).

Materials and Methods
Patients with symptomatic DIER and no pregnancy wish were randomly allocated to either surgical excision (followed by 24 months of progestin to prevent recurrences, SU) or medical treatment (3 months of GnRHa followed by 18 months of progestin intake; ME). Outcomes were assessed at 24 months in intention to treat.

Results
There were enrolled 36 women in the SU arm (receiving 19 shavings, 7 disc excisions and 10 rectal resections) and 38 women in the ME arm. In the ME arm, 17 patients (44.7%) ultimately received a surgery during the follow up because the lack of hormonal treatment's efficiency. Hysterectomy rates was 41.7% vs. 31.6%. Reoperation rate was 8.3% vs 2.9%.

In the two arms, severe adverse events rates related to surgical treatment were 11% vs. 18.4%, and those that could be related to hormonal treatment were 13.9% vs 7.9%. Intracranial meningiomas occurred in 8.3% vs. 5.3% with consecutive arrest of hormonal treatment.

Improvement of digestive function, pelvic pain and quality of life was comparable between the two arms.

Conclusion
Surgical excision and hormonal treatment may be proposed in symptomatic DIER. When medical treatment is recommended, half of patients can receive surgery within 2 years for unsatisfactory improvement of complaints. Patients must be informed about the risk of adverse events, among which meningioma occurrence requires the arrest of hormonal treatment.

Key words
Rectal endometriosis, progestins, randomized trial

FREE COMMUNICATION SESSION 2

SESSION 2A: POTENTIAL BREAKTHROUGH TREATMENT OPTIONS

LIPOCALIN-TYPE PROSTAGLANDIN D SYNTHASE EXPRESSION DECREASES IN ADENOMYOSIS: A BREAKTHROUGH IN DIAGNOSIS AND TREATMENT?

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Country where research was undertaken:
France

Introduction/Background
Adenomyosis is a common benign gynecological condition whose pathophysiology is not yet fully understood. The involvement of the Prostaglandin D2 pathway has been studied in several pathologies, but never in human adenomyosis. Understanding the interaction between Prostaglandin D2 and adenomyosis could improve management strategies for affected women.

Materials and Methods
This was a cohort study on human uterus samples. We analyzed 25 anonymous cases of uterine specimens, 15 with adenomyosis and 10 controls. We quantified the expression of CD45, a marker of inflammation, and of Prostaglandin D synthases, Lipocalin-Type

Prostaglandin D Synthase (L-PGDS) and Hematopoietic-Type Prostaglandin D Synthase (H-PGDS) in seven uterine compartments by immunohistochemical analysis. QuPath software was used to annotate and define regions of interest (ROIs) and automatically quantify intensity of biomarker staining.

Results
We found a significant decrease in Lipocalin-Type Prostaglandin D Synthase expression in the uteri of patients with adenomyosis compared with controls (p=0.015). This difference was observed in almost all uterine compartments, with the greatest significant difference in the endometrium and external myometrium. No significant difference was found in Lipocalin-Type Prostaglandin D Synthase expression according to the severity of involvement (p=0.63). No difference was found in the expression of Hematopoietic-Type Prostaglandin D Synthase in adenomyosis compared with controls (p=0.28). Adenomyosis lesions (ectopic glands) were significantly more infiltrated by CD45-positive inflammatory cells than eutopic glands in controls (p=0.03).

Conclusion
We found a significant decrease in Lipocalin-Type Prostaglandin D Synthase expression in the uteri of adenomyosis patients. These data confirm the involvement of the prostaglandin D2 pathway in adenomyosis. This study suggests that Lipocalin-Type Prostaglandin D Synthase could be a new biomarker for early diagnosis and a potential therapeutic target.

Key words
Adenomyosis, Lipocalin Type-Prostaglandin D Synthase, Prostaglandin D2

INTERLEUKIN-33 DRIVEN GROUP 2 INNATE LYMPHOID CELL - REGULATORY T CELL AXIS IN ENDOMETRIOSIS PATHOPHYSIOLOGY

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Country where research was undertaken:
Canada

Introduction/Background
The alarmin interleukin-33 (IL-33) contributes to endometriosis lesion alterations (fibrosis, angiogenesis, immune infiltration). These changes are largely driven by group 2 innate lymphoid cells (ILC2s), which orchestrate type 2 immune response. Regulatory T-cells (Treg) can temper this response, yet how both cell types shape the endometriotic lesion microenvironment remains unknown.

Materials and Methods
IL-33 (1ug) was administered every other day for one week via intraperitoneal injection to syngeneic mice (C57Bl6) with or without endometriosis induction (uterine biopsy engraftment). Endpoints include cytokine analysis of the peritoneal microenvironment, immunoprofiling of endometriosis associated tissues (spleen, peritoneal fluid (PF), uterus, lesion) by flow cytometry, and bulk RNA sequencing of fluorescence-activated cell sorted ILC2s and Tregs from the PF and lesion. Cell types were defined by canonical markers: Tregs (CD4+CD25+FOXP3+) and ILC2s (Lin-CD90+GATA3+).

Results
Preliminary experiments demonstrate that IL-33 drives increases in both ILC2 and Treg cell populations in the localized peritoneal microenvironment. Expression of the IL-33 receptor ST2, compliments these findings, whereby ST2 expression on Tregs and ILC2s was significantly higher in endometriosis mice treated with IL-33. These findings highlight the increased receptivity of both ILC2s and Tregs to IL-33 in endometriosis and suggest their involvement in mediating the associated type 2 inflammation, as confirmed through detection of type 2 cytokines (IL-5, IL-9, IL-13) in the peritoneal microenvironment. Through bulk RNA sequencing (in progress) we look to identify potential ligands and receptors enriched in ILC2s and Tregs to provide insight into mechanisms of cell interaction and whether they are tissue specific.

Conclusion
Our findings unravel the interplay between ILC2s and Tregs and their influence on the endometriosis lesion microenvironment, suggesting a potential role for Tregs in maintaining control over the ILC2 mediated type 2 immune response. These findings provide insight as to how dysregulation of the ILC2-Treg axis could exacerbate endometriosis pathophysiology.

Key words
Group 2 innate lymphoid cells, regulatory T-cells, interleukin-33

INVESTIGATING THE IMPACT OF OVARIAN HORMONES AND ENDOMETRIOSIS ON THE ENDOCANNABINOID SYSTEM IN THE ENDOMETRIAL CELLS USING ENDOMETRIAL ORGANOIDS

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Country where research was undertaken:
Australia

Introduction/Background
Endocannabinoids, such as anandamide, play a significant role in endometrial biology. Endocannabinoid activity is regulated by the endocannabinoid system (ECS), a complex interaction of proteins regulating synthesis, binding, transport and degradation. Their expression is predominately epithelial and modulated across the menstrual cycle, and potentially impacted in endometriosis.

Materials and Methods
To determine the impact of menstrual hormone on epithelial ECS expression, endometrial organoids (n=6) from women with and without endometriosis were generated. Organoids were treated with oestradiol for 5 days followed by oestradiol, Medroxyprogesterone acetate and cAMP for 7 days to mimic the menstrual cycle. Both RNA and protein was extracted at day 5 (*proliferative)*, 7 (*early secretory*) and 12 (*late secretory*), and RNA sequencing and Western Blotting on selected ECS proteins was performed.

Results
70 ECS genes were extracted from the RNA-seq data for analysis. 8 showed no discernible expression, and analysis of the remaining 62 genes revealed a coordinated change in gene expression across the simulated menstrual cycle. Genes responsible for the synthesis of anandamide, N-acyl phosphatidylethanolamine-specific phospholipase D (*NAPEPLD*) were downregulated, whereas genes associated with breakdown fatty-acid amide hydrolase 1 (FAAH) and N-acylethanolamine acid amidase (NAAA) were both upregulated. Analysis of protein levels confirmed the upregulation of FAAH and NAAA after exposure to progesterone with a subsequent decrease in NAAA after long exposure, but a further increase in FAAH. NAPEPLD protein expression was also increased after progesterone exposure and remained high after prolonged exposure. A comparison between endometriosis cases and controls did not reveal any significant differences.

Conclusion
There was extensive expression of the ECS in epithelial organoids modulated by steroid hormones, mirroring changes in the menstrual cycle. Gene expression highlights a tightly regulated anandamide control, and the higher expression of NAPEPLD protein, contrary to its gene expression, suggests its prolonged stability in maintaining control over anandamide concentrations.

Key words
Endometrial organoids, endocannabinoids, anandamide

DYSREGULATED ENDOCANNABINOID FAMILY MEMBERS IN THE PATHOPHYSIOLOGY OF ENDOMETRIOSIS AND THERAPEUTIC TARGETING

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Country where research was undertaken:
Canada

Introduction/Background
The endocannabinoid system (ECS) influences cardinal features of endometriosis (EM) including pain, vascularization, lesion proliferation but the exact mechanisms are unknown. Using EM patient samples and multiple mouse models of EM (cannabinoid receptor (CNR)1, CNR2 knock out (ko)) and wild type (WT) controls, we provide comprehensive evidence into the dysregulation of endocannabinoids and their involvement in EM pathophysiology.

Materials and Methods
Mass spectrometry analysis of endocannabinoids, gene expression (targeted Q-PCR array) and immunohistochemistry analysis of tissue microarray were conducted on endometriosis patients and control samples. Mouse models of endometriosis include CNR1 ko, CNR2 ko, and WT mice. Imaging mass cytometry and bulk RNA

sequencing were done for in-depth analysis of mouse endometriosis lesions in CNR1 ko, CNR2 ko and WT mice. Flow cytometry was performed on peritoneal fluid and spleens to capture immune cell alterations.

Results
Amongst the ECS members investigated (2AG, OEA, AEA and PEA), palmitoylethanolamide (PEA) levels were significantly higher in EM lesions compared to control endometrial samples. Genes involved in the endocannabinoid signaling pathways were differentially expressed in the EM lesions compared to matched eutopic patient samples and healthy endometrial samples. Immunohistochemistry of tissue microarray revealed significantly lower CNR2 receptor expression in EM lesions compared to controls. In WT mouse model of EM, PEA levels were significantly elevated in plasma and ectopic lesions from EM mice compared to sham controls. Imaging mass cytometry analysis and bulk-RNA sequencing revealed novel immune related and T cell specific changes in EM lesion microenvironment in CNR1 ko, CNR2 ko compared to WT mice.

Conclusion
Our data provides solid evidence in dysregulation of endocannabinoid system in EM patients and validation in mouse models of EM. These findings will advance the knowledge on the role of endocannabinoids in EM and their potential implications as specific therapeutic targets

Key words
Endocannabinoids, endometriosis, immune-dysfunction

INHIBITION OF TRPM3 BY PRIMIDONE PROVIDES A POTENTIAL THERAPEUTIC METHOD FOR ADENOMYOSIS MANAGEMENT

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Country where research was undertaken:
China

Introduction/Background
Among all complaints from women with adenomyosis, dysmenorrhea and other types of pain are at the top of the list and are the most debilitating. Our study is to reveal the expression profile of transient receptor potential channels (TRPs) in adenomyosis patients and evaluate the effects of TRPM3 inhibitor, primidone on tamoxifen-induced adenomyosis mice.

Materials and Methods
Eutopic endometrium from adenomyosis patients (n=20) was collected and subjected to mRNA analysis of TRPs. TRPA1, TRPV1 and TRPM3 in another fifty adenomyosis patients and tamoxifen-induced adenomyosis mice (n=6) were examined by immunohistochemistry. From 10 weeks after birth, primidone (2mg/kg/d) were given separately to adenomyotic mice by intraperitoneal injection for 3 weeks. The hotplate test was conducted once a week, and then uterine samples were harvested for HE staining and RNA-seq at 13 weeks.

Results
The mRNA expression of 15 TRPs was significantly increased in the proliferative phase of the adenomyotic endometrium. TRPV1, TRPM3 or TRPA1 staining levels were positively correlated with dysmenorrhea severity, menstrual volume and uterine size. In tamoxifen- induced adenomyosis mice, primidone had a significant effect on both the depth of myometrial infiltration and analgesia. Forty-seven differentially expressed genes (DEGs) were identified after primidone treatment, and bioinformatics analysis predicted that they were enriched in the cell cycle and cell division. Further verification was conducted on the expression of CHIL1, COL9A2, PSMC3IP, NEIL3, and SPC24, which play an important role in multiple pathological mechanisms, including inflammation, tissue remodeling, injury, DNA repair and cell mitosis.

Conclusion
The expression profile of TRPs varies significantly in adenomyosis patients, and the TRPM3 inhibitor primidone may provide a potential therapeutic method for adenomyosis management.

Key words
TRPs, primidone, pelvic pain

PRE-CLINICAL VALIDATION OF A NOVEL IMMUNOTHERAPEUTIC TREATMENT FOR ENDOMETRIOSIS AND ASSOCIATED CHRONIC PAIN

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Country where research was undertaken:
Australia

Introduction/Background
Endometriosis growth and associated chronic pain (CP) are highly influenced by proinflammatory and neuroangiogenic factors. Regulating both neuroangiogenesis[1] and immune cell activity[2] is netrin-1. Here, we investigate whether treatment with NP137, a clinically approved monoclonal antibody targeting netrin-1, can reduce endometriosis growth and CP in a mouse model of endometriosis.

Materials and Methods
Endometriosis (Endo) was surgically induced in ovariectomized/estradiol treated mice, together with sham counterparts, as previously described[3]. Between 4-9 weeks of development, mice were treated with either NP137 or control antibody NP001 (10mg/kg intraperitoneally). Endometriosis growth and CP was then assessed by quantifying: i) lesion size, ii) vaginal and colonic pain (visceromotor response to distension), iii) thermal and mechanical sensitivity (hot plate and von Frey hair), iv) bladder function (voiding patterns), and v) overall well-being (nesting).

Results
NP137 treatment significantly reduced the growth of lesions developed in Endo mice (32.2% reduction in size compared to lesions in Endo mice treated with NP001). Moreover, NP137 reduced endometriosis-induced vaginal and colonic pain sensitivity to low (<40mmHg) distension pressures (56% and 78.5% reduction, respectively), as well as sensitivity to mechanical (35.4% reduction) and thermal stimuli (17.5% reduction). NP137 treatment also reduced endometriosis-altered spontaneous behaviors, including improved bladder function (26.9% normalization in voiding patterns, specifically small size urine spots) and an increase in overall wellbeing (13.4% improvement of nest building capacity). Importantly, all evoked and spontaneous pain-like responses measured in Endo mice treated with NP137 were normalized to levels comparable to those measured in Sham mice treated with NP001.

Conclusion
Treatment with NP137 significantly reduced both endometriosis growth, and the enhanced widespread pain-like responses developed by mice with endometriosis. This study strongly supports NP137 as a feasible, non-invasive therapeutic strategy and an effective treatment for endometriosis growth and associated CP. Ongoing studies aim to elucidate mechanisms underlying our findings.

Key words
Monoclonal antibody, endometriosis growth, chronic pain

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SESSION 2B: INNOVATIVE APPROACHES TO SURGICAL MANAGEMENT

COMPARATIVE EFFECT OF DIFFERENT SURGICAL TREATMENTS FOR OVARIAN ENDOMETRIOMA ON AMH: A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS

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Country where research was undertaken:
Switzerland

Introduction/Background
Ovarian endometriomas are common in women of reproductive age. If surgical management is indicated, different surgical techniques are possible. We aimed to compare all relevant surgical techniques for endometriomas in terms of their impact on ovarian reserves.

Materials and Methods
We conducted a systematic review and network meta-analysis (NMA), searching PubMed, Embase and Cochrane Register of Trials for randomized controlled trials. We assessed the quality of included studies with the Cochrane risk of bias tool 2 and performed a network meta- analysis, comparing the head-to-head effect of different surgical strategies, calculating mean differences (MD) and 95% confidence intervals (CI).

Results
21 studies with 1519 participants, comparing eight different surgical techniques (cystectomy with ovarian suturing, cystectomy with hemostatic sealants, cystectomy with tranexamic acid, cystectomy alone, drainage with hemostatic sealants, drainage alone, laser ablation and transvaginal sclerotherapy) were included in the systematic review and 17 studies in the NMA. Regarding Anti-Müllerian hormone (AMH) at 3-6 months after surgery, drainage with hemostatic sealants (MD: 0.96; 95%CI [0.60-1.33]; high level of certainty), cystectomy with ovarian suturing (0.69 [0.39-0.98]; moderate certainty) and cystectomy with hemostatic sealants (0.37; [0.12-0.61]; low certainty) resulted in higher values of AMH compared with cystectomy alone. Regarding antral follicle count (AFC) at 3-6 months after surgery, laser ablation showed higher values of AFC (MD: 2.30; 95% CI: 0.20-4.40) compared with cystectomy alone at 3-6 months after surgery, followed by cystectomy with ovarian suturing (MD: 1.88 95% CI: 0.98-2.79). The overall risk of bias of included studies was low.

Conclusions
Considering the estimated effect sizes and certainty of evidence for both AMH and AFC, the interventions with the less negative impact on ovarian reserves were cystectomy with ovarian suturing and drainage with hemostatic sealants.

Key words
Endometrioma, ovarian reserve

ENDOMETRIOSIS APPEARANCE WITH HORMONAL CONTRACEPTIVES AT LAPAROSCOPY: A PROSPECTIVE COHORT STUDY (ENDO-COLOR TRIAL)

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Country where research was undertaken:
Australia

Introduction/Background
Hormonal medications are commonly used in the management of endometriosis but their impact on the appearance of endometriotic lesions is not known. We hypothesised that haemosiderin-laden macrophages contribute to a black appearance of lesions and that hormonal medication users may be more likely to have white or red lesions.

Materials and Methods
The ENDO-COLOR study is a prospective cohort study that aims to assess if hormonal medication use influences the appearance of endometriosis lesions at laparoscopy. The study compares hormonal medication users (HUs) to non-users (NUs), with a primary outcome of frequency of black coloured lesions at laparoscopy. Secondary outcomes include frequency of lesion colour, endometriosis stage, pelvic pain scores, EHP-30 quality of life scores, histological diagnosis of endometriosis and frequency of haemosiderin-laden macrophages.

Women over 18 years of age undergoing laparoscopy for diagnosis and a primary excision of suspected endometriosis were recruited into the study.

Results
Data for the primary outcome was available for 66 participants, 42 HUs and 24 NUs. There were 6 (14.3 %) participants with black coloured lesions in the HU group and 4 (16.7 %) in the NU group ($\chi^2 = 0.021$, $p = 0.88$). There was no difference in overall lesion colour distribution ($\chi^2 = 1.17$, $p = 0.76$). The

majority of lesions were mixed (NU group 50.0%, HU group 57.1%) or white in both groups (NU group 29.2%, HU group 19.0%).

Conclusion
These results suggest that hormonal contraceptive use does not significantly alter the colour of endometriotic lesions at laparoscopy.

Key words
Endometriosis, laparoscopy, hormonal medications

SHOULD WE SCLEROTIZE ENDOMETRIOMAS WITH ETHANOL?— ANSWERS FROM THE LAB

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Country where research was undertaken:
The Netherlands

Introduction/Background
Evidence is piling up on the effectiveness of sclerotherapy with ethanol for the treatment of ovarian endometrioma, but it is still unknown whether ethanol can pass through the cyst wall and reach toxic concentrations in the ovary, thus potentially impairing fertility. Experimental or histopathological data are basically non-existent.

Materials and Methods
Using donated patient material, we measured the permeability of the endometrioma wall to ethanol and its diffusion rate in the ovary. These results, combined with Hall's solution of Fick's laws of diffusion (Hall 1961), allowed us to calculate the maximum ethanol concentration behind the endometrioma wall after sclerotherapy with 96% ethanol. We modelled relevant exposure conditions in ex vivo ovarian cortex and medulla samples, and assessed tissue viability through histomorphological analysis and glucose uptake assays.

Results
Ethanol permeates the endometrioma wall and diffuses in the ovary with a concentration-dependent diffusion coefficient in the range of 1.0-7.5 x 10^{-6} cm^2 s^{-1}. Permeation is initially slow but increases rapidly within the first hour. Sclerotization for longer than 15-30 minutes with 96% ethanol results in ethanol concentrations > 1% in a region up to 8 mm deep surrounding the cyst. Ex vivo ovarian cortex and medulla samples exposed to these concentrations showed reduced glucose uptake, extensive decellularization, and altered morphology. Distinct cell populations were differentially affected by exposure to 1% and 5% ethanol, while 10% ethanol completely abolished glucose uptake in all samples. At lower concentrations, cell and tissue morphology were preserved and glucose uptake did not significantly differ from controls.

Conclusion
Ethanol as used for sclerotherapy permeates the endometrioma wall, reaching cytotoxic concentrations in a region up to 8 mm deep surrounding the cyst. Regions farther from the cyst are exposed to lower concentrations and likely remain viable. We are testing this by assessing in vitro growth potential of exposed follicles.

Key words
Sclerotherapy, ethanol, endometrioma

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THE ROLE OF COLONOSCOPY IN PRE-SURGICAL STAGING OF COLORECTAL ENDOMETRIOSIS

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Country where research was undertaken:
Australia

Introduction/Background
The role of colonoscopy in evaluating suspected colorectal endometriosis has historically been limited. This brings to question its effectiveness as a preoperative investigation [1]. Colonoscopy may not alter the surgical approach but can delay treatment. This study assesses the diagnostic role of colonoscopy for suspected colorectal endometriosis.

Materials and Methods
This retrospective case series was conducted at a single tertiary unit over a five-year period (June 1, 2019 to May 31, 2024). The inclusion criteria consisted of women with a clinical suspicion of colorectal endometriosis who underwent both colonoscopy and laparoscopic surgery. Data was sourced from integrated electronic medical records (ieMR), including colonoscopy reports and histopathology results. Histological findings from laparoscopic biopsy served as the reference standard. Diagnostic performance was assessed using sensitivity, specificity, and diagnostic odds ratio.

Results
A total of 46 consecutive women, aged 21-50 years, with suspected colorectal endometriosis were included in the analysis. Of these, 39 (85%) were confirmed to have colorectal endometriosis based on laparoscopic findings. Endometriosis was identified in 20 serosal lesions (51%), 1 subserosal lesion (3%), 10 muscularis lesions (26%), 4 submucosal lesions (10%), and 4 involving the mucosal layer (10%).

Colonoscopy only detected endometriosis in 8 of the 39 women (20.5%). 31 of 39 women were missed. Sensitivity was 20.51%, specificity 85.71%, and the diagnostic odds ratio was 1.55. Colonoscopy identified 3 of 4 mucosal cases, 1 of 4 submucosal, 1 of 10 muscularis. Colonoscopy failed to detect any subserosal or serosal involvement.

Conclusion
Colonoscopy has poor diagnostic performance in the setting of suspected colorectal endometriosis. It plays a limited role in select cases or to rule out alternate bowel pathology. Optimizing preoperative evaluation with imaging modalities such as MRI may help avoid unnecessary interventions, improve efficiency, reduce costs, and minimize potential colonoscopy-related complications.

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ROBOTIC APPROACH ON A RARE LOCALIZATION OF DEEP ENDOMETRIOSIS INVOLVING THE FEMORAL NERVE BEHIND THE PSOAS MUSCLE

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Country where research was undertaken:
France

Objective
The movie presents the robotic approach in rare localizations of deep endometriosis, such as that involving the femoral nerve.

Design
Video describing a surgical technique.

Material and Technique
The nodule was responsible for the palsy of the right quadriceps, pectineus and sartorius muscles, as well as for the abolition of the patellar tendon reflex in a 47-year-old woman. We consider that the robotic assistance may be particularly useful in achieving a minimally invasive surgery in such a hidden space. The patient was placed in left lateral decubitus, and the trocars were inserted in the right upper and middle quadrants. We used the DaVinci X device with 4 arms. The angle of the view is roughly orthogonal on the right psoas muscle. Contact is taken with the lateral limit of the right psoas muscle and peritoneum in incised longitudinally until the inferior limit of the right kidney. Hence the grasper is employed to push up the psoas muscle, with the Maryland bipolar and the monopolar scissors are used for a prudent and progressive dissection behind the muscle, until the lateral limit of the nodule is identified. The dissection reveals a first nerve involved by the disease, the lateral cutaneous femoral nerve, which provides sensory innervation of the skin of the right lateral thigh. The setting of monopolar current is reduced, to avoid uterine contractions and nerve stimulations. The nodule is progressively excised by small fragments. Behind the psoas muscle and medially from the lateral femoral cutaneous nerve, we identify the femoral nerve of larger diameter. In this patient, the epinerve of the femoral nerve appears interrupted, with an infiltration of the disease inside the nerve and destruction of several nervous fibers. The dissection is pursued medially from the femoral

nerve, with the identification of the right obturator nerve. The medial limit of the dissection plane behind the psoas muscle may dangerously come on contact with the lateral bord of the right common iliac vein, conversely injuries of the right ureter are very unlikely.

Conclusions
In our opinion this approach may be suitable for rare lesions located in this area, such as endometriosis nodules or lumbar nerves schwannomas. We believe that in the future the excision of such deep endometriosis nodules could benefit from the assistance of the augmented reality, to achieve a more precise complete excision of the disease.

Key words
Robotic surgery, deep endometriosis, femoral nerve, lumbar nerve, psoas muscle

COMPARATIVE EFFECTIVENESS BETWEEN HYSTEROSCOPIC EXCISION WITH AND WITHOUT LEVONORGESTREL-RELEASING INTRAUTERINE SYSTEM (LNG-IUS) IN SYMPTOMATIC MYOMETRIAL ADENOMYOSIS PATIENTS

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Country where research was undertaken:
China

Introduction/Background
Adenomyosis (AM) is a common gynaecological disease in women of reproductive age, mainly manifesting as dysmenorrhea and menorrhagia. Hysterectomy is the traditional radical treatment for women without fertility desire. In recent years, the treatment of AM has gradually evolved into a conservative method of preserving uterus.

Materials and Methods
Symptomatic women with adenomyosis who underwent hysteroscopic excision (excision group) or hysteroscopic excision combined with Levonorgestrel-releasing intrauterine system (LNG-IUS) (combined group) were retrospectively recruited from our hospital between January 2017 and December 2022. The degree of dysmenorrhea and menorrhagia was respectively evaluated by visual analogue scale (VAS) and Mansfield-Voda-Jorgensen Menstrual Bleeding Scale (MVJ), the scores of which were recorded preoperatively at 3rd, 6th and 12th month after surgery, respectively.

Results
28 women in excision group and 45 women in combined group were included at last. Compared to the baseline data, both treatments significantly reduced the degree of menorrhagia and dysmenorrhea at 3rd, 6th, and 12th months after surgery ($P<0.05$). In combined group, VAS and MVJ scores were both continually significantly decreased ($P<0.01$) as time goes on. Compared between two groups, at 3rd and 6th month, there was no significance for VAS score [combined group vs excision group: mean difference -0.091 (-1.520~1.337), -0.793 (- 2.117~0.531), $P>0.05$], while the difference was significant at 12th month [-1.420 (-2.791~- 0.485), $P<0.05$]. On the other hand, the mean difference of MVJ score was significant (combined group vs excision group) at each postoperative follow-up point [-0.816 (-1.527~- 0.105), -1.371 (-2.074~-0.668), -1.677 (-2.464~-0.891), $P<0.05$].

Conclusion
Hysteroscopic excision can improve the symptom of menorrhagia and dysmenorrhea in women with myometrial adenomyosis. Furthermore, when the method is combined with Levonorgestrel-releasing intrauterine system, the effect of relieving symptoms is strengthened and will provide a continuous improvement during follow-up, especially for menorrhagia.

Key words
Adenomyosis, hysteroscopic excision, levonorgestrel-releasing intrauterine system

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SESSION 2C: PAIN AND A MULTIDISCIPLINARY APPROACH TO ITS MANAGEMENT

A DIETARY INTERVENTION REDUCES ACYCLIC PELVIC PAIN AMONG PEOPLE WITH ENDOMETRIOSIS: A RANDOMIZED CONTROLLED TRIAL

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Country where research was undertaken:
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Introduction/Background
The role of diet in endometriosis symptomatology has gained increased attention, yet there are no published randomized controlled trials (RCTs) supporting dietary recommendations for endometriosis symptom management. Given the well-documented placebo effect of dietary changes on pain, RCTs are essential to establish evidence-based dietary recommendations for people with endometriosis.

Materials and Methods
People with endometriosis who reported a pelvic pain score of at least 6/10 and scored <75 on the Alternative Healthy Eating Index (AHEI) were randomized to receive a 12-week individually-delivered AHEI-compliant dietary change program or continue their usual diet. The primary outcomes were acyclic pelvic pain and dysmenorrhea measured with the visual analog scale (VAS) from the WERF EPHect questionnaire. Linear mixed models were used to compare change in pain scores over the study period.

Results
100 participants were block randomized to the dietary intervention (n=46) or control (n=54) groups. Participants in the intervention arm experienced significant improvement in acyclic pelvic pain (mean [95% CI] worst pain in the past month, baseline to 12-week: 7.1 [6.3-7.9] to 4.6 [3.7-5.6], p<0.0001). No improvement was observed in the control arm (7.1 [6.3-7.8] to 6.7 [5.8-7.5], p=0.23), with a statistically significant difference in change in acyclic pain between the intervention and control arms(p=0.02). Participants in the intervention arm experienced statistically, but not clinically, significant improvement in dysmenorrhea (8.6 [8.2-9.1] to 7.2 [6.4-8.0], p=0.0002) with a similar change observed in the control arm (8.7 [8.4-9.1] to 7.3 [6.6-8.0], p=0.0003)(p=0.73). There were no differences between arms in percentage of participants who did not complete the study.

Conclusion
In people with endometriosis, a 12-week dietary intervention based on the AHEI led to significant improvements in acyclic pelvic pain compared to control participants who maintained their usual diet. Our results indicate that AHEI guidelines could be used to establish foundational, evidence-based dietary recommendations for people with endometriosis.

Key words
Diet, trial, pain

NOVEL PAIN MECHANISM IDENTIFICATION IN WOMEN WITH ENDOMETRIOSIS-ASSOCIATED PAIN (EAP)

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Country where research was undertaken:
Australia

Introduction/Background
Endometriosis-associated pain (EAP), often refractory to treatment, burdens women's health. However, the underlying pain mechanisms are yet to be fully identified. We aimed to classify EAP mechanisms through psychophysical testing which uniquely

distinguishes peripheral and central pain pathways. Underlying neuropathological pain pathways may then be targeted for treatment.

Materials and Methods
Quantitative sensory testing (QST), a psychophysical test, meticulously applies thermal, mechanical and dynamic stimuli to the hand dorsum, midline lower back and abdomen evoking a controlled verbal response. QST is prescribed by the German Research Network on Neuropathic Pain (DFNS). We assessed women with EAP and endometriosis (n = 20), EAP and suspected undiagnosed endometriosis (n = 9), and pain-free women without endometriosis (n = 14) for abnormal QST changes compared with DFNS reference datasets.

Results
Women with EAP with or without endometriosis (n = 29) exhibited a greater proportion of abnormal QST values from noxious stimuli at the back ($p = 0.066$), abdomen ($p = 0.024$) and hand ($p = 0.041$) and lower threshold for mechanical pain at the back ($p = 0.014$) compared with pain-free women without endometriosis (n = 14).

Abnormal QST values were categorised as either a gain, loss or mixed change in sensory function to develop QST sensory phenotypes. The major QST sensory phenotype was noxious pinprick (mechanical) gain at the back for women with EAP with or without diagnosed endometriosis (n = 58 tests) vs pain-free women without endometriosis (n = 28 tests) ($\chi^2 = 5.45$, df = 1, $p = 0.020$).

Conclusion
Women with EAP, with or without endometriosis, demonstrated pinprick hyperalgesia which indicates secondary hyperalgesia. Secondary hyperalgesia, as a mechanism of central sensitisation, is not due to persistent nociceptive barrage, is restricted to mechanical stimuli and requires neuroaxis input. This specific neuropathic pathway has not been previously identified in EAP.

Key words
Neuropathic pain mechanism

MULTIPLE LESION INDUCTIONS SENSITIZE THE PERIPHERAL AND CENTRAL NERVOUS SYSTEM IN A MOUSE MODEL OF ENDOMETRIOSIS

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United States of America

Introduction/Background
Although understanding endometriosis pathogenesis is crucial, many studies rely on single- induction rodent models. While these models can develop endometriosis-like lesions, menstrual cycles repeatedly occur in women, and each retrograde menstruation induces composite inflammation. We thus carried out repeated cycles of lesion inductions in mice to examine disease pathophysiology.

Materials and Methods
To induce endometriosis-like lesions in mice, endometrial fragments were inoculated into the peritoneal cavity of recipient mice a single time (1x) or multiple times (6x) at 2-week intervals. Von Frey testing was performed to evaluate mechanical hyperalgesia, and then mice were euthanized at 2 or 6 weeks after the last induction, and peritoneal fluid, lesions, bilateral lumbar (L4-6) dorsal root ganglion (DRG), brain, and spinal cord were collected.

Results
Multiple-induction mice showed a remarkable increase in lesion numbers, and von Frey tests showed that the 6x group was more sensitive than the 1x group. More macrophages and increased vascularization and innervation were observed in the lesions with multiple-inductions. In support of the results, proinflammatory cytokines, TNFα, IL-1β, and IL-6, were significantly elevated in the 6x group. Furthermore, increased $MHCII^{hi}$ and decreased $TIM4^{hi}$ peritoneal macrophages were exacerbated in the 6x group. High levels of CGRP, SP, and TRPV1-positive cells were sustained in the DRG in the 6x group. We also examined markers of microglia (IBA1) and astrocytes (GFAP) in the brain and spinal cord. IBA1 and GFAP- positive cells and area were elevated in the cortex, hippocampus, thalamus, hypothalamus, and/or spinal cord by multiple inductions.

Conclusion
These results suggest that multiple-inductions (a better mimic for repeatedly occurring menstruation) could be critical to establishing a chronic peritoneal inflammatory environment

that promotes lesion progression, enhances central glial activation, and leads to exacerbated endometriosis-associated pain.

Key words
Endometriosis, pain, chronic inflammation

IMPACT OF PAIN AND FEELINGS OF INFERTILITY ON DEPRESSION, ANXIETY AND STRESS SYMPTOMS IN INDIVIDUALS WITH ENDOMETRIOSIS: AN INTERNATIONAL SURVEY

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Country where research was undertaken:
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Introduction/Background
The link between endometriosis-related pain, infertility, and mental health is not fully understood. In chronic pain conditions there are known relations with mental health symptoms. This study explores the relationship between of pain and infertility symptoms on depression, stress, anxiety and post-traumatic stress disorder (PTSD) symptoms in individuals with endometriosis.

Materials and Methods
This cross-sectional international online survey was disseminated to endometriosis support groups utilising validated questionnaires of the Endometriosis Health Profile (EHP-30), Depression Anxiety Stress Scales-21 (DASS-21), and Post-traumatic Stress Disorder Checklist for DSM-5 (PCL-5). Demographic and previous history data was collected (age, country, pregnancy history, previous fertility treatment). Participants included people assigned female at birth with self-reported endometriosis. Relation of outcome measures of EHP-30 pain and fertility scores, DASS-21 scores and PCL5 scores were assessed.

Results
3,449 individuals across 81 countries responded to the survey between March 2021 and May 2021. Most (76.8%) were aged between 25 and 44. Results revealed significant associations for EHP-30 pain and EHP-30 fertility scores in relation depression, anxiety, stress and PTSD scores ($p<0.0001$ for each) in individuals with endometriosis (e.g., pain score 50, fertility score 80 resulted in DASS-21 depression score of 9.4). In the domains of depression, stress and PTSD there was an interaction between pain and fertility severity with the effect of each being larger when the other is large. Previous pregnancy significantly reduced depression ($p=0.001$), anxiety ($p=0.006$) and PTSD scores ($p= 0.006$) but not stress scores. Access to fertility treatment reduced depression score ($p=0.014$) and was independent of live birth outcome ($p=0.061$).

Conclusion
There is a direct linear relationship for both pain and fertility score magnitude in relation to depression, anxiety, stress and PTSD scores in individuals with endometriosis. Future research should target developing predictive models to identify individuals with endometriosis at higher risk of mental health deterioration, providing timely and directed support.

Key words
Pain, mental health, fertility

A NOVEL MULTIDISCIPLINARY SERVICE TREATING WOMEN WITH ENDOMETRIOSIS AND CHRONIC PELVIC PAIN: SERVICE USER PROFILE

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Country where research was undertaken:
Australia

Introduction/Background
Australian guidelines recommend a multidisciplinary team approach for managing endometriosis and pelvic pain. The 2018 National Action Plan committed to establishing 20 specialised clinics, leading to Queensland launching the first publicly funded

multidisciplinary service for endometriosis and pelvic pain in the state. This study presents data from users of this service.

Materials and Methods
Launched in February 2024, this multidisciplinary service is a hospital-based groundbreaking model of care distinguished by its holistic, patient-centred, and tailored approach. We reported preliminary data on the service user profile. Retrospective quarterly patient data from February to April 2024 was collected from routine data and Integrated Electronic Medical Records (ieMR). Preliminary findings have been presented, with plans to include up to 12 months of data in the conference presentation.

Results
This multidisciplinary service includes clinical nurse consultants, gynaecology consultants, pain specialists, social workers, physiotherapists, psychologists, and dietitians, accessible through GP referral. Patients attend a group neuroscience pain education session, followed by individual appointments with a clinical nurse consultant and a gynaecologist. Treatment pathways are tailored through multidisciplinary case conferences. Within three months, the service treated 124 patients (mean age 31, SD 8.27; 4% identified as First Nations). The primary issues were pelvic pain (67%) and infertility (18%). Common symptoms included headache (88%), bowel symptoms (88%), dysmenorrhoea (88%), and dyspareunia (82%). Regarding pain, 84% had moderate-extreme central sensitisation severity levels, 82% had low pain self-efficacy, and 47% had high pain catastrophisation. Preliminary data revealed a 65% decline in emergency department presentations compared to three months pre-referral.

Conclusion
We provided a comprehensive profile of patients attending a multidisciplinary service for females with endometriosis and pelvic pain, highlighting symptom prevalence. This data underscores the need for a tailored, multidisciplinary care approach and sets the stage for future research on the impact of such an approach on endometriosis patients.

Key words
Model of care, multidisciplinary approach, health service

COGNITIVE AND ELECTROPHYSIOLOGICAL BIOMARKERS OF CHRONIC PELVIC PAIN IN WOMEN WITH ENDOMETRIOSIS

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Country where research was undertaken:
New Zealand

Introduction/Background
Endometriosis, a condition affecting 10% of women, is linked to chronic pelvic pain, cognitive complaints, and reduced quality of life. Despite limited research, recent findings reveal altered neural connections in affected women. This study employed cognitive tests and electroencephalography to identify impacted cognitive areas and further understand these neural differences.

Materials and Methods
Our cross-sectional study measured cognitive performance and electroencephalography (P300 and spectral power) in three groups of women: endometriosis with chronic pelvic pain (CPP), endometriosis without CPP, and age- and education-matched healthy controls. Cognitive performance, P300 event-related potential (ERP) amplitudes/latencies, and spectral power were compared across groups. We also analyzed whether pain levels, psychological measures, and modifiable lifestyle factors were potential moderators of cognitive performance and electroencephalographic differences between groups.

Results
Women with endometriosis exhibited poorer cognitive performance relative to age- and education-matched healthy controls, with significantly greater deficits observed in those experiencing endometriosis with CPP. Pain levels (at session and over the past 6 months), and depressive, anxious, and stress symptomatology emerged as significant moderators of cognitive performance differences. The data support that pain severity may be especially associated with poorer performance. We identified augmented ERPs in the parietal planes of women with endometriosis, particularly in P3b component amplitudes. While P3a latencies remained stable, group- and task-dependent differences emerged in P3b latencies. An overall trend was noted in which smaller ERP amplitudes (both P3a and P3ba) were associated with

poorer performance on speeded tasks, with spectral power differences further supporting ERP augmentations.

Conclusion
We provide evidence of objective cognitive deficits and augmented neural functioning in individuals with endometriosis. These findings underscore the importance of addressing cognitive health in the management of endometriosis. Our results also lay the groundwork for future research to develop targeted interventions that address cognitive deficits in this population.

Key words
Endometriosis, cognition, pain

SESSION 2D: BIOPSYCHOSOCIAL CONSIDERATION IN ENDOMETRIOSIS

A RANDOMIZED CONTROLLED TRIAL OF TELEHEALTH COGNITIVE BEHAVIOUR THERAPY, YOGA VERSUS EDUCATION TO IMPROVE ENDOMETRIOSIS HEALTH-RELATED QUALITY OF LIFE

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Country where research was undertaken:
Australia

Introduction/Background
Interdisciplinary care is recommended in treating endometriosis, but the efficacy of commonly used psychological and mind-body interventions such as cognitive behaviour therapy (CBT) and yoga is unknown. What is the efficacy of telehealth cognitive behaviour therapy (CBT) and telehealth yoga, versus an active control (online education), on health-related quality of life (HRQoL) for endometriosis?

Materials and Methods
This parallel randomized controlled trial (RCT) randomised 334 participants between April 2021 and February 2024. English-speaking adults in Australia, with a diagnosis of endometriosis, with pain for at least 6 months, and access to internet were recruited via support groups and doctors' clinics. Participants were randomly allocated to CBT, yoga or education groups. CBT involved an 8-week telehealth, therapist-led CBT group; yoga an 8-week telehealth therapist-led yoga group; and education involved weekly educational handouts via email. Outcomes: Endometriosis-specific HRQoL (EHP-30); and generic HRQoL (EQ-5D-5L) at post-treatment (8 weeks). Mixed-effects models were used to examine group x time differences.

Results
The CBT group reported statistically significant improvements in EHP Pain (B = - 2.65, CI -4.89 - -0.41), EHP Control (B = -1.73, CI -3.33 - -0.12), EHP Treatment (B = -1.37, CI -2.46 - -0.27) and overall generic HRQoL (B = 7.18, CI 0.46 – 13.90) compared to the control group, with small to medium effect sizes (Cohen's D = .32 to .41). No statistically significant improvements relative to the control group were evident for yoga.

Conclusion
Telehealth CBT demonstrated efficacy for improving endometriosis-specific and generic HRQoL in people with endometriosis, compared to education. We recommend psychological care as part of interdisciplinary management for people with endometriosis, including endometriosis-tailored CBT that can be delivered online to address access and mobility barriers.

Key words
Psychological therapy, yoga, quality of life

Study funding/competing interest(s)
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ETHICS OF A MEDICAL ASSISTANCE IN DYING REQUEST FOR ENDOMETRIOSIS AND CHRONIC PELVIC PAIN

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Country where research was undertaken:
Canada

Introduction/Background
In 2021, Canada amended legislation on medical assistance in dying (MAiD) to remove the criterion that 'natural death has become reasonably foreseeable'[1,2], such that people

with chronic, grievous, and irremediable conditions and no reasonably foreseeable death – like people with chronic pelvic pain – may access MAiD if they meet certain criteria.

Materials and Methods
An ethical analysis of the provision of MAiD care to patients with chronic pelvic pain and endometriosis was conducted using the IDEA[3] framework. The analysis is based in ethical principles including autonomy, protection of rights, maleficence, justice, equity, common good, and stewardship. The analysis is based in the context of Canadian legislation and access to care. An illustrative case is provided.

Results
Relevant facts, such as the documented suffering of people with chronic pelvic pain (CPP) and endometriosis and long delays in diagnosis and access to care, are outlined. The relevant ethical principles are identified including autonomy of the person suffering and protection of rights, such as the legal right to request MAiD if one believes they have met the criteria. The options are explored, such as assisting the patient in accessing an assessment for MAiD and other services and ensuring the patient has capacity to make such a decision. The clinician should act to support the patient, refer appropriately, and to advocate for improved resource allocation to reduce suffering for people with CPP and endometriosis.

Conclusion
Endometriosis and/or chronic pelvic pain as the sole causal conditions are eligible conditions to be assessed for MAiD. MAiD should not replace the dire need to solve chronic health care system issues of access to chronic pain services, mental health care, and social challenges.

Key words
Euthanasia, chronic pain

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THE IMPACT OF DIFFERENT SOCIAL MEDIA HEALTH INFORMATION FORMATS ON WOMEN'S ENDOMETRIOSIS TREATMENT-SEEKING INTENTIONS: ANECDOTES VS NEUTRAL FACTS

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Country where research was undertaken:
Australia

Introduction/Background
Women increasingly use social media to learn about and manage endometriosis due to its varied symptom profile and diagnostic challenges. As social media content often lacks scientific evidence and credibility, this study aimed to explore how different endometriosis-related health information formats (varying by format and credibility) impact women's treatment-seeking intentions.

Materials and Methods
Australian women were randomised to one of four Instagram posts in a 2x2x(2) design where content (personal anecdote vs neutral, evidence-based information) and source credibility (high-credibility World Health Organisation (WHO) account vs low-credibility layperson account) were varied. After viewing the post, participants read a hypothetical scenario outlining pain medication and laparoscopy as potential treatment options. A within-subjects component investigated change in intention when informed laparoscopy is only recommended if pain medication is ineffective.

Results
A total of 1473 women aged 18-45 years who had no prior endometriosis diagnosis were included in the analysis. Instagram posts featuring an anecdote produced higher treatment- seeking intentions (*MD* = 0.22, *F* (1,1469) = 5.99, *p* = .015) and more favourable attitudes towards getting a laparoscopy compared to posts containing neutral evidence-based information (*MD* =

0.13, F (1,1469) = 4.68, p = .031). Whilst the WHO account was perceived as more credible (MD = 0.29, F (1,1469) = 23, p = <.001), there were no differences in intentions, perceived norms, or self-efficacy towards laparoscopy compared to the layperson account. Providing information about the new laparoscopy guidelines reduced intention (MD = 0.29, F (1,1469) = 50.44, p < .001), irrespective of condition.

Conclusion
Findings demonstrate the power of anecdotes in shaping women's treatment preferences amidst new evidence and changing clinical guidelines for endometriosis. The complex influence of source credibility on medical decision-making highlights the urgent need to promote digital literacy and integrate experiential knowledge into endometriosis-related health communication on social media.

Key words
Endometriosis, social media, medical decision-making

DEVELOPMENT AND APPLICATION OF THE PELVIC PAIN AND IMPACT TANGLE: A BIOPSYCHOSOCIAL APPROACH TO THE PELVIC PAIN "SUPER-SYNDROME"

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Country where research was undertaken:
Australia

Introduction/Background
The *Pelvic Pain and Impact Tangle* is an innovative tool developed at a federally funded, multidisciplinary clinic within the *Endo 22* initiative. The Pain Tangle visualizes the interwoven impact of biological, psychological, and social stressors, helping patients conceptualize pelvic pain as a "super-syndrome" involving predictable interactions across body systems. (49 words)

Materials and Methods
The *Pelvic Pain and Impact Tangle* was created through structured Biopsychosocial workshops, gathering narrative accounts from patients to represent the biological, psychological, and social dimensions of their pelvic pain experiences. These narratives were analysed and integrated into a visual model, mapping pain drivers and their relationships. By enabling patients to "pull at threads" within the Pain Tangle, this tool helps identify stressor interactions across body systems, promoting insights into individual and common pain drivers. (70 words)

Results
Our clinic focuses on persistent pelvic pain and endometriosis, with an emphasis on lived experiences and quality of life. The Pain Tangle facilitated patients' understanding of their pelvic pain as an interconnected "super-syndrome," where each "thread" in the web of pain represents stressors across biological, psychological, and social dimensions. Participants identified how work-related stress, sleep issues, and relational dynamics could intensify pain, while others highlighted links between dietary triggers, emotional health, and physical strain. By visualizing these interactions, patients gained individualized strategies for holistic pain management, empowering them to better navigate their conditions with targeted, actionable approaches. (96 words)

Conclusion
The *Pelvic Pain and Impact Tangle* offers a transformative approach to managing pelvic pain as a "super-syndrome," facilitating a holistic and individualized management strategy that enhances quality of life. This tool underscores the importance of multidisciplinary, patient- centred care in addressing endometriosis and related pelvic pain within the Biopsychosocial framework. (46 words)

Key words
Pelvic pain, biopsychosocial model, super-syndrome

INTERGENERATIONAL IMPACT OF PELVIC PAIN: EXPLORING FAMILIAL AND CATASTROPHISING FACTORS IN ADOLESCENT PAIN EXPERIENCES

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Country where research was undertaken:
Australia

Introduction/Background
While studies have reported familial risks of endometriosis[1,2], hereditary aspects of persistent pelvic pain are yet unexplored. We present baseline characteristics from a longitudinal cohort of adolescents (aged 10-18) and their parent/guardians. We analysed adolescents' medical history, pain scores, pain catastrophising, and parental catastrophising specific to their child's pain.

Materials and Methods
The LongSTEPPP study recruited adolescents aged 10 to 18 who sought medical care for dysmenorrhea or pelvic pain. Participants included both the adolescent and their parent/guardian who answered questionnaires on medical history, pain and pain-related catastrophising. Baseline data and trends were analysed to explore the role of family history and parental depression, anxiety and catastrophisation on the child's self-reported pain. We also explored if there was any correlation between child and parent catastrophising.

Results
Data from 233 adolescents (mean age 15.6 years) were analysed, and most parent/guardians identified as mothers. Comorbid pain conditions (chronic pain, fibromyalgia, migraine) were reported in over a quarter of both adolescents and mothers. History of gynecological surgery was noted in 14% of adolescents and 55% of mothers (with a mean of 3 laparoscopies, range 1-18). Half of adolescents reported a family history of endometriosis, with one-third citing a first-degree relative. Similar patterns were observed for persistent pelvic pain. Adolescents tended to report family history (of endometriosis) more frequently than their mothers. Average pain scores were higher in those with a family history of endometriosis. Among adolescents, there was a moderate link between pain scores and catastrophizing, but it was much weaker in parents.

Conclusion
Adolescents tended to overreport a family history of endometriosis, which correlated with higher average pain scores. This highlights the need for qualitative research exploring discrepancies between adolescents and parents in gynaecological contexts. Further exploration of adolescent-parent pain catastrophising and its impact on adolescent's health-seeking behaviors and pain are also warranted.

Key words
Dysmenorrhea, pelvic pain, family history

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A BIOPSYCHOSOCIAL ASSESSMENT OF ENDOMETRIOSIS-ASSOCIATED PAIN REVEALS NOVEL MECHANISMS OF CENTRAL SENSITISATION AND THE INFLUENCE OF PSYCHOSOCIAL FUNCTIONING

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Country where research was undertaken:
Australia

Introduction/Background
Central sensitisation (CS), identified in endometriosis-associated pain (EAP), is thought to arise from peripheral nociceptive barrage due to neuro-inflammatory aspects of endometriosis. Yet, there is not a linear relationship between pain experience and endometriosis. We aimed to elucidate all neural mechanisms along the entire somatosensory pathway contributing to EAP.

Materials and Methods
We used the Initiative on Methods, Measure and Pain Assessment in Clinical Trials (IMMPACT) guidelines to complete psychophysical (QST) and psychosocial (pain severity, affective, cognitive and physical functioning questionnaires) assessment of women with EAP, with or with suspected undiagnosed endometriosis (n = 29) and pain-free, endometriosis-free women (n = 14). QST distinguishes pain pathways, pinpointing peripheral and central inputs. Questionnaires deliver neuroaxis (psychosocial) inputs. Together, psychophysical and psychosocial testing build a biopsychosocial model of EAP.

Results
We associated the QST-determined pain mechanisms with psychosocial functioning via

Spearman's correlations. Women with EAP, with or without diagnosed endometriosis, demonstrated a dynamic relationship at the primary EAP referral sites, the back and abdomen, between self-reported severe pain; QST-determined central sensitivity, specifically secondary hyperalgesia, temporal summation and long-term potentiation; and self-efficacy or catastrophising cognitions. Those with high self-efficacy experienced the pain (severity) and modulated its unpleasantness (sensitivity) (r_S = –0.80, n = 10, p = 0.006). At the same body sites, those with catastrophising cognitions experienced the pain (severity) with increasing unpleasantness (sensitivity) (r_S = 0.71, n = 10, p = 0.021). Those with catastrophising also displayed a lowered pain threshold at the hand (r_S = -0.68, n = 10, p = 0.032).

Conclusion
The biopsychosocial model framed novel insights into pathophysiological pain mechanisms in women with EAP. Capturing the dynamic interactions between pain outcomes, psychosocial functioning and specific central mechanisms reveals how EAP arises and is experienced. This offers the potential of expanding mechanism targeted treatment for EAP.

Key words
Central sensitization, biopsychosocial

SEMINAR SESSION 5: LIFESTYLE AND MEDICAL TREATMENTS IN ENDOMETRIOSIS

LIFESTYLE DISEASES AND ENDOMETRIOSIS

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Endometriosis is a chronic inflammatory condition characterized by the presence of endometrial- like tissue outside the uterus, leading to pain, infertility, and other systemic symptoms. The pathophysiology of endometriosis involves complex interactions between hormonal, immune, and genetic factors, which may also play roles in the development of lifestyle diseases such as type 2 diabetes, gestational diabetes, metabolic syndrome, and cardiovascular diseases. The relationship between endometriosis and lifestyle diseases is multifaceted. Chronic inflammation, dysregulation of estrogen and microbiome imbalance in endometriosis can contribute to the development of lifestyle diseases such as insulin resistance, metabolic syndrome, diabetes and cardiovascular disease. Diet may play a role in the prevention and management of endometriosis including in the management of pain in endometriosis. A review of evidence on dietary and nutritional interventions will be provided. This include interventions on dietary patterns, nutrients and supplement in endometriosis and cardiometabolic diseases. Knowledge gap and future directions in dietary management of endometriosis will be discussed. In summary, the interplay between endometriosis and lifestyle diseases underscores the importance of a holistic approach to the management of endometriosis. This emphasizes the role of diet and lifestyle modifications to prevent or improve the management of endometriosis, thereby improving the quality of life associated with reproductive health in women.

Key words
Diabetes, endometriosis, cardiovascular

LONG-TERM EXTENSION STUDY TO ASSESS THE EFFECT OF LINZAGOLIX IN WOMEN WITH ENDOMETRIOSIS-ASSOCIATED PAIN (EDELWEISS-6 TRIAL)

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Countries where research was undertaken:
Austria, Bulgaria, Czech Republic, France, Poland, Romania, Spain, Ukraine, United States of America

Introduction/Background
Linzagolix is a GnRH antagonist that is currently under development for the reduction of pain associated with endometriosis. In this extension study (EDELWEISS-6), we assessed the long- term effects of linzagolix in women with moderate to severe endometriosis-

associated pain (EAP) who have completed the phase 3, double-blind, placebo-controlled EDELWEISS-3 trial.

Materials and Methods
Following completion of the principal EDELWEISS-3 trial, participants were invited to continue treatment for a further six months with either linzagolix 75mg or 200mg plus hormonal add-back therapy (1mg estradiol/0.5mg norethindrone acetate) for their EAP. Co- primary endpoints were a clinically meaningful reduction in dysmenorrhea (DYS) and non- menstrual pelvic pain (NMPP) up to month 12. Key secondary endpoints assessed sustained efficacy in dyschezia, overall pelvic pain (OPP) and pain interference with daily activities up to 12-months.

Results
Of the 484 women completing EDELWEISS-3, 353 enrolled and were analysed in the EDELWEISS-6 study. At the outset of this extension study (at month-6), 84.7% of women in the linzagolix 200mg+ABT group and 49.6% in the linzagolix 75mg group showed a clinically meaningful reduction in DYS, increasing to 91% and 55.9% by month-12, respectively. For NMPP, response rates rose from 61% and 54.0% at month 6 to 67.6% and 59.5% by month-12 for the 200mg+ABT and 75mg groups, respectively. Additional improvements in dyschezia, OPP, and pain interference with daily activities were observed from month-6 to -12 with both treatment arms. Hot flushes (3.4–6.9%) were the most common adverse event, and bone mineral density change from baseline was <2% at month-12 across all groups.

Conclusion
Improvements in DYS and NMPP observed at month-6 further increased by month-12 in both the linzagolix 75mg and 200mg+ABT groups. Similarly, efficacy on key secondary endpoints demonstrated at month 6 continued to improve up to month-12. Overall, linzagolix was well-tolerated over the 12-months treatment course in EDELWEISS-3 and -6 trials.

Key words
Linzagolix, GnRH antagonist, endometriosis

LINZAGOLIX OUTCOMES IN WOMEN WITH CONCURRENT ENDOMETRIOSIS AND ADENOMYOSIS: A POST-HOC ANALYSIS OF THE EDELWEISS-3 AND 6 TRIALS

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Countries where research was undertaken:
Austria, Bulgaria, Czech Republic, France, Hungary, Spain, Romania, Poland, Ukraine, United States of America

Introduction/Background
Endometriosis, a chronic inflammatory disorder characterised by troublesome dysmenorrhoea (DYS) and pelvic pain often co-exists with adenomyosis, a condition characterised by the infiltration of endometrial tissue into the uterine wall. Here, we evaluated outcomes of patients with co-existing endometriosis and adenomyosis treated with linzagolix in the EDELWEISS- 3 and 6 trials.

Materials and Methods
EDELWEISS-3 was a multi-center, randomized, double-blind phase 3 trial evaluating linzagolix versus placebo for endometriosis-associated pain. Patients were randomised to receive linzagolix 75mg, 200mg plus add-back therapy (1mg estradiol/0.5mg norethindrone acetate), or placebo for 6-months. Upon completion, patients were then invited to continue treatment with linzagolix for a further 6-months in the EDELWEISS-6 trial. This post-hoc analysis examines outcomes in patients with endometriosis (Endo) alone versus those with concurrent adenomyosis (Endo+Adeno) in the EDELWEISS trials.

Results
Of the 484 patients enrolled, 145 (30%) had concurrent adenomyosis. For DYS, a greater proportion of patients in the Endo+Adeno group (78.4%; OR:11.24, p<0.001) showed improvement with linzagolix 200mg+ABT compared to the Endo group (69.5%; OR:7.01, p<0.001) at 3-months, with sustained improvements observed at 6 and 12-months. In the 75mg arm, DYS improvements were generally lower. For NMPP, linzagolix 200mg+ABT improved symptoms in 47.6% (OR:2.05, p=0.021) of the Endo group and 49% (OR:1.92, p=0.243) of the Endo+Adeno group

at 3-months, with statistical significance in the Endo group only. By 6- months however, significant improvements in NMPP were observed in both Endo+Adeno and Endo groups (p=0.026 and p=0.034, respectively) which was maintained up to 12-months. Linzagolix 75mg showed no significant improvement in NMPP in either group.

Conclusion
Linzagolix 200mg+ABT significantly improved DYS in patients with concurrent endometriosis and adenomyosis, indicating this higher dose may be optimal for this subgroup. Further investigation is warranted.

Key words
Linzagolix, adenomyosis, endometriosis

THE ALYRA DEVICE: FIRST-IN-HUMAN, FIRST-IN-CLASS, CLINICAL TRIAL OF A NEUROIMMUNE- MODULATING INTRAUTERINE DEVICE TO REDUCE PELVIC PAIN IN WOMEN

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Country where research was undertaken:
Australia

Introduction/Background
Women with dysmenorrhea report pain symptoms consistent with a systemic neuroimmune inflammatory process[1]. Increased Interleukin-1β (IL-1β) expression in endometrial stromal cells mediates pain in women with endometriosis[2]. A neuroimmune circuit linking excess intrauterine Toll-Like Receptor 4 (TLR4)-mediated immune activation with central neuroglial activation, cytokine release and immune activation is proposed.

Materials and Methods
A Phase 1B, single-centre, randomised, double blind, parallel-group study of 12 participants with dysmenorrhea was undertaken to investigate the pharmacokinetic properties and uterine tolerability of a novel dual drug reservoir intrauterine device releasing amitriptyline and levonorgestrel. Amitriptyline is a TLR4-inhibitor used clinically for pelvic pain and migraine[3,4]. Trial devices were inserted for 3 months. Endometrial biopsies were taken at baseline, device removal, and 1 month after removal.

Results
Peak plasma concentrations of amitriptyline were below <2ng/ml. This is the systemic threshold for adverse effects[5]. Endometrial biopsies confirmed that the levonorgestrel effect on endometrium observed in women using levonorgestrel-only devices is conserved in amitriptyline/levonorgestrel device users. High endometrial tolerability was observed, and endometrial histology returned to baseline 1 month after device removal. Michigan Symptom Severity Scores (0-31) reduced from an average of 10 to 5 over the 3-month trial period. No serious adverse effects occurred. Dynamic cytokine analysis undertaken before and after device use confirmed the strong cytokine response to TLR4-agonist stimulation among this pain population.

Conclusion
This first-in-human study of a dual levonorgestrel and TLR-4 inhibitor releasing IUD confirmed that the drug release profile and initial uterine tolerability were fit for purpose. Study criteria were met, and no serious adverse effects were found. This study supports further evaluation of this device in a larger participant cohort.

Key words
Toll-like receptor 4, pain, intrauterine device

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A NEW ERA IN ENDOMETRIOSIS DIAGNOSIS: VALIDATING SONOPODOGRAPHY FOR SUPERFICIAL ENDOMETRIOSIS

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Country where research was undertaken:
Canada

Introduction/Background
Advances in non-invasive diagnostic methods for endometriosis, such as transvaginal ultrasound (TVS), have improved detection rates for deep (DE) and ovarian endometriosis (OE), yet superficial endometriosis (SE) remains elusive. SonoPODography (SPG), which introduces saline into the pouch of Douglas (POD), has shown promise in improving SE diagnoses, though it has required validation.

Materials and Methods
This prospective diagnostic accuracy study evaluated the accuracy (Acc), sensitivity (Sens), specificity (Spec), positive predictive value (PPV), and negative predictive value (NPV) of SPG for SE detection. We compared two approaches—TVS alone and TVS with SPG—using laparoscopy and histology as reference standards in diagnosing SE. Both ultrasounds and surgeries were performed by the same surgeon-sonologist, though the histologist was blinded. Participants were scheduled for laparoscopy, excluding cases with non- patent fallopian tubes or POD obliteration.

Results
Among 65 participants, pathologically confirmed SE was present in 80% (52/65) of participants. The accuracy of TVS alone, using laparoscopy as the reference, was Acc 42.1%, Sens 39.6%, Spec 75.0%, PPV 95.5%, and NPV 8.6%. Compared to histology, TVS accuracy was Acc 53.6%, Sens 45.5%, Spec 83.3%, PPV 90.9%, and NPV 29.4%. With SPG, accuracy using laparoscopy as the reference was Acc 93.1%, Sens 94.0%, Spec 87.5%, PPV 86.2%, and NPV 97.9%. Compared to histology, SPG accuracy was Acc 86.0%, Sens 91.5%, Spec 60.0%, PPV 91.5%, and NPV 60.0%. SPG was successfully performed in 92% of cases, failing in 8% due to inadequate fluid accumulation in the POD.

Conclusion
SE remains the most common subtype of endometriosis yet often evades detection, contributing to diagnostic delays. SPG, a non-invasive outpatient technique, may significantly enhance the diagnostic accuracy of TVS for SE, supporting its potential to reduce delays and enable earlier management.

Key words
Endometriosis, diagnostic accuracy, transvaginal ultrasound

SPAGOPIX-02:A PHASE IIA,SINGLE-CENTRE, OPEN-LABEL,PROOF-OF-CONCEPT STUDY CONCERNING EFFICACY OF THE NOVEL INTRAVENOUS CONTRAST AGENT SN132D IN PATIENTS WITH SUSPECTED ENDOMETRIOSIS (NCT05664828)

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Country where research was undertaken:
Sweden

Introduction/Background
Endometriosis lesion development and growth are angiogenesis dependent. Pegfosimer manganese is a novel manganese-

based nanosized MRI contrast agent under development. The uptake mechanism of action utilizes the Enhanced Permeability and Retention phenomenon allowing accumulation in leaky vessels in endometriosis lesions, thereby enabling MRI visualization by longitudinal T1 relaxation contrast-enhancement of lesions. Detection of lesions has the potential to assist in diagnosis, surgical interventions, and treatment of individuals with endometriosis.

Aims
The aim of the proof-of-concept clinical study SPAGOPIX-02 was to assess the safety profile and MRI-enhancing properties of SN132D (Pegfosimer manganese) in women with endometriosis.

Materials and Methods
Women with endometriosis at transvaginal ultrasound were enrolled at Skåne University Hospital, Sweden and received Pegfosimer manganese by intravenous infusion at a dose of 20µmol Mn/kg. MR images were read by a blinded, qualified reader. The MR images used to evaluate the primary and secondary endpoints were assessed by 2 independent radiologists with >10 years of experience.Qualitative and safety review based on the assessment of the available MRI and safety data was performed (Data Monitoring Committee).

Results
No SAEs, clinically significant changes in safety laboratory parameters, ECG, vital signs, physical examination were observed following a single i.v administration of Pegfosimer manganese of 20 µmol Mn/kg. Overall, 7 participants (88%) reported a total of 21 AEs. All events were of mild or moderate severity. The most frequent AEs were nausea, flushing, injection site pain.

Skeletal muscle as reference tissue provided Pegfosimer manganese-mediated contrast-to-noise ratio enhancement, which was marginally better than healthy endometrium as reference tissue.

Conclusions
Contrast agent Pegfosimer manganese has the potential to improve the detection and assist in the diagnosis, surgical interventions, and treatment options of individuals with endometriosis, particularly deep pelvic lesions which are challenging to identify. Further evaluation of Pegfosimer manganese contrast-enhancing efficacy in such lesions is warranted.

SEMINAR SESSION 6: BENEFITS AND BUGBEARS OF MODELING ENDOMETRIOSIS OUTSIDE OF THE HUMAN BODY

CLINICALLY RELEVANT EXPERIMENTAL MODELS OF ENDOMETRIOSIS

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Country where research was undertaken:
United Kingdom

Introduction/Background
Experimental models of endometriosis are critical to understanding disease mechanisms and testing therapies, yet many fail to capture the condition's true complexity. This presentation examines key models and emerging frameworks for standardisation, framing the limitations of current models and outlining opportunities to develop models that truly reflect the clinical reality.

Materials and methods
A comparative overview of existing and emerging models. We outline collaborative efforts from the WERF Endometriosis Phenome and Biobanking Harmonisation Project (EPHect) Experimental Models working group to unify SOPs and reporting standards and also make recommendations on best practice. Additionally, we present an overview of data using a syngeneic mouse model of endometriosis, demonstrating a translational arc from model implementation to deployment in discovery science and preclinical testing that has now informed a clinical trial.

Results
No single model captures the full complexity of endometriosis, thus understanding their strengths and limitations is key to using them appropriately and combinations of approaches often provide the most relevant insights. Importantly, significant variation in model design, experimental approach and endpoint reporting exists in the field. The WERF EPHect Experimental Models consortium's work to harmonise SOPs in homologous, heterologous, pain, and organoid models

begins to address these variations and will improve reproducibility amongst groups. Using our own experience with syngeneic mouse models of endometriosis, we reflect on our journey, lessons learnt and key questions outstanding. The research that will be presented in the broader session will be briefly covered.

Conclusion
Recognising both the strengths and gaps in current models is essential for building the next generation of clinically meaningful tools. This presentation and broader session call for acknowledgement that models are not just technical tools, they are philosophical choices about what we think matters in disease. Going forward, we need models that probe underlying aetiology

Key words
Experimental models

MEDIOBASAL HYPOTHALAMIC KNOCKDOWN OF ESR1 IN FEMALE RHESUS MACAQUES INCREASES INCIDENCE OF ENDOMETRIOSIS AND ENDOMETRIOSIS-ASSOCIATED OVARIAN NEOPLASMS

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Country where research was undertaken:
United States of America

Introduction/Background
Knockdown of ESR1, the gene for estrogen receptor alpha (ERα), in mediobasal hypothalamus (MBH) of female rhesus macaques induced higher incidence of endometriosis compared to controls. Here, we describe whole exome sequencing (WES) and spatial transcriptomic (ST) analyses to lay the foundation for a novel nonhuman primate model for endometriosis.

Materials and Methods
Adenovirus-8 borne ESR1 shRNA (ERαKD, n=6) and scrambled shRNA (control, n=5) were infused into the MBH of adult female rhesus macaques. Circulating hormonal levels were monitored over three years followed by pathologic examination of the reproductive tract at necropsy. WES was conducted on endometriotic lesions, endometrium and liver from healthy control (n=4), spontaneous endometriosis (n=4), ERαKD (N=1) cohorts and human endometriosis samples (n=3). ST was conducted on all cohorts (n=3/cohort) using the 10X Genomics platform.

Results
ERαKD macaques exhibited PCOS-like hypergonadotropin ovarian hyperandrogenism, luteal insufficiency and increased body weight. An unanticipated increase in endometriosis was observed in ERαKD compared to control macaques (5/6, 83% versus 1/5, 20%, respectively). One ERαKD female with endometriosis also presented with an endometrioid-like ovarian neoplasm. Pathologic examination of endometriotic lesions from ERαKD animals confirmed endometriosis with alterations in ARID1A and other relevant proteins. WES of the ERαKD female with endometriosis revealed a missense mutation in BRCA1 with a ClinVar classification of pathogenic and a CADD score of 31 predicting it is among the 0.1% most deleterious changes in the human genome. In macaques with spontaneous endometriosis, WES identified mutations in KRAS, PIK3CA, and BRCA2. Analyses of spatial transcriptomics of endometriotic lesions and endometrium are underway.

Conclusion
Hypothalamic ERαKD induces endometriosis and endometrioid-type ovarian neoplasm in adult female rhesus macaques, with pathologic and molecular similarities to spontaneously occurring endometriosis in macaques and women. This new non-human primate model provides novel insights into the implication of neural estrogen activity in the pathogenesis of endometriosis and endometrioid ovarian cancer.

Key words
Rhesus macaque, ESR1 knockdown, endometriosis

INVESTIGATING MACROPHAGE ONTOGENY AND PHENOTYPE IN ENDOMETRIOSIS LESIONS USING MS4A3CREROSATDTOMATO AND FOLR2-KO MICE

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Countries where research was undertaken:
United Kingdom, Singapore

Introduction/Background
Macrophages, key immune cells in tissue repair and inflammation, are abundant in endometriosis lesions and peritoneal fluid. Macrophages originating from yolk-sac-derived erythro-myeloid progenitors may differ in phenotype from those derived from circulating monocytes. We investigated the origin and phenotype of macrophages with a focus on Folr2- expressing macrophages.

Materials and Methods
In a 'menses' mouse model of experimental endometriosis we used Ms4a3creRosaTdTomato mice (monocytes and monocyte-derived macrophages (MDMs) express fluorescent TdTomato) and JM8A3.N1 Folr2$^{tm1b(EUCOMM)Hmgu}$ (Folr2-KO) mice to examine the role of MDMs and Folr2+ macrophages in lesion development and maintenance. Endometriosis was induced in these models over different timepoints (day 3, 7, 14 & 21), allowing for longitudinal tracking of macrophage origin, phenotype, and contribution to lesion dynamics. Flow cytometry and immunofluorescence were used to characterise macrophage populations and assess spatial localisation in lesions.

Results
In the Ms4a3creRosaTdTomato mice, MDMs were the predominant immune cells in endometriosis lesions and peritoneal fluid (PF) across timepoints. Both monocytes and MDMs exhibited high TdTomato expression, confirming their origin. The highest cell counts for MDMs appeared at day 3, decreasing over time, while other immune cells, except neutrophils, remained stable. Notably, monocytes peaked at days 7 and 21 in the PF. Folr2 expression was elevated in lesion and PF MDMs, aligning with published scRNA sequencing data identifying Folr2 as a pro-disease lesion resident macrophage marker. Preliminary findings from Folr2- KO mice suggested a trend toward fewer lesions at day 14 compared to wildtype littermate controls, though further experiments are needed to confirm this observation and over different timepoints.

Conclusions
Our study suggests that monocyte-derived, Folr2+ macrophages may drive endometriosis progression, with preliminary Folr2-KO data indicating fewer lesions. Understanding macrophage origins and phenotypes in endometriosis could reveal potential therapeutic targets, offering new strategies to address this chronic condition and improve patient outcomes.

UNRAVELING KRAS SOMATIC MUTATIONS IN ENDOMETRIOSIS: INSIGHTS FROM EUTOPIC MOUSE MODELS

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Country where research was undertaken:
Canada

Introduction/Background
KRAS mutations are the most common observed somatic mutation in endometriosis, affecting half of patients and associated with high stage. We evaluated the effects of activating Kras- G12D mutations in otherwise normal endometrial epithelial cells to understand the impact on this cell type and microenvironment[1,2].

Materials and Methods
Two models were employed, one a genetic cross resulting in activation of Kras-G12D in sexually mature endometrial epithelium and another using adeno-associated viral CRE delivered to the endometrial lumen to activate the same Kras-G12D knock-in allele. Mutant and control animal were monitored for 6-8 weeks (post-activation) and tissues collected at either estrous or proestrous. Endometrial tissues were evaluated for gene expression changes, hormone receptor, Ras-pathway activation, Ki67 and CD3.

Results
Kras-mutant endometrial epithelium showed increased p-ERK, confirming mutant activity, and bulk gene expression of uterine tissue showed a greater number of differentially expressed genes were observed in proestrous Kras-G12D affected uteri showed increases in ras-regulators (DUSP6, DUSP4), and

proliferation/progenitor markers (Ccnd1, Hmga2, Klf4, Stat4, Etv4). Markers of differentiation and epithelial development, in particular Wnt-pathway members (Wnt3/5a/16, Fzd2, Dvl1/2/3) were reduced, as were cell adhesion components Itga6/7/9 and Laminin a5/c2/c3. Immune-modulating cytokines were broadly dysregulated with increases in Il10 and Ccr7, and reduction in Il1a and Il24.

Immunohistochemistry (IHC) supported RNA data showing >6 fold increased CD3+ cells in Kras-G12D affected endometrial epithelium and increased Ki67 staining in both epithelial (>6 fold) and stromal (>4 fold) cells. There were no signs of malignancy or hyperplasia despite oncogene activation.

Conclusion
Kras mutation was insufficient to drive malignancy but did result in dysregulation of normal endometrial expression patterns throughout the estrus cycle. This resulted in increased proliferation in targeted epithelial cells and adjacent (unmodified) stromal cells, as well as increased T-cell infiltration. Observations suggest Kras activation may result in pro-stemness characteristics.

Key words
Somatic mutation, endometrium, mouse model

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GENOME WIDE EFFECT OF GREB1 REGULATORY REGION SNPS ON ENDOMETRIOSIS USING PATIENT-DERIVED COMPLEX IN VITRO MODELS AND GENETIC PERTURBATION

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Country where research was undertaken:
Australia

Introduction/Background
Genome wide associated studies have identified SNPs in *GREB1* regulatory region that increase endometriosis risk[1]. GREB1 is a hormone regulated gene that interacts with transcription factor motifs [2] and regulates progesterone responsive genes [3]. The genome wide effect of these SNP and how they contribute to endometriosis pathophysiology is unknown.

Materials and Methods
Using patient-derived endometrial biopsies we cultured stromal cells and endometrial organoids. We then designed *GREB1* regulatory regions for CRISPR activation and inhibition (CRSIPRa/i). Perturb-seq analysis through single cell sequencing was performed on primary stromal cells for the genome wide gene expression effect. We developed a single cell dissociation protocol to generate organoids from individual stem cells, and to perform transduction of stem cells for *GREB1* CRISPRi and confirmed with qPCR GREB1 inhibition from two patients.

Results
We analyzed RNA-seq data of more than 5,000 cells with *GREB1* activation and more than 6,000 cells with *GREB1* inhibition in patient derived endometrial stromal cells. Results indicate IL1R, *TNFR, IGFBP2/3* and *CDKN1A* were among the top 100 genes impacted by greb1 inhibition while *SMYD3, VEGFC, DAAH*, IGFBP5 were among the top 100 genes affected by GREB1 activation. To replicate this study in the epithelial cell compartment of endometrial tissue, we have developed CRISPR-based gene editing pipeline in endometrial organoids from the single cell level (novel). We have validated the efficiency of our pipeline with FACS and qPCR and established a biorepository of patient-derived endometrial organoids with GREB1 and RAB1A inhibition from two biological replicates.

Conclusion
GREB1 regulatory region perturbation affect critical genes involved in inflammation, maintenance of stemness, and cell viability. Expands our understanding of how SNPs in regulatory regions influence cell behavior and endometriosis. We have also established a novel genome engineering pipeline to transduce epithelial stem cell to develop into organoids.

Key words
Functional validation, endometriosis, endometrial organoids

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GROWING ALL TYPES OF ENDOMETRIOSIS: THE DEVELOPMENT OF PHENOTYPE-SPECIFIC ORGANOID MODELS OF ENDOMETRIOSIS FOR PRECLINICAL RESEARCH

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Country where research was undertaken:
Australia

Introduction/Background
Developing efficacious endometriosis treatments is limited by an incomplete understanding of disease mechanisms and a lack of functional preclinical models. Organoids represent a promising avenue by recapitulating 3D microenvironments and behavioural complexities of human tissues. Current endometriosis organoid models are incompletely described and lack clinical context, limiting their translational potential.

Materials and Methods
Patients receiving surgical treatment for endometriosis were invited to participate. Those with ≤2 lesions were excluded. Excised lesions were cryopreserved within 4h and stored at -80°C. Tissue was weighed, minced, and dissociated in collagenase, before embedding in Matrigel and cultured in defined media. Organoids were passaged, cryopreserved and revived, and successful models were captured, fixed and paraffin embedded for immunohistochemistry and immunofluorescence against hormone receptors, proliferative and cell phenotype markers.

Results
15 organoid models were successfully established from 27 sites in 21 patients (15/27, 55.6%). All successful organoids recapitulated primary lesions in structure and hormone receptor expression. Endometriomas (OMA; 5/7, 71.4%) and deep infiltrating lesions (DIE; 7/10, 70.0%), including peritoneum (3/4, 75.0%), bladder (1/1, 100%), diaphragm (1/2, 50.0%), and fallopian tube (2/2, 100%) were more successful than superficial (SUP; 3/10, 30.0). OMA organoids showed the greatest variability, forming cystic and solid structures and had the lowest proliferative index. Success rates were similar in early (I/II; 2/7, 53.3%) vs. late stages (III/IV; 7/12, 58.3%) and primary (5/7, 71.4%) vs. recurrent surgeries (10/20, 50.0%). Subfertility (4/4, 100%) and no hormonal treatment (12/14, 85.7%) improved success compared to pain (10/23, 43.5%) or hormonal treatment (3/13, 23.0%).

Conclusion
Organoid models can capture the clinical heterogeneity of endometriosis, including superficial and hormone-treated disease. Ongoing optimisation of culture conditions is required, particularly for endometriomas. By capturing the molecular and structural diversity of endometriosis, organoids are pivotal for advancing preclinical research and personalised medicine.

Key words
Organoids, experimental models, cellular mechanisms

FREE COMMUNICATION SESSION 3

SESSION 3A: SINO-AUSTRALIAN SESSION

MAST CELLS MEDIATE ESTROGEN-INDUCED PAIN SENSITIZATION IN ENDOMETRIOSIS

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Introduction/Background
It has been established that elevated levels of estrogen, as well as increased numbers of

total mast cells (MCs) and degranulated MCs in endometriotic lesions, are closely associated with endometriosis-related pain. However, the precise mechanism by which MCs mediate estrogen- induced sensitization of endometriosis-associated pain remains unclear and warrants further investigation.

Materials and Methods
The levels of estradiol and the number of MCs were quantified in endometrial tissues collected from women with and without endometriosis. The expression of estrogen receptors on MCs and mediators released by MCs were analyzed. The influence of MCs on neurite outgrowth of dorsal root ganglion (DRG) cells was examined. A rat model of endometriosis was established and treated with mast cell stabilizers.

Results
Our findings demonstrated a significant correlation between estradiol levels and the number of degranulated mast cells in endometriotic lesions ($P < 0.05$). The expressions of G-protein-coupled receptor 30 (GPR30) and estrogen receptor-α (ER-α) on MCs were markedly upregulated in endometriotic lesions compared to control endometria ($P < 0.05$), and their expression was enhanced by estradiol stimulation. Estradiol activated MCs via the GPR30-non-classic estrogen pathway and ER-α-nuclear-initiated signaling pathway, leading to the upregulation of fibroblast growth factor 2 (FGF2) and NOD-like receptor family pyrin domain containing 3 (NLRP3). Mediators such as FGF2 and nerve growth factor (NGF), released by activated MCs, promoted neurite outgrowth of DRG cells. Treatment with mast cell stabilizers, including ketotifen and sodium cromoglycate, significantly reduced the number of degranulated MCs in endometriotic lesions and DRG tissues in the rat endometriosis model, as well as the release of mediators such as NGF and tumor necrosis factor-α (TNF-α).

Conclusion
Degranulated mast cells in endometriotic lesions mediate estrogen-induced pain sensitization through the GPR30-non-classic estrogen pathway and ER-α-nuclear-initiated signaling pathway. Mast cell stabilizers may provide a promising avenue for targeted drug therapy in endometriosis.

Key words
Endometriosis, mast cells, estrogen

NEUROLOGICAL PRESERVATION DURING DEEP ENDOMETRIOSIS SURGERY

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Introduction/Background
Nerve-sparing (NS) surgery for deep endometriosis, introduced two decades ago, draws on pelvic neuroanatomy and oncological techniques. It aims to preserve autonomic nerve fibres to reduce iatrogenic injury and visceral dysfunction, without compromising excisional efficacy. Its evolution is supported by growing literature on anatomy, dissection techniques, surgical and functional outcomes.

Materials and Methods
We conducted a bibliographic search in the Medline/PubMed Database using Key words such as "nerve-sparing," "nerve preservation," "nerve anatomy," "neuroanatomy," "neuropelveology," "functional outcomes", "bladder dysfunction," "voiding dysfunction," "bowel dysfunction," "sexual dysfunction," and "endometriosis." Cross-references were examined to identify additional relevant articles. The search was limited to publications in English and French up to January 2024.

Results
Over the past two decades, literature on NS surgery for deep endometriosis has progressed from early feasibility studies to larger cohort analyses with extended follow-up. Prospective trials indicate that intraoperative and postoperative complication rates are comparable to conventional excision. NS techniques are associated with a reduced incidence of postoperative voiding dysfunction, though transient symptoms may occur in those with pre-existing issues. Pain relief and fertility outcomes are preserved, supporting the therapeutic effectiveness and fertility-optimization potential of NS surgery. Recurrence rates range from 2.1% to 40%, depending on the surgical technique, but are broadly comparable to non-NS approach. While bowel and sexual function improvements are variable, NS appears to

prevent de novo dysfunction in these domains. Further multicentre studies using standardized outcome measures are needed to better define long- term efficacy and functional benefits.
Conclusion

NS surgery for deep endometriosis minimizes postoperative functional impairment without increasing perioperative risks or compromising therapeutic effectiveness and completeness of excision. It maintains a safety and efficacy profile comparable to conventional techniques while potentially reducing the risk of new-onset visceral dysfunction.

Key words
Nerve-sparing surgery, deep endometriosis, functional outcomes

ADENOMYOMECTOMY WITHOUT POST-OPERATIVE MEDICATION FOR SYMPTOMATIC ADENOMYOSIS: A TWO-YEAR FOLLOW-UP STUDY

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Country where research was undertaken: China

Introduction/Background
Adenomyosis is responsible for dysmenorrhea and heavy menstrual bleeding (HMB). Adenomyomectomy is a viable treatment modality for patients with symptomatic adenomyosis who either intend to preserve their uteri or are refractory to medical treatment or contraindicated for long-term medication. However, most adenomyomectomy studies used post-operative medication

Materials and Methods
After informed consent, 102 patients with magnetic resonance imaging (MRI)-diagnosed adenomyosis who complained of severe dysmenorrhea and/or HMB, were refractory to medical treatment and intended to preserve their uteri were recruited. Laparoscopic or laparotomic double- flap adenomyomectomy was performed, followed by symptom evaluation 1, 3, 6, 9, 12, 18, and 24 months after surgery without post-operative medication. MRI and ultrasound evaluation, along with assessment of quality of life (QoL) and sexual function, also were made.

Results
All but 3 patients were followed up for over two years after surgery. Adenomyomectomy significantly and remarkably reduced, starting from the 1st month after surgery, the severity of dysmenorrhea and HMB, as well as the uterine size and CA-125 levels, and elevated serum hemoglobin levels. It also significantly improved QoL per SF-36, and sexual functions per female sexual function index (FSFI). The 1- and 2-year recurrence rate of dysmenorrhea, defined to be visual analog scale (VAS) score of 5 or higher, was 2.0% and 7.8%, respectively. A multivariate analysis identified that the imaging evidence for residual lesions is the only risk factor for recurrence. For HMB, only 2 and 3 patients still reported HMB 1 and 2 years after surgery.

Conclusion
Adenomyomectomy, especially with sufficient radicality, can effectively and substantially relieve symptoms with low recurrence rate for the first two years after surgery, even without post- operative medication. It also significantly improves QoL and sexual functions. Further medication may be justified, but perhaps only for those having a high risk of recurrence.

Key words
Adenomyosis, adenomyomectomy; recurrence

CHARACTERIZATION OF ENDOMETRIAL IMMUNE CELL PROFILES IN INFERTILE PATIENTS WITH ADENOMYOSIS

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Country where research was undertaken: China

Introduction/Background
Adenomyosis, characterized by the invasion of endometrial cells into the myometrium, is linked to infertility due to its impact on endometrial receptivity. Endometrial immune cell adaptation is crucial for preparing the endometrium during the window of implantation (WOI), a process that may be disrupted in adenomyosis.

Materials and Methods
A retrospective study compared endometrial immune cell profiles between infertile women with adenomyosis (ultrasound-diagnosed) and fertile controls. Endometrial samples collected on days LH surge +7~9 and stained for CD56, CD57, CD68, CD163, CD1a, Foxp3, CD8, T-bet, and GATA3 using Bond III Immunostainer. Percentages of immune cells relative to stromal cells were quantitatively analyzed with the HALO Image Analysis System. Group differences were determined using the independent t-test (normal distribution) or Mann-Whitney U test (non-normal distribution).

Results
A total of 120 fertile controls with live births and 153 infertile women with adenomyosis seeking assisted reproductive technology were included. Demographic parameters were similar between the two groups. Compared to fertile controls, women with adenomyosis had significantly higher percentages of endometrial $CD56^+$ NK cells (4.07% vs. 5.01%, $p = 0.0005$), $CD1a^+$ Langerhans cells (0.036% vs. 0.043%, $p = 0.0223$), $CD163^+$ M2 macrophages (0.74% vs. 1.085%, $p < 0.0001$), $CD8^+$ cytotoxic T lymphocytes (1.25% vs. 1.71%, $p < 0.0001$). In contrast, the percentages of $Foxp3^+$ regulatory T cells (0.087% vs. 0.059%, $p < 0.0001$) and T-bet^+ Th1 cells (0.912% vs. 0.803%, $p=0.0423$) were significantly lower in women with adenomyosis. No significant differences were observed for $CD57^+$ cells, $CD68^+$ macrophages, or $GATA3^+$ Th2 cells between the two groups.

Conclusion
The endometrial immune cell profiles during the WOI differ significantly between infertile women with adenomyosis and fertile controls, suggesting that changes in endometrial immune cells are associated with impaired endometrial receptivity in adenomyosis. However, further studies are needed to determine the causal relationship.

Key words
Adenomyosis, endometrium, immune cells

FOXP1 MEDIATING TH17/TREG IMBALANCE AND PROMOTING PROGRESSION OF ENDOMETRIOSIS

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Country where research was undertaken:
China

Introduction/Background
Endometriosis is an estrogen dependent chronic inflammatory disorder. Imbalance of T-helper- 17 (Th17) and Regulatory T (Treg) cells may be involved in pathogenesis of endometriosis. FOXP1 may play a key role in the differentiation of CD4+ T cells. However, the mechanism is unclear.

Materials and Methods
We detected the colocalization and expression of FOXP1, IL-17A+, TGF-βand FOXP3 markers cells in endometrioma and eutopic endometrial tissues using multiplex immunohistochemical. Co-culture with supernatant of FOXP1 high expressed stromal cells in CD4+ T-cells. We upregulated the expression of FOXP1 in Immortalized Human Endometrial Stromal Cells (HESC) to identify the proportion of Treg and Th17 cells. A mouse model of endometriosis was constructed and silenced the expression of FOXP with the CRISPER-Cas9 technology.

Results
We observed increased colocalization and expression of FOXP1 and IL-17A+, decreased of TGF-β, and FOXP3 markers in both endometrioma and ectopic endometrial tissues using multiplex immunohistochemistry and flow cytometry. In co-culture experiments, the supernatant from FOXP1-overexpressing stromal cells significantly influenced CD4+ T cell differentiation. Specifically, upregulation of FOXP1 in both immortalized human endometrial stromal cells (HESC) and primary cultured endometrial stromal cells led to an altered ratio of Treg (FOXP3+) and Th17 (IL-17A+) cells, with a notable increase in the Th17 cells and decrease in Treg cells. Furthermore, in a mouse model of endometriosis where FOXP1 expression was silenced using CRISPR-Cas9 technology, there was a reduction in the Th17 cell proportion and increasing in Treg cells.

Conclusion
In conclusion, FOXP1 upregulation in endometrial stromal cells promotes Th17 cell differentiation, suggesting its role in enhancing inflammation and potentially driving the progression of endometriosis.

Key words
Endometriosis, FOXP1, Th17/Treg cells

ROBOTIC TREATMENT OF CESAREAN SCAR DEFECT ENDOMETRIOSIS – A POSSIBLE NEW SITE OF RETROGRADE MENSTRUATION THEORY OF ENDOMETRIOSIS.

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Country where research was undertaken:
Taiwan

Introduction/Background
This report presents the surgical process and outcomes of a patient with isthmocele (Cesarean scar defect). The retrograde menstruation theory, the oldest explanation for endometriosis, suggests that endometrial cells or debris flow backward through the fallopian tubes into the pelvic cavity during menstruation, contributing to the development of endometriosis.

Materials and Methods
This case report presents a 39-year-old woman who received treatment at our hospital. She had a prior low transverse cesarean section 8 years ago and experienced prolonged dysmenorrhea, dysuria, and infertility for 3 years. After two failed IVF cycles, an ultrasound revealed a 2x1.8x1.0 cm Cesarean scar defect. Robotic repair was performed. The analysis includes a review of outpatient records, hospitalization, surgical details, follow-up history, and laboratory data.

Results
The surgical findings revealed a dense endometriotic mass at the site of the scar defect and extending onto the bladder flap. A purple-colored mass was identified, along with additional areas of endometriosis observed on other pelvic structures. The accompanying surgical video illustrates these findings, demonstrating the extent of pelvic endometriosis.

Conclusion
A previous Cesarean scar defect may serve as a new site for retrograde menstruation, contributing to the development of endometriosis. This theory suggests that endometrial tissue can be transported into the pelvic cavity through the scar during menstruation.

Key words
Theory of endometriosis

THERAPEUTIC EFFICACY OF PRODRUG OF EGCG (PRO-EGCG) IN THE MANAGEMENT OF ENDOMETRIOSIS-ASSOCIATED PAIN (EAP): INSIGHTS FROM THE MURINE MODEL

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Countries where research was undertaken:
Hong Kong SAR, China

Introduction/Background
Endometriosis affects 10-15%[1] of women worldwide, with 50%[2, 3] suffering chronic pain. Current treatments for EAP are limited, mainly nonsteroidal anti-inflammatory drugs (NSAIDs) and hormonal medications[4]. Our previous studies identified Pro-EGCG's effectiveness in inhibiting endometriotic lesion growth. However, further investigation is needed to clarify its potential in alleviating EAP.

Materials and Methods
After the synchronization of estradiol-17β (E2) level through intramuscular injection, endometriosis model was established by surgically transplanting autologous endometrial fragments onto the abdominal wall of 8-week-old female C57BL/6 mice. Once the successfulness of endometriotic model was confirmed on day 28 after surgery, mice were

divided in three groups (n=8/group): negative control (NC), vehicle and Pro-EGCG for therapeutic efficacy exploration. On day 56, mice were sacrificed and lesions were collected for analysis of pain-related marker expression.

Results
Initially, hematoxylin-eosin (HE) staining was used to confirm the presence of endometrial stroma and glands in the lesions. Then, immunohistochemistry (IHC) staining for nerve fiber- related markers (NGF, TRPV1, β-tubulin Ⅲ) was conducted. In the stromal area, the expression levels of these markers were significantly lower in the Pro-EGCG group compared to the NC and vehicle groups. Histological scores were calculated for each marker: NGF [Pro- EGCG: 0.82±0.18; NC: 3.35±1.82, *P*<0.05; Vehicle: 2.74±1.62, *P*<0.05], TRPV1 [Pro-EGCG: 3.93±0.38; NC: 9.82±3.20, *P*<0.05; Vehicle: 12.92±1.18, *P*<0.0001], and β-tubulin Ⅲ [Pro- EGCG: 3.77±1.72; NC: 11.76±3.51, *P*<0.05; Vehicle: 10.86±2.20, *P*<0.001].

Conclusion
Following the establishment of an effective model, HE staining confirmed the presence of endometrial stroma and glands. IHC staining revealed significantly lower expression of pain-related markers NGF, TRPV1, and β-tubulin Ⅲ in the Pro-EGCG group, indicating its potential therapeutic efficacy in EAP alleviation.

Key words
Endometriosis, pain-related, Pro-EGCG

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UTILIZING AI FOR THE IDENTIFICATION AND VALIDATION OF NOVEL THERAPEUTIC TARGETS AND REPURPOSED DRUGS FOR ENDOMETRIOSIS

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Introduction/Background
Endometriosis affects over 190 million women globally. Dysregulated steroidogenesis is one commonly studied mechanism, emphasizing hormonal therapy as an effective treatment for the disease, but their long-term effects still remain unknown. Thus, a pressing, unmet clinical need exists to develop new, effective as well as safe therapeutics for endometriosis.

Materials and Methods
We utilized an artificial intelligence (AI)-driven target discovery platform, PandaOmics, to identify novel druggable targets and analyze approved drugs that could be repurposed to treat endometriosis. To validate these targets, we conducted targeted knockdown experiments using siRNA on proliferation and apoptosis of ectopic endometrial cells both in-vitro and in-vivo. Furthermore, an approved drug was identified as a candidate drug through PandaOmics and evaluated as repurposing drug with therapeutic value in treating endometriosis in-vitro and in- vivo.

Results
We identify two unreported therapeutic targets,

guanylate-binding protein 2 (GBP2) and hematopoietic cell kinase (HCK), along with a drug repurposing target, integrin beta 2 (ITGB2) for the treatment of endometriosis. GBP2, HCK, and ITGB2 are upregulated in human endometriotic specimens. siRNA-mediated knockdown of GBP2 and HCK significantly reduced cell viability and proliferation while stimulating apoptosis in endometrial stromal cells. In subcutaneous and intraperitoneal endometriosis mouse models, siRNAs targeting GBP2 and HCK notably reduced lesion volume and weight, with decreased proliferation and increased apoptosis within lesions. Both subcutaneous and intraperitoneal administration of Lifitegrast, an approved ITGB2 antagonist, effectively suppresses lesion growth. Collectively, these data present Lifitegrast as a previously unappreciated intervention for endometriosis treatment and identify GBP2 and HCK as novel druggable targets in endometriosis treatment.

Conclusion
The study leveraged an AI target discovery platform to analyze transcriptomic datasets from patients with endometriosis and healthy controls. This innovative approach identified multiple novel targets and drug repurposing opportunities, underscoring AI's potential to accelerate the discovery of novel drug targets and facilitate the repurposing of treatment modalities for endometriosis.

Key words
Artificial intelligence, target discovery, drug repurposing

IMMUNOREGULATORY EFFECTS OF A NOVEL PRODRUG OF EGCG (PRO-EGCG) ON MYELOID- DERIVED SUPPRESSOR CELLS (MDSCS) IN ENDOMETRIOSIS

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Countries where research was undertaken:
Hong Kong, China

Introduction/Background
Our previous study demonstrated the critical role of MDSCs in promoting the progression of endometriosis. Additionally, we identified Pro-EGCG as a promising novel treatment to prevent and inhibit the development of endometriosis. However, it remains unclear whether Pro-EGCG exerts its effects by regulating MDSCs in this context.

Materials and Methods
Peripheral blood from EMS patients and controls was analyzed for MDSC subpopulations using flow cytometry. *In vitro*, PBMCs were differentiated into monocytic MDSCs (M- MDSCs) with GM-CSF and IL-6, then purified using CD33 beads. The effects of Pro-EGCG on M-MDSCs were assessed by cell proliferation, apoptosis, and ROS production. *In vivo*, EMS was surgically induced in mice which were treated with 50 mg/kg pro-EGCG or vehicles for 4 weeks. MDSC percentages were compared by flow cytometry.

Results
Compared to non-EMS controls (n=16), EMS patients (n=15) showed a significantly higher percentage of MDSCs ($CD45^+HLA\text{-}DR^-CD33^+CD11b^+$/total cells) (2.938 ± 1.568 % vs 8.625
± 8.437 %, P = 0.0194) and M-MDSCs ($CD14^+CD15^-$/MDSCs) (1.706 ± 0.8249 % vs 11.72 ±
9.104 %, P= 0.0261), with no significant changes in polymorphonuclear MDSCs (PMN-MDSCs) in the peripheral blood. *In vitro*, pro-EGCG treatment reduced MDSC proliferation, induced apoptosis, and lowered ROS levels, suggesting a decrease in their immunosuppressive function. *In vivo*, pro-EGCG significantly reduced lesion size and weight (n=8). Flow cytometry revealed that pro-EGCG treatment decreased M-MDSC ($CD45^+CD11b^+Ly6G^{lo/-}Ly6C^{hi}$) and PMN-MDSC ($CD45^+CD11b^+Ly6G^{hi}Ly6C^{lo}$) populations in both bone marrow and peritoneal fluid, while also lowered PD-L1 expression on MDSCs. No liver cytotoxicity was observed in the treatment group.

Conclusion
Pro-EGCG reduces MDSC populations and their immunosuppressive functions in endometriosis, potentially leading to smaller lesions and inflammatory inhibitions. These findings suggest that pro-EGCG may be a safe and novel promising therapeutic for endometriosis with effective immune modulatory effects.

Key words
Endometriosis, MDSCs, pro-EGCG

CORRELATIONS BETWEEN TSC EXPRESSION AND CLINICOPATHOLOGIC PARAMETERS IN ADENOMYOSIS PATIENTS

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Country where research was undertaken:
China

Introduction/Background
The TSC (tuberous sclerosis) complex plays an important role in endometrial-related diseases[1-3]. Meanwhile, TSC can regulate vascular endothelial growth factor (VEGF) participating in the pathogenesis of adenomyosis[4, 5]. We aimed to investigate the expression of TSC proteins in adenomyosis and determine the correlation between TSC expression and clinicopathologic parameters in patients with adenomyosis.

Materials and Methods
Twenty-one patients with histologically diagnosed adenomyosis were enrolled in this study. Specimens of healthy endometria were obtained from twenty-one patients with cervical carcinoma in situ. Patient characteristics were collected via a standard questionnaire. The severity of dysmenorrhea and menorrhagia was quantified via the visual analogue scale and the menstrual pictogram[6]. Samples of serum and endometrial tissue were collected. TSC and VEGF expression was determined via immunofluorescence, and VEGF expression in the serum was quantified via ELISA.

Results
We found that in patients with AM, epithelial TSC expression was significantly decreased during the secretory phase. Endometrial TSC1 and TSC2, but not TBC1D7, expression was correlated with menstrual volume, VAS score, and uterine volume. Additionally, high levels of VEGFs increased the likelihood of moderate-to-severe menorrhagia in adenomyosis patients.

Conclusion
Our results suggest that TSC may be associated with clinical symptoms such as dysmenorrhea and menorrhagia. In addition, VEGFD may be a potential quantitative predictor during the secretion phase of AM.

Key words
Adenomyosis, TSC expression, menorrhagia

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AREG PROMOTES ENDOMETRIAL REPAIR AND PROLIFERATION

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Country where research was undertaken:
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Introduction/Background
The amphiregulin (AREG) is constitutively expressed by a number of epithelial and mesenchymal cell types. Epithelial-derived AREG promotes tissue repair and integrity. Cessation of menses requires reepithelialisation of the remaining denuded basal endometrium. However, the mechanisms and regulation of endometrial repair are not well understood.

Materials and Methods
Endometrial shedding and repair was simulated in ovariectomised mice. Mice were culled by cervical dislocation at the time of P4-withdrawal (T0) 24or 48 after P4-withdrawal (T24, T48). C57BL/ AREG $^{flox/+}$ PR-CRE $^{+/-}$ mice underwent the simulated menstruation protocol. Uteri of female C57BL/ AREG $^{flox/+}$ PR-CRE $^{+/-}$ mice were collected at T24, T48 and transcriptomes were determined by RNA-Seq. Analysis of two groups (i.e. histological breakdown/repair scores) utilised unpaired t tests where the distribution of data was normal.

Results
AREG $^{flox/+}$ mice have delayed endometrial repair. In contrast, during the repair phase at T24 and T48, the score was significantly lower in AREG $^{flox/+}$ mice versus controls, consistent with delayed endometrial repair. we examined its presence by immunohistochemistry in AREG $^{flox/+}$ versus wild-type mice at T24. CD31 and Ki67 staining was reduced in AREG $^{flox/+}$ mice, consistent with a reduced Estrogen response in these mice. GO and KEGG pathway analyses identified significantly enriched pathways in DEGs, including epithelial cell proliferation, endothelial cell proliferation, vasculature development, regulation of angiogenesis and MAPK signaling pathway, PI3K-Akt signaling pathway and RAS signaling pathway.

Conclusion
AREG-deficient delays endometrial repair. The GO and KEGG analysis revealed that AREG play an important role in the process of endometrial proliferation. Therefore, we identified an important factor that AREG function in endometrial repair and epithelial cell proliferation.

Key words
Endometrial repair, thin endometrium, AREG

SESSION 3B: INDO-AUSTRALIAN SESSION

NEW ZEALAND IS NOT LIKE AUSTRALIA: A COMPARISON OF ENDOMETRIOSIS DIAGNOSIS, MANAGEMENT AND GOVERNMENT POLICY

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Endometriosis is a major global health concern affecting millions of patients. It frequently results in persistent pelvic pain, infertility, and a diminished quality of life. Despite its widespread occurrence, the approach to diagnosis and treatment differs significantly across countries. This presentation explores the commonalities and distinctions in managing endometriosis in New Zealand and Australia, emphasising affected demographics, healthcare expenditures and policy, delays in diagnosis, treatment options, and research funding.

The main comparison points feature healthcare system structures, treatment accessibility and cost, and the efficiency of national policies. The presentation addresses obstacles to prompt diagnosis, such as delays in specialist referrals and surgical access, while also exploring non- invasive diagnostic methods and pelvic pain management. Furthermore, it assesses government funding for research and patient assistance, pinpointing areas for enhancement and partnership between the two countries.

ENDOMETRIAL DNA DAMAGE RESPONSE AND ITS REGULATION BY MBD4 IN ENDOMETRIOSIS

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Country where research was undertaken:
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Introduction/Background
Eutopic (EUE) and ectopic endometrium (ECE) from women with endometriosis are known to experience inflammation, oxidative and proliferative stress. These stimuli can contribute to DNA damage, as evidenced by presence of somatic mutations in EUE and ECE. It remains to be established how ectopic cells proliferate despite expressing DNA damage.

Materials and Methods
RT^2 profiler array was employed to assess the expression of 81 DNA Damage Response (DDR) genes in endometrial stromal cells ($CD10^+$) from paired EUE and ECE samples (n=5; proliferative phase endometrioma). Differentially expressed genes were validated by immunoblotting (EUE, n=32) (endometrium from control (EUC), n=23) and immunofluorescence (EUE, n= 8; EUC, n= 12). DNA damage induced endometrial stromal cell line (tHESC) were investigated for DNA damage (comet assay and H2AX foci) and expression of DDR-genes.

Results
Expression of DDR genes was found significantly higher in the endometrial stromal cells from ECE compared to its paired EUE. Amongst these was Methyl CpG Binding Domain 4 (MBD4), a glycosylase protein of base excision repair (BER) pathway, which recognizes and removes U:G mismatch. Significant higher MBD4 expression was observed in proliferative ($p<0.01$) and secretory phase ($p<0.05$) EUE compared to EUC. Another glycosylase, Thymine DNA glycosylase (TDG) showed no change between EUE and EUC. In-vitro data revealed higher expression of MBD4 in tHESC exposed to DNA damage stimuli (oxidative stress, double stranded break and 17β estradiol). The stimuli contributed to significantly higher number of □H2AX foci. MBD4 silenced tHESC cells exposed to oxidative stress and double stranded breaks, showed reduced □H2AX foci and DNA comet.

Conclusion
Stromal cells from ECE demonstrated higher MBD4 expression compared to EUE. This may have occurred in response to higher DNA damage. EUE also had higher MBD4, compared to EUC. MBD4 silencing impaired DDR. We propose, MBD4 overexpression is an adaptive response to higher DNA damage, likely to promote cell survival.

DEVELOPMENT AND VALIDATION OF AN ARTIFICIAL INTELLIGENCE ENABLED SCREENING TOOL FOR EARLY RISK ASSESSMENT OF ENDOMETRIOSIS IN BANGLADESH

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Country where research was undertaken:
Bangladesh

Introduction/Background
Endometriosis affects 10% of women globally [1]. Lack of awareness, stigma, limited healthcare access cause diagnostic delays, leading to serious consequences. This study aims to develop and validate an artificial intelligence (AI) powered self-administered or community- health-worker-assisted, questionnaire-based screening tool for endometriosis risk assessment, identify risk groups, and refer for further intervention.

Materials and Methods
We conducted thorough literature review, as well as in-depth interviews (IDI) with gynecologists and patients, which helped to develop the questionnaire. Then, we conducted a cross-sectional survey among 100 diagnosed cases from 2 selected hospitals. We convened a consultative validation workshop with a team of gynecologists, epidemiologists and AI experts to enhance and validate the tool. The validated questionnaire integrated into a digital healthcare platform with mobile application tailored to Bangladeshi culture.

Results
We reviewed 77 relevant studies and existing screening tools that help to identify risk factors, major symptoms of endometriosis. IDI ensured the clinical and cultural relevance of our tool. Survey analysis focused on the frequency of responses to questionnaire items, which showed patterns similar with known endometriosis risk factors and symptoms including: 91.9% patients had dysmenorrhea; among married patients 44.4% reported dyspareunia and 37.8% infertility. Additionally, 82.0% had depression; 65.7%, 26.3% and 41.7% of patients experienced irritable-bowel-syndrome-like symptoms, dyschezia and dysuria, respectively. These findings ensured preliminary development and confirmation of the tool's efficiency. Feedback from the validation workshop improved the tool's clarity and applicability, making it suitable for deploying through a digital platform to ensure accessibility for all.

Conclusion
This culturally contextualized, AI-enabled digital platform may serve as a tool for early risk detection, directing risk groups to medical intervention. It has the potential to reduce diagnostic delays and promote early intervention to democratize access to endometriosis care in Bangladesh. Further research is needed to assess its clinical effectiveness.

Key words
Endometriosis, artificial-intelligence, risk-assessment

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LUMWA- LAPAROSCOPIC AND ULTRASOUND GUIDED MICROWAVE ABLATION TECHNIQUE, A UTERUS PRESERVING CONSERVATIVE PROCEDURE IN MANAGEMENT OF ADENOMYOSIS AND ENDOMETRIOSIS

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Country where research was undertaken:
India

Introduction
Adenomyosis along with Endometriosis is a serious gynecological condition affecting the women of reproductive and child bearing age. The most common symptoms seen in these women are dysmenorrhea, menorrhagia, anemia and infertility. It has a serious effect on both physical and mental health of the women. Laparoscopic and Ultrasound guided Microwave Ablation Technique (LUMWA) is an effective fertility preserving procedure in management of adenomyosis with endometriosis.

Aims/Objectives
To evaluate the efficacy of Laparoscopic and Ultrasound guided Microwave Ablation Technique as an effective conservative procedure for fertility preserving and uterus sparing technique in adenomyosis and endometriosis.

Materials and Methods
Prospective clinical study, A 40 year old lady presented with painful periods, heavy bleeding and she was anxious to conceive. She was diagnosed with huge Adenomyoma of vol 400cc and endometriosis. She was treated with Laparoscopic and Ultrasound guided microwave ablation technique as uterine preserving conservative procedure along with endometriosis excision.

Results
Post operative symptomatic relief, 5 months post treatment. Reduction in pain, menorrhagia.

Volume of Adenomyoma has reduced by 50% 5 months post treatment.

Key words
Microwave ablation technique, adenomyosis, endometriosis

LEVONORGESTREL RELEASING INTRAUTERINE SYSTEM (LNG) VERSUS DIENOGEST FOR THE TREATMENT OF ADENOMYOSIS

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Country where research was undertaken:
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Introduction/Background
Adenomyosis is a gynecological condition where endometrial tissue (the lining of the

uterus) grows into the muscular wall of the uterus. It often leads to symptoms like heavy menstrual bleeding, dysmenorrhea (painful menstruation), and pelvic discomfort.

Objective
This study aimed to compare the clinical efficacy of the Levonorgestrel-Releasing Intrauterine System (LNG-IUS) and Dienogest in the management of symptomatic adenomyosis, their effects on pain, menstrual bleeding, and overall patient satisfaction.

Materials and Methods
A prospective, randomized controlled trial was conducted involving 60 women diagnosed with symptomatic adenomyosis. Participants were randomly assigned to receive either the LNG-IUS or oral Dienogest for a period of 18 months. The primary outcomes measured were the reduction in menstrual blood loss, improvement in dysmenorrhea (measured by the visual analog scale), and changes in overall pelvic pain.

Results
LNG-IUS group demonstrated a greater reduction in menstrual blood loss, with 65% of participants reporting amenorrhea or significantly reduced bleeding by the end of the study period, compared to 40% in the Dienogest group. LNG-IUS provided a more consistent reduction in pelvic pain and dysmenorrhea over the 6-month period. Side effects were more common in the Dienogest group, including weight gain, mood swings, and headache .Patient satisfaction was higher in the LNG-IUS group, with 75% reporting a preference for the intrauterine system due to its long-term efficacy and fewer systemic side effects.

Conclusion
Both LNG-IUS and Dienogest are effective in managing the symptoms of symptomatic adenomyosis. LNG-IUS offers superior control of menstrual bleeding, more consistent pain relief, and a better overall safety profile. Dienogest may be considered as an alternative for women who prefer oral therapy .

Key words
Adenomyosis , levonorgestrel , dienogest

FOCAL ADENOMYOSIS OF OUTER MYOMETRIUM – A PHENOTYPE TO BE ADDRESSED DURING DEEP INFILTRATING ENDOMETRIOSIS EXCISION

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Country where research was undertaken:
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Objective
The purpose of this study was to observe the clinical profile and outcomes in patients after complete excision of Focal Adenomyosis of Outer Myometrium (FOAM) and Deep Infiltrating Endometriosis (DIE).

Materials and Methods
Our study was an observational retrospective study in a Multi-disciplinary Endometriosis Care Centre over a period of 18 months which included 30 patients who underwent laparoscopic or robotic excisional surgery for DIE and FOAM by a single surgeon between Nov 2020 to May 2022 at Apollo Hospitals, Hyderabad.

Results
The study group involved patients with a mean age of 30.43years and the mean age of onset of symptoms was 24.47years. On laparoscopy, lesion distribution was noted according to the #ENZIAN scoring system. Peritoneal lesions 42.9%, ovarian involvement on left side in 66% and right ovary in 62.7 % of cases whereas bilateral ovarian involvement was noted in 46.2%. Post-operative Visual Analogue pain Score (VAS) for dysmenorrhoea was noted as 1.1 as compared to pre-operative VAS score of 6.3. Of the 46.2% women who were trying for pregnancy 9.48% of them conceived.

Conclusion
Excision of FOAM along with Endometriosis could have a better reduction in the pain scores and the operative technique of closure after excision of FOAM also ensures that the myometrial thickness is maintained but a larger prospective controlled study is needed to have a consensus regarding the effectiveness of surgical approach of FOAM along with DIE and for better understanding and management of patients with FOAM.

PREGNANCY OUTCOMES IN WOMEN WITH ENDOMETRIOSIS: INSIGHTS FROM A NATIONWIDE STUDY IN INDIA

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Country where research was undertaken:
India

Introduction/Background
Endometriosis globally affects about 10% of women of reproductive age, with impacts on conception and pregnancy outcomes. The present study focused on determining pregnancy outcomes in women with endometriosis across different geographical zones in India and amongst different endometriosis lesion types [superficial peritoneal endometriosis (SUP), ovarian endometrioma (OMA) and deep infiltrating endometriosis(DIE)].

Materials and Methods
A total of 1775 women with surgically confirmed endometriosis were recruited from 18 study sites, across five distinct geographical zones in India from 2020 to 2024, as a part of the Endometriosis Clinical and Genetic Research in India (ECGRI) study. The data was collected using a modified WERF-EPHect Endometriosis Patient Questionnaire (EPQ) and standard surgical form (SSF). Data was analyzed to evaluate pregnancy outcomes based on geographic distribution and lesion types.

Results
About 60%(n=1066) women with endometriosis were recruited at government hospitals and 39.9%(n=709) from private hospitals. Out of 1775 women recruited, 47.8%(n=848) were ever pregnant with the mean age (Standard Deviation) at the time of conception being 26(4.5), 23.1(3.8), 25.8(5.2), 28.4(4.3) and 25.2(4.8) years in the central, north, north-east/east, south and west zone of India, respectively. Pregnancy outcomes included 72% single live-birth, 1% twins/triplets and 26.8% adverse outcomes. Miscarriage (17.1%, n=143) was the most common adverse pregnancy outcome reported in Indian women with endometriosis with the highest proportion in central(29.4%), followed by west(19.3%), east-northeast(18.1%), north(9.5%) and least in the south(8.9%) zone of India. Amongst the different lesion types, women with SUP showed the highest proportion of adverse pregnancy outcomes (36.2%) followed by DIE(30.9 %) and OMA(13.8%).

Conclusion
The first nationwide study in India demonstrates that one in every four pregnancies in women with endometriosis results in an adverse outcome, a two-and-half-fold increase over the general population in India. These findings warrant the need for provision of appropriate obstetric care for women with endometriosis.

Key words
Endometriosis, miscarriage, pregnancy outcomes

ISOLATED OVARIAN TUBERCULOSIS MIMICKING AN ENDOMETRIOMA: A CASE REPORT

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Country where research was undertaken:
India

Introduction/Background
Ovarian tuberculosis presenting as an isolated ovarian mass is a rare form of extra-pulmonary tuberculosis. Most cases are initially diagnosed as ovarian malignancy due to atypical symptoms and similar radiological features. This is the first report of an ovarian tuberculosis mimicking an endometrioma in an infertile woman.

Case Report
A 31-year-old woman with history of regular cycles, BMI 21 presented with primary infertility of 3 years. Vaginal examination revealed a retroverted fixed uterus with right adnexal tenderness.

Her Hb was 10 g/dl and WBC count was 14200cells/mm3. Anti Mullerian Hormone (AMH) was low (<0.3).

Transvaginal ultrasound revealed bilateral retropositioned adherent ovaries. Right ovary showed well-defined thin walled cystic lesion of 4.8 x 3.8 cm with hypoechoic solid intra-cystic component within it suggestive of endometrioma. Left ovary had 2-3 antral follicles. Hysterosalpingography showed bilateral tubal block.

Laparoscopy with hysteroscopy was planned. Chest X-ray was normal. Bilateral adherent

ovaries encased within a fibrous sheet was seen on posterior uterine wall with a right ovarian cyst. While performing adhesiolysis, cheesy material oozed out of the cyst. Histopathology report of paratubal encased cheesy material showed a nodule with caseous necrosis in the lumen and a fibrous wall infiltrated by lymphocytes, epithelioid cells, few histiocytes and an occasional giant cell. Endometrial tissue showed proliferative changes with no granulomas. The findings were compatible with a tuberculous nodule with extensive necrosis in paratubal region.

Patient is presently on anti-tubercular treatment and has been counselled for Invitro fertilization with donor ovum.

Conclusion
Ovarian tuberculosis can present as an ovarian mass mimicking an endometrioma on sonography. Infertility is due to reduced ovarian reserve or complete ovarian destruction. Our case highlights the importance of laparoscopic evaluation for confirmation of diagnosis to ensure immediate and adequate treatment, especially in countries where tuberculosis is endemic.

Key words
Infertility, endometrioma, ovarian tuberculosis

SEMINAR SESSION 7: SO MANY STAGING SYSTEMS; SO MANY PROBLEMS

REDEFINING STAGING OF ENDOMETRIOSIS FROM CLINICAL TO CELLULAR SCIENCE

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Country where research was undertaken:
China

Introduction/Background
Currently, the revised American Society for Reproductive Medicine (rASRM) staging is the most widely used for staging endometriosis, but its limitations are well known. There are several other staging systems, such as the ENZIAN classification, but they often reflect surgical complexity. Arguably, none of them depict the progression of endometriosis.

Materials and Methods
This talk provides an overview of the existing and emerging endometriosis staging systems, focusing on their relationship with the progression of endometriosis. A staging system that reflects the progression of endometriosis would be important to prognostic stratification, treatment guidance, standardization of communication, research and clinical trials, patient counseling, resource allocation, and epidemiological tracking. Evidence in support for the use of lesional fibrosis as an important domain of a staging system is provided.

Results
Research in the last decade has profiled the natural history of endometriotic lesions, which can manifest in different guises, locations, sizes, and colorations. Yet depending on their location and thus different microenvironment, they all undergo repeated tissue injury and repair, resulting ultimately in fibrosis. As a proxy measure of endometriosis progression, the extent of lesional fibrosis correlates closely with lesional “age” in mouse and baboon models, and with the coloration of lesions as well as the density and viscosity of cyst fluid (a surrogacy of the number of bleeding episodes) in human ovarian endometriomas. Quantitated non-invasively by elastography, the extent of lesional fibrosis is also associated with the extent of epigenetic aberrations and vascularity of endometriotic lesions, and correlated positively with the severity of dysmenorrhea.

Conclusion
The extent of lesional fibrosis, which can be quantitated non-invasively by elastography, seems to offer the best proxy for disease progression as of now. It correlates with the extent of epigenetic aberrations and vascularity in lesions, as well as dysmenorrhea severity. It should be incorporated into the future staging system.

Key words
Endometriosis, progression, staging

MIRNA BLOOD-BASED MOLECULAR BIOMARKER AND MICROBIOME ANALYSIS TO DIAGNOSIS ENDOMETRIOSIS: MULTI-OMICS APPROACH

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Countries where research was undertaken:
United States of America and China

Introduction/Background
Endometriosis clinical presentation varies widely, complicating efforts to timely diagnose patients with accuracy. We have employed bioinformatics and machine learning to explore whether data on circulating miRNA biomarkers in blood and the uterine microbiome could serve as a novel diagnostic in patients with histologically confirmed disease pathology.

Materials and Methods
Under IRB approval, uterine tissue biopsies (n=95) and blood serum were obtained from women (n=170) prior to laparoscopy surgery with histology for suspected endometriosis. The endometrial microbiome profile was determined based on barcoded sequencing of the bacterial 16S rRNA gene. Using qPCR, serum levels were measured for a 5-miRNA panel from patients with and without endometriosis based on laparoscopy and histopathology.

Bioinformatic/Random Forest analysis was employed to determine performance in detecting endometriosis compared to histology.

Results
Of 95 uterine tissues, 52 were histologically confirmed to be endometriosis positive. Molecular analysis of the microbiome revealed that 35 of 54 histologically confirmed cases (71%) had an abnormal microbiome composition. When comparing early to late-stage endometriosis, 7 of 10 (87%) and 30 of 44 (68%) cases, respectively, displayed abnormal microbiomes with a higher prevalence of Gardnerella and Streptococcus. Of the 43 endometriosis negative cases, microbiome composition was abnormal in 17 (40%) cases. Serum miRNAs were evaluated using 10 different random forest predication models that yielded an optimal model with 92% AUC based unique menstrual phase as compared to histology with 90% sensitivity, 95% specificity, 88% NPV and 97% PPV. In cases where both miRNA and microbiome were evaluated, combined accuracy of 95% was observed.

Conclusion
Detection of endometriosis with an equivalency to invasive gold-standard methods using circulating miRNAs alone or in combination with microbiome evaluation is both feasible and influenced by menstrual phase at time of sampling. Further studies to better understand the clinical significance of serum miRNA markers and uterine microbiome biosignatures are underway.

Key words
Endometriosis diagnosis, microbiome, machine learning, miRNA

NON-INVASIVE DIAGNOSTIC INNOVATIONS FOR ENDOMETRIOSIS DETECTION: A COMPREHENSIVE APPROACH USING MENSTRUAL BLOOD

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Country where research was undertaken:
Austria

Introduction/Background
Endometriosis affects approximately 10% of women globally and is often diagnosed after 5-10 years. A non-invasive diagnosis is urgently needed to reduce diagnostic delays and improve patient outcomes. Our study introduces a non-invasive diagnostic tool that utilizes mRNA biomarkers found in menstrual blood, enabling early and accurate detection of endometriosis.

Materials and Methods
We analyzed RNA-sequencing patient samples (n=1.142) from endometrium and blood and identified specific biomarkers for endometriosis. In parallel, we conducted experiments on RNA purity and the amount of RNA in menstrual blood by testing various factors, including the collection time point during the menstrual cycle, temperature, stabilizer volume, collection method, and RNA stability over time. We validated our biomarkers with an independent test set (n=19) of menstrual blood using qPCR.

Results
We identified specific biomarkers for endometriosis. We systematically excluded biomarkers due to specificity and sensitivity cut-off of >=70%. Then we ended up with a list of 27 biomarkers, excluding those without physiological relevance, and tested them in menstrual blood. The independent test set

(n=20) confirmed a initial diagnostic accuracy of 93% (100% specificity,75% sensitivity) using qPCR. Parallel experiments examining the potential of menstrual blood as diagnostic sample confirmed RNA purity and amount across varying conditions, including collection time point, temperature, RNA extraction kit, and stabilizer volume. The best combination of these factors was chosen to optimize RNA yield and quality, with menstrual blood RNA remaining stable for up to 7 days. These results highlight the robustness of our approach for non-invasive endometriosis diagnostics, acknowledging the need for larger-scale validation.

Conclusion
The menstrual blood diagnostic kit represents a breakthrough in endometriosis diagnosis, offering women a pain-free, cost-effective, and accurate solution for early detection and treatment. This innovation could significantly reduce the diagnosis time from years to days.

Key words
Non-invasive diagnosis, menstrual blood, biomarkers

MRI OR ULTRASOUND, THAT IS THE QUESTION. IMAGING VS INTRAOPERATIVE FINDINGS; RETROSPECTIVE STUDY FROM THE UK ENDOMETRIOSIS CENTRE

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Objectives
Endometriosis is a chronic inflammatory disease affecting 5-10% of women of reproductive age. Early diagnosis is essential for symptoms' management and reproductive health. Standardised protocols resulted in accurate non-invasive diagnosis of endometriosis using imaging, in particular transvaginal ultrasound (TVUS) and magnetic resonance (MRI).

The aim of our study was to compare the diagnostic accuracy of pre-operative TVUS and MRI for the detection of deep endometriosis (DE) using intraoperative surgical findings as a reference standard.

Methods
We searched a single Endometriosis Centre database between 1.1.2020. and 31.12.2023. to identify patients with DE who underwent laparoscopic surgery. All patients included in the study had either TVUS, MRI or both in the same centre. Scans were done by examiners with a high level of expertise in gynaecological imaging and they were expected to describe location and size of DE. All surgeons were experts in minimally invasive surgery with particular interest in treatment of endometriosis.

Results
We identified 110 DE patients who satisfied the inclusion criteria.

43/110 (39%) had only TVUS, 19/110 (17%) had only MRI and 48/110 (44%) had both tests. The diagnostic performance of was evaluated using AUC (Area Under The Curve) ROC (Receiver Operating Characteristics) metrics, and interpreted as follows: 0.7-0.8 acceptable, 0.8-0.9 good and >0.9 excellent result.

AUC was 0.94 MRI vs 0.95 TVUS for vesicouterine disease, 0.92 MRI vs 0.94 TVUS for ovarian endometriosis, 0.86 MRI vs 0.92 TVUS for uterosacral ligaments deposits, 0.81 MRI vs 0.90 TVUS for rectovaginal septum disease, and 0.95 MRI vs 0.93 TVUS for bowel deposits.

Conclusions
Our study demonstrated comparable performance of MRI and TVUS for the diagnosis of vesicouterine, ovarian and bowel endometriosis whilst TVUS was better for the diagnosis of posterior compartment endometriosis. The study limitations were its retrospective nature and only a minority of patients underwent both TVUS and MRI.

Key words
Deep endometriosis, transvaginal ultrasound, magnetic resonance

ULTRASOUND AS A NON-INVASIVE DIAGNOSTIC TOOL FOR DETECTION OF DEEP ENDOMETRIOSIS USING THE INTERNATIONAL DEEP ENDOMETRIOSIS ANALYSIS (IDEA) TERMINOLOGY

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Countries where research was undertaken:
Belgium, Austria, Hungary, Australia, Italy, Spain, Israel and Switzerland

Introduction/Background
Diagnosing endometriosis remains challenging. Non-invasive diagnosis using imaging techniques increasingly gain recognition. Of these, transvaginal ultrasound (TVS) is considered the first-line imaging technique. The objective was to evaluate the performance of TVS using the International Deep Endometriosis Analysis (IDEA) terminology in the detection of deep endometriosis (DE).

Materials and Methods
Prospective observational international multicenter diagnostic accuracy study involving eight academic centers in eight countries (September 2019 - November 2023). Patients with suspicion of DE were included. The index test was TVS performed in accordance with the IDEA consensus statement. Reference standard was the direct visualization of endometriosis at laparoscopy. Area under the curve (AUC), sensitivity, specificity, positive and negative predictive value (PPV and NPV) were calculated to assess the performance of TVS to detect DE.

Results
1796 consecutive patients underwent a TVS performed according to the IDEA terminology of which 1182 subsequently underwent laparoscopic surgery. Based on direct surgical visualization 1140/1182 (96.4%) had endometriosis, of whom 923/1182 (78.1%) patients presented with DE. For DE overall, the diagnostic performance of TVS was as follows: AUC 0.88 (95% CI 0.85-0.90), sensitivity 95% (95% CI 94%-97%), specificity 80% (95% CI 75%-85%), PPV 95% (95% CI 93%-96%), NPV 82% (95% CI 77%-87%). Sensitivity was highest for bowel DE (87%, 95% CI 83%-90%) followed by left uterosacral ligament (USL) (78%, 95% CI 74%-82%). The sensitivity was lowest for the rectovaginal septum (51%, 95% CI 44%- 58%). Specificity was highest for bladder DE (99%, 95% CI 99%-100%) and lowest for the left USL (87%, 95% CI 84%-89%).

Conclusion
Non-invasive diagnosis of DE with TVS performed in accordance with the IDEA consensus statement has a high diagnostic accuracy. Implementation of the IDEA methodology in daily gynecological practice has the potential to shorten the diagnostic delay and reduce the negative impact of undiagnosed and untreated endometriosis patients.

Key words
Diagnostic accuracy, deep endometriosis, transvaginal sonography

VALIDATION OF A NOVEL PLASMA PROTEIN BIOMARKER TEST FOR DIAGNOSING ENDOMETRIOSIS

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Country where research was undertaken:
Australia

Introduction/Background
Endometriosis is a common gynaecological

condition with gold standard diagnosis normally via invasive laparoscopy. Diagnosis is often delayed due to the lack of non-invasive diagnostic biomarkers. The objective of this study, therefore, was to develop and validate a non-invasive plasma protein biomarker test for the early detection of endometriosis.

Materials and Methods
Plasma samples were obtained from 464 women with laparoscopy/pathology confirmed endometriosis, 132 women with abdominal symptoms but surgically confirmed absence of endometriosis (symptomatic controls) and 153 general population controls without symptomatic endometriosis. A bi-model algorithm was developed to differentiate endometriosis cases from controls, combining age and BMI with the plasma concentration of 10 novel protein biomarkers measured with targeted mass spectrometry. Test scores from 0- 100% are presented as low-, moderate-, or high-risk for endometriosis.

Results
The developed test demonstrated excellent performance for differentiating endometriosis cases from symptomatic and general population controls (area under the receiver operator curve (AUC) 0.93). At the low/moderate-risk cut-off, the test showed high sensitivity (83%) and a high negative predictive value (77%). At the moderate/high-risk cut-off, it exhibited a low false positive rate (4%) and a high positive predictive value (96%). In the internal validation cohort, the test correctly identified 96% of high-risk patients as having endometriosis and 77% of low- risk patients as not having endometriosis.

Conclusion
The developed test provides a non-invasive, accurate method for the early diagnosis of endometriosis, offering significant potential to improve patient outcomes and reduce the economic burden associated with delayed diagnosis and invasive procedures.

Key words
Endometriosis, diagnosis, biomarkers

DIENOGEST IMPACT ON DIE LESIONS AND PROGNOSTIC TREATMENT SELECTION THROUGH GENE EXPRESSION AND HISTOLOGICAL PRESENTATION

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Country where research was undertaken:
Australia

Introduction/Background
Progestins are a heterogeneous group of compounds with varying affinities for steroid hormone receptors, leading to variation in patient response. Dienogest is a fourth-generation progestin with highly selective binding to progesterone receptors. A direct impact on lesions that contributes to its effectiveness has been postulated and leveraged for treatment selection.

Materials and Methods
Using 33 DIE lesions from 10 untreated, 13 Dienogest responders and 10 non-responders we generated sequences from 40,015 nuclei of archival tissue. Cellular composition and gene expression were compared between groups and the impact of treatment and markers of non- response identified. The CMAP database was interrogate with gene signatures to identify therapeutics for non-responders and high throughput drug screening performed on organoid to determine the impact of these drugs on patient derived tissue.

Results
Untreated DIE lesions have a strong inflammatory phenotype with high lymphocyte content (18.5%), that was significantly reduced after Dienogest treatment. This mechanism was mediated through the suppression of epithelial CXCL1, 2 and 4, stromal CXCL12 and 14 and lymphocyte CXCR4 expression. Patients' refractory to DNG had increased gene expression markers for fibrosis mediated by stromal TGFB and epithelial SDC4. Increased fibrosis and non-response could be identified prognostically by H&E staining. Interrogation of the CMAP database strongly support the use of glucocorticoid agonists to target stromal and lymphocyte cells in non-responding lesions. NFKB and HSP90 inhibitors were implicated to target epithelial cells. The impact of NFKB and HSP90 inhibitors Triptolide and Luminespib on endometrial epithelial cells was validated in high content screening of organoids.

Conclusion
Gene signatures and histological appearance of DIE lesions can be utilized for prognostic treatment selection. Glucocorticoid agonist activity was strongly indicated for Dienogest refractory patients. Novel compounds for

epithelial dominated endometriotic lesions were identified. Together this study provides a genuine pathway to stratify the current approach to endometriosis treatment.

Key words
Treatment, progestins, personalized treatment

SEMINAR SESSION 8: FERTILITY FACTS AND FICTION IN ENDOMETRIOSIS

USING SINGLE-CELL TRANSCRIPTOMIC AND 3D MODELS TO STUDY ENDOMETRIAL AND IMMUNE CELLS INTERACTIONS IN ENDOMETRIOSIS

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Country where research was undertaken:
France

Introduction/Background
Endometriosis is associated with increased risks of infertility, pregnancy loss and several pregnancy complications. A defective endometrium and/or immune dysfunction may explain these increased risks. However, the interactions between the different cell types within the endometrium and the maternal fetal interface are not clearly understood, especially in endometriosis.

Materials and Methods
We used single nuclei transcriptomics to study the maternal fetal interface of term human pregnancies with and without endometriosis as well as a mouse model of endometriosis to study the disease impact on the maternal fetal interface early development. In addition, we are developing 3D culture models (organoids, assembloids, Organ-on-chip) to dissect the interaction between immune cells and endometrial cells derived from the menstrual blood of women with and without endometriosis.

Results
We showed that endometriosis affects the maternal fetal interface transcriptome, especially during its early development, with alteration of pathways related to inflammation, proliferation and hormonal response. An immunomodulatory treatment was able to correct these alterations in the mouse model. A specific assessment of the immune cells within the maternal fetal interface revealed alteration of gene expression by endometriosis in particular in myeloid and NK cells. These changes were partially restored by the immunomodulatory treatment. In order to assess endometrium at the window of implantation in endometriosis patients, including its immune cells component, we study the capacity of 3D culture models incorporating various cell types to recapitulate the physiological endometrium from endometriosis affected and unaffected women.

Conclusion
Endometriosis affect pregnancy through an alteration of early maternal fetal interface, affecting cells of both maternal and fetal origin. These may participate in the programming of female offspring genital tract, favoring future endometriosis development and explaining part of the missing heritability.

Key words
Endometrium, maternal fetal interface, immunity

ALTERED OVARIAN STEROIDOGENESIS IN WOMEN WITH ENDOMETRIOSIS UNDERGOING IN VITRO FERTILIZATION: A COMPARATIVE STUDY OF HORMONAL PROFILES IN FOLLICULAR FLUID

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Country where research was undertaken:
Italy

Introduction/Background
Endometriosis is a chronic condition characterized by endometrial tissue outside the uterine cavity, affecting approximately 5% of women of reproductive age, and is frequently associated with infertility. While the correlation between endometriosis and infertility is well known, the underlying pathophysiological mechanisms behind this association remain unclear.

Materials and Methods
The study aims to evaluate ovarian steroidogenesis in women with endometriosis undergoing in vitro fertilization (IVF) compared to women with infertility from other causes. Patients with endometriosis were prospectively recruited and matched with controls. Follicular fluid, aspirated during oocyte retrieval and frozen at -80°C, was analyzed using Liquid Chromatography Tandem Mass Spectrometry (LC-MS/MS) to measure the levels of 15 steroid hormones, including estradiol, progesterone, testosterone, cortisol, DHEA, and others, in both groups.

Results
A total of 166 women were enrolled (83 with endometriosis and 83 controls). No significant differences were found between the groups regarding IVF cycle characteristics. However, significant differences in steroid hormone concentrations in follicular fluid were observed. In women with endometriosis, 11-deoxycortisol and corticosterone were significantly higher, while aldosterone, progesterone, 17-OH-progesterone, and 11-deoxycortisone were significantly lower compared to controls. A subgroup analysis of follicular fluid from the ovary with an endometrioma showed a significant reduction only in 11-deoxycorticosterone. Another analysis comparing hormonal concentrations in women with endometriomas to controls revealed similar patterns to those in the primary analysis.

Conclusion
Follicular fluid in women with endometriosis shows distinct hormonal levels compared to controls, indicating altered steroidogenesis. These findings suggest a systemic, rather than localized, impact on hormone levels. The clinical relevance of this altered ovarian steroidogenesis in ART outcomes remains unclear, requiring further studies to explore potential therapeutic strategies.

Key words
Ovarian steroidogenesis, endometriosis, in vitro fertilization

SERUM ANTI-MULLERIAN HORMONE IS REDUCED IN WOMEN WITH SUPERFICIAL PERITONEAL ENDOMETRIOSIS AND IS ASSOCIATED WITH CHANGES TO CIRCULATING INFLAMMATORY CYTOKINES

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Country where research was undertaken:
United Kingdom

Introduction/Background
In/subfertility is common in women with endometriosis. Levels of anti-Mullerian hormone (AMH) are reduced with ovarian endometrioma (OMA), but whether superficial peritoneal endometriosis (SPE) alters AMH/follicular function is under-researched. Altered systemic inflammation is also implicated in subfertility but correlations with AMH are lacking.

Materials and Methods
Serum and peritoneal fluid (PF) samples were collected from women undergoing laparoscopy for suspected endometriosis and were classified as follows: no endometriosis lesions (n=39, 'controls'/no previous OMA), SPE alone (n=46), and OMA (n=29). AMH (as a measure of follicular activity) was assayed in serum using the picoAMH ELISA, and inflammatory cytokines determined using 13-plex Luminex (serum/PF). Body weight, age and use of hormonal contraceptives (HC) were recorded. Data are described as mean±SD.

Results
All clinical groups were of a similar age (controls 29.23±5.53, SPE 31.17±7.53, OMA 32.00±5.00). In women not using HC, serum AMH levels were reduced with SPE (0.91±0.75ng/mL; p=0.043) and OMA (0.73±0.46ng/mL; p=0.005), compared to controls (1.54±0.99ng/mL). Women with OMA taking HC were older but demonstrated no difference in AMH between groups (controls 1.045±0.66, SPE 1.096±56, endometrioma 1.067±0.63). Serum inflammatory markers were increased in SPE without HC compared to controls: interleukin 17 (4.54±0.37pg/mL vs 3.83±0.42pg/mL; p=0.004), and TNFalpha (4.50±1.30pg/mL vs 2.87±1.55pg/mL; p=0.053) but were unchanged in SPE with HC. Serum PGE2 was lower in SPE with HC (237.5±171.4ng/mL versus control 403.8±259.9ng/mL; p=0.042) but levels were unchanged in matched PF. These data demonstrate AMH, and peritoneal inflammation are altered by HC use in women with SPE.

Conclusion
AMH/follicular function is altered in women with SPE and associated with systemic inflammation. HC use abrogates differences in serum AMH and inflammatory markers with SPE. HC is also effective for modulating endometriosis-associated peritoneal inflammation. Assays are underway to validate these findings in an expanded dataset.

Key words
Fertility, inflammation, anti-Mullerian hormone

DEFINING THE DYSREGULATED HORMONE RESPONSE OF THE ENDOMETRIUM IN PATIENTS WITH ENDOMETRIOSIS

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Country where research was undertaken:
Australia

Introduction/Background
30-50% of women with endometriosis are infertile, likely due to the inability of the endometrium to undergo hormone-induced endometrial remodelling critical in making it receptive to the implanting embryo. The underlying mechanisms remain largely unknown. Our aim was to define the hormone response of endometrial epithelia from women with endometriosis.

Materials and Methods
Endometrial epithelial organoids (EEO) derived from women with (stage I-II and III-IV) and without endometriosis were treated for two days with estradiol-17β (E2) and then either with vehicle control, E2 or E2 and medroxyprogesterone acetate (MPA) for 6 days. Secretome of hormone-treated EEO was analysed by mass spectrometry. Hormone receptors *ESR1*, *ESR2* and *PGR* were examined by RT-qPCR. EEO-stroma co-cultures were established to determine the impact of endometrial epithelia on stromal cell decidualisation in endometriosis.

Results
The basolateral secreted proteome of hormone-treated EEO derived from endometriosis patients was analysed, showing 39 differentially abundant proteins compared to those from healthy patients and between hormone treatments. These included CRISP3 (FC=20.39, P<0.0001), INHBB (FC=8.17, P<0.001), MGAT1 (FC=4.11, P<0.01) and WNT7A (FC=8.46, P<0.05). *ESR1*, *ESR2* and *PGR* expression patterns were altered in EEO from endometriosis patients demonstrating dysregulated hormone signalling. In stromal cells from patients with endometriosis but not without, *PRL* (P<0.0001) and *IGFBP1* (P<0.05) expression significantly decreased in response to E2+MPA in the EEO-stroma co-culture relative to the stromal monocultures.

Conclusion
EEO from endometriosis patients have an altered response to menstrual cycle hormones resulting in an impaired endometrial epithelial secretory transformation. Our results provide potential mechanisms for the inability of the endometrium to become receptive in endometriosis, leading to endometrial infertility. This forms essential foundations for developing treatments targeting endometriosis-associated infertility.

Key words
Endometrium, infertility, organoids

ENHANCING PREGNANCY OUTCOMES IN WOMEN WITH ADENOMYOSIS: THE ROLE OF GONADOTROPIN RELEASING HORMONE AGONIST (GNRHA) PRIOR TO FROZEN-THAWED EMBRYO TRANSFER

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Country where research was undertaken:
Taiwan

Introduction/Background
Adenomyosis is linked to reduced implantation and pregnancy rates, possibly due to impaired endometrial receptivity. Pretreatment with depot GnRHa before frozen-thawed embryo transfer (FET) has shown promise in improving reproductive outcomes by enhancing endometrial readiness. This study investigates whether GnRHa pretreatment enhances pregnancy outcomes in women with adenomyosis undergoing FET.

Materials and Methods
This retrospective cohort study was conducted from 3/2020 to10/2022 with 162 women diagnosed with adenomyosis. Adenomyosis diagnosis was established through surgical history or ultrasound. Participants were categorized into two groups: one receiving a single 3.75 mg dose of depot leuprorelin during the early follicular phase before FET initiation (n=124), and the other without this pretreatment (n=38). Exclusion criteria included premenopausal and menopausal status, intrauterine adhesion, or other persistent uterine abnormalities impacting the implantation process.

Results
Pituitary suppression resulted in lower luteinizing hormone levels (1.20±1.90 vs 3.77±3.88) ($p<0.001$). There were no differences in the number of embryo transfers (1.77±0.93 vs 1.97±0.97), or the proportion of good embryos transferred (78.2% vs 81.6%) ($p>0.05$). Women with GnRHa pretreatment experienced higher implantation rates (36.1% vs 22.7%) ($p<0.05$). While the observed improvement in clinical pregnancy rates was "marginally significant" (54.0% vs 36.8%) ($p=0.06$), this might be worth investigating further or interpreting cautiously in the context of adenomyosis. Although statistically insignificant, GnRHa pretreatment showed associations with a higher live birth rate (42.6% vs 21.1%) ($p=0.09$) and a lower early miscarriage rate (19.2% vs 21.4%) ($p=0.86$). No differences were noted in gestational age at delivery (37.3±3.6 vs 36.3±2.75 weeks) and birth weight (2519±768 vs 2270±433 grams) ($p>0.05$).

Conclusion
Pituitary suppression using depot GnRHa prior to FET significantly increases the pregnancy rate in women with adenomyosis, while demonstrating comparable neonatal outcomes to conventional FET cycles. Further randomized controlled trials are essential to validate the effectiveness of GnRHa and determine the optimal FET protocol for women with adenomyosis diseases.

Key words
Adenomyosis, GnRH pretreatment, FET

ENDOMETRIOSIS INDUCES DNA DOUBLE-STRAND BREAKS AND TRIGGERS APOPTOSIS IN OOCYTES OF PRIMORDIAL FOLLICLES AND ITS INHIBITION BY MELATONIN ADMINISTRATION.

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Country where research was undertaken:
Japan

Introduction/Background
Endometriosis causes ovarian reserve reduction by excessive activation of primordial follicles.[1] We hypothesized that endometriosis causes DNA double-strand breaks (DDSBs) in oocytes of primordial follicles, causing ovarian reserve reduction. This study aims to clarify the signaling mechanism by which endometriosis reduces ovarian reserve and whether melatonin can prevent its reduction.

Materials and Methods
Sixteen patients who had undergone surgery for endometriosis (E) and 12 control women (C) without ovarian pathology were included. Endometriosis model mice (mE) and control mice (mC) were established.[2] Melatonin was administered to mice daily from D3 to D14.

Immunohistochemical studies were performed using ovarian tissue of H2A histone X (γH2AX), phosphorylated-Ataxia Telangiectasia Mutated (pATM), and RAD51 to detect the DDSBs pathways.[3] Apoptosis was detected by TUNEL assay.[4] The positive-stained oocytes were counted and analyzed.

Results
The percentages of γH2AX-positive oocytes were significantly higher in E (62.9%) than in C (4.7%, $p < 0.05$) and mE (87.5%) than in mC (25.0%, $p < 0.05$). The percentage of pATM-positive oocytes was significantly lower in E (11.4%) than in C (25.2%, $p < 0.05$) and mE (18.25%) than in mC (24.75%, $p < 0.05$). The percentages of TUNEL-positive oocytes were significantly higher in E (85.2%) than in C (24.7%, $p < 0.05$) and mE (81.75%) than in mC (20.75%, $p < 0.05$). The percentage of RAD51-positive oocytes was significantly higher in mE (87.0%) than in mC (14.5%, $p < 0.05$). Melatonin administration significantly reduces percentage of γH2AX-positive oocytes (72.1% vs 50.5%, $p < 0.05$) and TUNEL-positive oocytes (83.0% vs 22.0%, $p < 0.05$).

Conclusion
This study proved that endometriosis induces DDSBs and triggers apoptosis in primordial follicle oocytes, which may result in ovarian reserve reduction. Moreover, we also demonstrated that melatonin rescued oocytes from DDSBs and apoptosis in endometriosis model mice, indicating the pharmacological potential of melatonin to prevent ovarian reserve reduction in endometriosis.

Key words
Endometriosis, DDSBs, apoptosis.

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SEMINAR SESSION 9: ENDOMETRIOSIS AT SCALE AND WHAT WE CAN LEARN FROM A LIFE-COURSE APPROACH

INVESTIGATING CAUSES AND CONSEQUENCES OF ENDOMETRIOSIS

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Country where research was undertaken:
Untied States of America

While for the majority of patients with endometriosis the disease itself is localized to the pelvic area, we know that endometriosis results in systemic changes within the body. Various genetic, biological, and epidemiologic risk factors have been associated with endometriosis development and diagnosis and emerging research highlights the importance of incorporating endometriosis heterogeneity in endometriosis risk factor research. Additionally, individuals with endometriosis have been observed to have an increased risk of co-existing conditions, particularly related to pain and the immune system, and later-life health outcomes including several cancers, heart disease, and stroke. However, it is currently unclear if these comorbid conditions are causes or consequences of existing endometriosis or if they develop separately along similar pathways. In addition, mechanisms through which later-life health outcomes may occur for those with endometriosis are not entirely understood. This seminar presentation will delve into risk factors for endometriosis as well as associations with comorbid and later-life health outcomes throughout the lifecourse including implications of endometriosis-specific research challenges in addition to future research opportunities.

Key words
Risk factors, comorbidities, endometriosis

ASSOCIATION BETWEEN CIRCULATING METABOLITES AND ENDOMETRIOSIS RISK: A METABOLOME-WIDE ASSOCIATION STUDY IN A FRENCH POPULATION-BASED COHORT

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Country where research was undertaken:
France

Introduction/Background
Aberrant metabolism involving endocrine and proinflammatory mechanisms may be involved in endometriosis pathophysiology. However, there is limited evidence from population-based prospective studies supporting these hypotheses. We investigated the association between levels of circulating metabolites and lipids and endometriosis risk in a French prospective study.

Materials and Methods
We conducted a case-cohort study with 120 incident endometriosis cases reported as surgically confirmed and 462 non-cases from the French E3N cohort. Pre-diagnostic blood levels of 325 lipids and 92 metabolites were measured by liquid chromatography tandem mass spectrometry and flow injection analysis tandem mass spectrometry. Weighted Cox proportional hazard models were used to estimate endometriosis hazard ratios [HR] and 95% confidence intervals [CI] for a one-standard deviation increase in each normalized metabolite concentration.

Results
A total of 12 lipids and metabolites were associated with endometriosis risk (false discovery rate <0.10). Inverse associations were observed for two bile acids, including glycochenodeoxycholic acid (HR=0.47, 95%CI: 0.32, 0.69) and taurodeoxycholic acid (HR=0.51, 95%CI: 0.32, 0.79). Positive associations were observed for xanthine (HR=1.84, 95%CI: 1.40, 2.42), 3-methyl-histidine (HR=1.53, 95%CI: 1.21, 1.95), four acylcarnitines (C16, C18:1, C16:1 and C12-DC, with HRs ranging from 1.70 to 4.02), two cholesterol esters, including CE(14:1) (HR=1.77, 95%CI: 1.21, 2.57) and CE(20:3) (HR=1.84, 95%CI: 1.27, 2.65), as well as Hex2Cer(d18:1/14:0) (HR=2.22, 95%CI: 1.30, 3.77) and DG(16:0/16:1) (HR=1.84, 95%CI: 1.87, 2.86). Ongoing analyses using machine learning and data dimensionality reduction approaches are performed to identify a metabolic signature associated with endometriosis risk.

Conclusion
These preliminary results suggest that blood lipids and metabolites may play a role in endometriosis pathophysiology and will provide new insights for the identification of disease pathways and biomarkers. Further evaluations are needed to understand the interplay between these metabolites, other biologic measures, lifestyle, and environmental factors.

Key words
Metabolomics, endometriosis risk, prospective study

LINKING CHILDHOOD AND ADULT TRAUMA TO ENDOMETRIOSIS THROUGH OBSERVATIONAL AND GENETIC ANALYSES

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Countries where research was undertaken:
Spain and United States of America

Introduction/Background
While psychological traumas have been associated with the diagnosis of endometriosis[1,2], limited information is available regarding the role of trauma type and interplay with genetic predisposition in this association.

Materials and Methods
Leveraging UK Biobank (UKB), we investigated the effect of different trauma types (childhood maltreatment and interpersonal and contact traumas) in 8,276 endometriosis cases and 240,117 female controls. A latent class analysis (LCA) was used to investigate the co- occurrence patterns of traumatic experiences in cases and controls. Using the largest endometriosis meta-analysis[3] and FinnGen[4] cohort, we conducted genetic correlation and polygenic risk scoring (PRS) analyses to assess

pleiotropy and interactive effects linking traumatic events to endometriosis.

Results
Accounting for sociodemographic factors, we observed that endometriosis cases were more likely to report traumatic experiences (e.g., increased odds of experiencing contact trauma (OR=1.26, 95%CI=1.16-1.37)). Our LCA highlighted an increased association with emotional and physical trauma (8% vs 5%, $p<2.2\times10^{-16}$) and sexual trauma (5% vs 4%, $p=2.9\times10^{-3}$) between endometriosis cases and controls, and more female controls were assigned to the "no trauma" latent class (20% vs 24%, $p=7.4\times10^{-14}$). Our genetic correlation analyses showed pleiotropic relationships between endometriosis and multiple trauma-related outcomes, including posttraumatic stress disorder (meta-analysis rg=0.31, $p=7.1\times10^{-16}$; FinnGen rg=0.26, $p=4.7\times10^{-15}$) and childhood maltreatment (meta-analysis rg=0.23, $p=1.3\times10^{-6}$; FinnGen rg=0.16, $p=1\times10^{-4}$). Endometriosis PRS was associated with increased odds of the disease (beta=0.31, $p<2.2 \times 10^{-16}$), but no interaction was observed with different types of trauma events.

Conclusion
The present study comprehensively investigated the impact of childhood and adulthood traumatic experiences and stressful events on endometriosis. In particular, our findings highlight the potential effect of contact traumas in increasing endometriosis risk. This appears to not interact with genetic predisposition to the disease, suggesting an independent pathogenic mechanism.

Key words
Traumatic experience, polygenic risk score, latent class analysis

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TYPE AND AGE OF MENOPAUSE AMONG WOMEN WITH ENDOMETRIOSIS: A POOLED ANALYSIS OF FIVE COHORT STUDIES

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Country where research was undertaken:
Australia

Introduction/Background
Endometriosis is associated with reduced ovarian reserve, but there is little evidence on the timing of menopause. This study aimed to quantify the association between endometriosis and menopause type (natural and surgical) and age (continuous and categorical).

Materials and Methods
We combined individual-level data from five cohort studies in Australia, Europe, and Japan. Endometriosis was assessed through linked administrative data and self-reported surveys. Surgical menopause was defined as premenopausal bilateral oophorectomy. Fine-Gray subdistribution hazard models were used to assess hazard ratio (HR) of natural and surgical menopause. Age at menopause was determined by age at final menstrual period or age at bilateral oophorectomy. Linear regression models were used to assess mean differences in menopause age. Multinomial logistic regression models were used to estimate relative risk ratio (RRR) for categorical menopause age (<40, 40-44, 45-49, 50-51, 52-54, and ≥55 years).

Results
Overall, 279,948 women were included, with 3.7% having endometriosis and 7.9% surgical menopause. Using a competing risk model, women with endometriosis were less likely to have natural menopause (HR:0.40, 0.33-0.49) while had a 7-fold increased risk of surgical menopause (HR:7.54, 6.84-8.32) compared with those without endometriosis. On average, they experienced natural menopause 0.4 years earlier (-0.46, -0.28). For those who experienced surgical menopause, it was 1.6 years earlier (-1.77, -1.42). They were 1.4 times (RRR:1.36, 1.17-1.57) more likely to experience spontaneous premature ovarian insufficiency (POI: <40 years) and twice (RRR:2.11, 2.02-2.20) as likely to experience premature surgical menopause (<40 years), rather than to have menopause at the age of 50-51 years. They were also more likely to have early natural and surgical menopause (40-44 years).

Conclusion
Long-term monitoring of endometriosis after menopause may be needed as women are at an elevated risk of POI/early menopause and surgical menopause, which have been linked to adverse health outcomes in later life.

Key words
Premature ovarian insufficiency, early menopause, surgical menopause

MUCOSAL IMMUNITY AS A POTENTIAL LINK BETWEEN ENDOMETRIOSIS AND LONG-COVID

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Country where research was undertaken:
United States of America

Introduction/Background
Immune dysregulation is a feature of endometriosis[1]. Despite evidence of increased risk for persistent SARS-CoV-2 (long-covid) in patients with endometriosis[2], the physiological drivers of this association are unknown. We examined salivary immunoglobulins(Ig), the primary feature of mucosal immunity, by endometriosis status and predicted long-covid risk.

Materials and Methods
The Women's Health Study:From Adolescence to Adulthood(A2A) is an ongoing longitudinal observational cohort that enrolled participants with surgically-confirmed endometriosis and clinic+community controls from 2012-2018, collecting WERF EPHect-compliant data and biologic samples[3]. In spring-summer 2023, participants completed a questionnaire focused on COVID-19 and provided saliva using OraSure Oral Fluid Collection Device. Long-covid was defined by USA-CDC criteria. Immunoglobulin phenotyping was performed on samples using the 8-plex Human Ig Isotyping Panel.

Results
Of the 262 participants with saliva Ig measured thus far, 91 (35%) had surgically-confirmed endometriosis and 66 met criteria for long-covid (25%). Prevalence of long-covid was higher in participants with endometriosis (44%) compared to controls (29%). Although largescale differences in levels of salivary immunoglobulins have not yet emerged, endometriosis cases had reduced IgG1 and elevated IgG2. Long-covid was more common in the subset of endometriosis cases not using hormones (71% vs 27%, p=.03 Fisher's exact test). Long-covid cases (endometriosis and controls) not using hormones had elevated IgA (vs. long-covid negative, p=.02, Kruskal-Wallis test). Assay of ~100 additional saliva samples is ongoing as are explorations of Ig levels by hormone use, pelvic pain severity, widespread pain, and comorbid immune conditions. Additional assays will target SARS-CoV-2-specific antibodies.

Conclusion
Altered mucosal immunity in endometriosis can be modified by hormone use. Preliminary results suggest that reduced IgA levels with hormone use may be protective for long-covid. Hormone therapy has previously been shown to decrease salivary IgA in women[4] and risk

of respiratory infections[5, 6]. Complete analysis expected by March 2025.

Key words
Endometriosis, SARS-CoV-2, immunoglobulins

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ASSOCIATION BETWEEN CIRCULATING LEVELS OF PERSISTENT ORGANIC POLLUTANTS AND ENDOMETRIOSIS RISK: A CASE-COHORT STUDY IN A FRENCH POPULATION-BASED COHORT

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Country where research was undertaken:
France

Introduction/Background
Several persistent organic pollutants [POPs] are known endocrine-disrupting chemicals and suspected to influence endometriosis risk in previous cross-sectional studies. However, there is limited evidence from population-based prospective studies supporting this hypothesis. We investigated the association between levels of 42 circulating POPs and endometriosis risk in a French prospective study.

Materials and Methods
We conducted a case-cohort study with 120 incident endometriosis cases and 462 non-cases from the E3N cohort. Pre-diagnostic blood levels of 42 POPs (12 organochlorine pesticides [OCP], five polybrominated diphenyl ethers [PBDE], 14 polychlorobiphenyls [PCB] and 11 per- and polyfluoro alkylated substances [PFAS]) were measured by liquid/gas chromatography and mass spectrometry. Weighted Cox models were used to estimate endometriosis hazard ratios [HR] and 95% confidence intervals [CI] for quartiles of POPs with 75% detection.

Results
Analyses showed positive associations between POPs and endometriosis risk for three PFAS (N-MeFOSAA [HRQ4vs.Q1= 3.46, 95%CI: 1.21, 9.91], PFNA [HRQ4vs.Q1= 4.93, 95%CI: 1.51, 16.08] and PFUnDA [HRQ4vs.Q1= 2.90, 95%CI: 1.01, 8.36]). We also observed inverse associations with endometriosis risk for four PCBs (PCB52 [HRQ4vs.Q1= 0.20, 95%CI: 0.06, 0.73], PCB105 [HRQ4vs.Q1= 0.31, 95%CI: 0.10, 1.00], PCB114 [HRQ4vs.Q1= 0.32, 95%CI: 0.11, 0.93], PCB118 [HRQ4vs.Q1= 0.15, 95%CI: 0.04, 0.59], and sum of dioxin-like-PCBs [HRQ4vs.Q1=0.31, 95%CI: 0.11, 0.92]), one OCP (Hexachlorobenzene [HRQ4vs.Q1= 0.14, 95%CI: 0.03,0.56]), and one PBDE (PBDE99 [HRQ4vs.Q1= 0.23, 95%CI: 0.07, 0.82]). Current analyses using Bayesian Kernel Machine Regression will investigate the joint effect of POP mixtures on endometriosis risk.

Conclusion
These preliminary results support findings from previous case-control studies for PCBs and OCPs and identified novel associations with PFAS and PBDEs. They strengthen evidence involving POPs in endometriosis etiology. Ongoing investigation of mixture effects in the E3N cohort will help understand the complex interplay between POPs and endometriosis risk.

Key words
Circulating persistent organic pollutants, endometriosis risk, prospective study

BURDEN OF SOMATIC MORBIDITY ASSOCIATED WITH A SURGICALLY VERIFIED ENDOMETRIOSIS AT A YOUNG AGE: A REGISTER-BASED FOLLOW-UP COHORT STUDY

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Country where research was undertaken:
Finland

Introduction/Background
Endometriosis is associated with an increased risk of several somatic disorders, including autoimmune, inflammatory, and pain-related disorders with higher utility of healthcare resources. There may be differences in the experience of pain relating to the subtypes of endometriosis. Depression and anxiety are linked to endometriosis and increase overall somatic comorbidity.

Materials and Methods
This longitudinal retrospective register-based cohort study examined hospital care among 2680 women under 25 diagnosed with endometriosis (1998-2012) and 5338 matched reference women. Follow-up continued until 2019, emigration, or death. We analyzed incidence rates, cumulative incidence, and hazard rate ratios (HR) with 95% confidence intervals across 15 somatic disorder groups. Subgroup analyses considered 1) type of endometriosis - ovarian-only (n=601) *vs.* combined (n=2079), and 2) pre-existing depression/anxiety (n=270) vs. none (n=2410).

Results
By a median follow-up of nearly 16 years (IQR 12-19), women reached a median age of 38 (34-42). Compared to the reference cohort, women with endometriosis had higher incidences of somatic disorders. By age 40, infertility affected 38% of women with endometriosis *vs.* 9% of the reference cohort (HR 5.88 [95% CI 5.24-6.61]). Dyspareunia was diagnosed in 3% *vs.* 1% (5.04 [3.32-7.63]), genital infections 24% *vs.* 6% (4.64 [4.03-5.36]), pain symptoms 62% *vs.* 28% (3.27 [3.04-3.51]), and uterine myomas 5% *vs.* 2% (2.73 [2.05-3.63]). Increased incidences were found for celiac disease, migraine, chronic pain, asthma, anemia, cardiovascular issues, and thyroid disorders. Women with ovarian endometriosis had lower HRs for cardiovascular issues, asthma, and pain conditions. Those with pre-existing depression/anxiety had higher HRs for somatic disorders.

Conclusion
Surgical diagnosis of endometriosis at a young age is followed by a burden of somatic disorders, emphasising importance of comprehensive approach to management of endometriosis. The results of this study suggest that pain and mental health may play a key role in the development of subsequent somatic disorders.

Key words
Endometriosis, somatic disorders, comorbidity

SEMINAR SESSION 10: HIGH THROUGHPUT PROFILING FOR IMPROVING ALL ENDOMETRIOSIS OUTCOMES

GENETIC INSIGHTS INTO ENDOMETRIOSIS: DISSECTING SUB-TYPES AND SHARED PATHWAYS WITH CO-MORBID CONDITIONS

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Countres where research was undertaken:
United States of America, United Kingdom, Iceland, Finland, Denmark, Estonia, Poland, Belgium, Netherlands, Italy, Greece, Turkey, Cyprus, Japan, Australia

Introduction/Background
Approximately 50% of endometriosis risk is due to genetics, with 26% linked to common variants. Our previous genome-wide-association-study (GWAS) in 60,674 cases and 701,926 controls identified 49 variants associated with endometriosis, showing larger effects in stage III/IV disease driven by endometriomas, hinting at differential genetic mechanisms underlying potential endometriosis subtypes.

Materials and Methods
We conducted the largest endometriosis GWAS to date, including 94,315 cases and 1,309,106 controls, expanding the International Endometriosis Genome Consortium (IEGC) to 30 studies. Thirteen sub-phenotype-specific GWAS explored macro-surgical and symptom-based endometriosis sub-phenotypes and co-morbid adenomyosis. Across the studies, cases and controls were defined from medical records or surgically-confirmed (57%) or self-reports (43%). Following phenotype-stratified GWAS, shared genetics between endometriosis sub- phenotypes and other gynecologic, cardio-metabolic, inflammatory, autoimmune, chronic-pain conditions and cancers were investigated.

Results
The GWAS analyses have been completed for all 13 phenotypes: (1) overall endometriosis (Cases N=94,315), (2) macro-surgical sub-phenotypes: endometrioma (N=14,469), deep endometriosis (N=4,814), superficial peritoneal lesions only (N=7,083); rASRM stage I/II (N=9,983) and stage III/IV disease (N=18,179), (3) symptomatologic sub-phenotypes: severe dysmenorrhea (N=8,508), dyspareunia (N=4,741), acyclical pain (N=21,176), gastro-intestinal pain (N=4,019), any gynecological pelvic pain (N=22,897) and infertility (N=9,165), (4) adenomyosis (N=3,558) associated signals and their novelty or sharing with endometriosis overall and sub-phenotypes. Results of GWAS meta-analyses illustrating identified novel genetic signatures underlying potential sub-phenotypes of endometriosis will be presented. Genetic correlation and multi-trait GWAS of conditions associated with increased risk in endometriosis patients highlighted shared genetic causal pathways with overall endometriosis and/or particular sub-phenotypes.

Conclusion
Utilising GWAS, we investigated whether there are genetically driven sub-phenotypes of endometriosis. Understanding whether endometriosis is a single progressive condition or condition with multiple genetically-heterogeneous sub-phenotypes will aid in development of targeted treatments, improving diagnostic accuracy, and personalising care for patients by addressing the specific underlying mechanisms of each sub-phenotype.

Key words
Genetics, sub-phenotypes, comorbidities

GENOME-WIDE SCAN FOR STRUCTURAL VARIANTS ASSOCIATED WITH ENDOMETRIOSIS IN 56,230 GENETICALLY DIVERSE PARTICIPANTS FROM THE ALL OF US RESEARCH PROGRAM

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Country where research was undertaken:
United States of America

Introduction/Background
While endometriosis (endo) is known to be 47% heritable, previous genome-wide association studies (GWASs) of common variants have only explained 7% of phenotypic variance. We hypothesize that a portion of the missing heritability may be found in structural variants (SVs) which have not been explored yet for endometriosis.

Materials and Methods
Publicly-available SVs were called in the All of Us (AOU) dataset using the GATK-SV pipeline. We included participants assigned female at birth. Two ICD-code case definitions were tested: endo (En) and endo excluding adenomyosis (EnEx). For variants with MAC > 5 and QUAL > 13, we performed ancestry-stratified GWAS (European, African, Admixed American) and meta-analysis with PLINK, adjusted by age and the first four principal components.

Results
In total, we included 56,230 women with both Electronic Health Record and SV data. The case counts for the meta-analyses were 1,632 for En and 855 for EnEx across all populations. At most 257,452 SVs were tested, yielding a corrected p-value threshold of 1.94 $x10^{-7}$. Seven unique variants were significant in the meta-analysis (three in En, five in EnEx, one overlapping) including four deletions and three insertions. Three variants were intronic to the following transcripts: *AOAH, MR1,* and *ARHGEF10/KBTBD11-OT1.* Four variants fell near transcription start sites for the following genes: *ADGRL3, ETS1, ARRDC4,* and *KCNJ18*.

Conclusion
Our genome-wide analysis of SVs in AOU identified seven novel variants associated with endometriosis. These variants affect genes previously implicated in asthma and tumor pathogenesis, suggesting potential shared biological pathways and expanding our understanding of endometriosis pathophysiology. Future validation and functional studies are warranted.

Key words
Structural variants, genetic study, disease mechanisms

EXOME-WIDE ASSOCIATION STUDY CHARACTERIZES GENETIC BURDEN ASSOCIATED WITH ENDOMETRIOSIS ACROSS DIVERSE POPULATIONS

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Country where research was undertaken:
United States of America

Introduction/Background
Genetic predisposition is a key risk factor for endometriosis, with up to 50% heritability. While genome-wide association studies (GWAS) have identified numerous non-coding variants, the contribution of rare and low-frequency coding variants remains largely unexplored. An exome- wide association study (ExWAS) approach offers a powerful means to uncover the role of these functional genetic variations in endometriosis etiology.

Materials and Methods
We performed an ExWAS in the Penn Medicine Biobank (PMBB) dataset to identify genetic variants associated with wide (W), wide excluding adenomyosis (WEX), procedure confirmed (PCN), and surgically confirmed (SCN) endometriosis. Meta-analyses were conducted separately for European American (EUR), African American (AFR) ancestries, as well as overall, comprising a total of 1,185 cases and 19,249 controls for the W, 426 cases and 19,249 controls for Wex, 376 cases and 5293 controls for PCN and 151 cases and 407 controls for SCN phenotypes.

Results
The ExWAS identified 2 genome-wide significant loci (p-value<2.7e-06; missense variants in *TRIM45* and pLoF/damaging missense varaints in *PPARGC1A*) associated with Wex phenotype in the overall meta-analysis. For the W, PCN, and SCN phenotypes, the analyses uncovered no genome-wide significant associations. However, the top association for PCN was *RTN4RL2* (p-value=1e-06). Further biological characterization of the identified variants is ongoing to elucidate the distinct molecular mechanisms underlying the diverse endometriosis manifestations.

Conclusion
Comprehensive ExWAS across multiple large datasets and ancestral populations revealed distinct genetic architectures for the major endometriosis phenotypes. These findings provide valuable insights into the underlying biology and may inform targeted therapeutic strategies for the diverse clinical presentations of this complex disorder.

Key words
Exome-wide association analyses, BioBanks

TRANSCRIPTIONAL CHARACTERIZATION OF SUPERFICIAL PERITONEAL ENDOMETRIOSIS

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Country where research was undertaken:
United States of America

Introduction/Background
Despite the varying clinical presentation of endometriosis, the molecular heterogeneity of
endometriosis is not well understood. To identify clinically relevant molecular subtypes of superficial peritoneal endometriosis(SPE) and elucidate potential underlying mechanisms that distinguish clinical phenotypes, we assessed the association between pain symptoms and cellular composition of SPE.

Materials and Methods
Using data and samples from the Women's Health Study: From Adolescence to Adulthood(A2A) and Endometriosis in Oxford University(ENDOX) WERF-EPHect- compliant cohorts, we profiled transcriptomes of 50,326 individual cells from 7 SPE samples, identified cell subpopulations and leveraged these results to deconvolute bulk RNA sequencing data from 425 SPE samples using the MuSIC algorithm. We performed agnostic hierarchical clustering to group the SPE samples and evaluated associations with lesion appearance and pain symptoms.

Results
We classified 425 SPE lesions into 6 subgroups defined by cell-type composition and characterized by enrichment for (1)PAX8+ epithelium(PAX8+, CLDN4+, KRT7+), (2)fibroblasts or endometrial stroma(WT-1, COL1A1+, DCN+), (3)myofibroblasts(TAGLN+, ACTA2+), (4) mesothelial cells(MSLN+, CALB2+), (5)myeloid cells(CD163+, CD68+), and (6)endothelial(VWF+, PECAM-1+) and smooth muscle cells(MYL9). Brown appearing SPE lesions were associated with higher prevalence of myeloid cells (32%vs15%,) and lower prevalence of fibroblast-rich classes(34%vs45%,) compared to non-brown appearing SPE lesions. Women reporting moderate/severe dysmenorrhea were more likely to have SPE enriched with endometrial stroma(48%vs42%) and myofibroblasts(11%vs4%) compared to those without, but a lower prevalence of endothelial cells(9%vs20%) while those reporting pain with bowel movement were more likely to have higher myofibroblasts(10%v5%) and endothelial cells(19%vs9%) but less likely to have SPE enriched with fibroblasts(41%vs51%) or myeloid cells(31%vs20%).

Conclusion
We defined six cell-type associated SPE subgroups which correlated with lesion appearance and pain symptoms. This provides insight into the underlying physiology of SPE lesions that could inform personalized treatment or novel therapies. Analyses are ongoing to determine the SPE subgroups associated with other clinical phenotypes.

Key words
Single-cell deconvolution, superficial-peritoneal

SPATIAL TRANSCRIPTOMICS REVEALS INTRA-LESION HETEROGENEITY IN DEEP INFILTRATING BOWEL ENDOMETRIOSIS AND ITS IMPACT ON HOST TISSUE HOMEOSTASIS

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Country where research was undertaken:
Denmark

Introduction/Background
Deep infiltrating bowel endometriosis [DIE] poses significant challenges for research due to its dense, fibrotic, and heterogeneous tissue structure. This study employs spatial RNA profiling to reveal the intra-lesion cellular heterogeneity from the core to the surface of bowel DIE lesions, revealing insights into the impact on host tissue homeostasis.

Materials and Methods
RNA spatial profiling was performed on fresh-frozen bowel biopsies and eutopic endometrium from four DIE patients using the GeoMx Human Whole Transcriptome Atlas. Antibody markers for stromal, epithelial, and smooth muscle cells [SMCs] identified regions of interest spanning lesion core, lesion boundary, and into surrounding healthy bowel tissues to investigate host-lesion interactions. Various R packages were employed to

analyze cellular composition [1], cellular heterogeneity, stage of menstrual cycle [2], and activity of biological pathways.

Results
Cell type RNA expression profiles varied markedly across spatial location within lesions. Cellular composition shifted from the core to the surface of lesions, with immune cells infiltrated in deep, smooth muscle cell-adjacent regions. Distinct stromal and epithelial cell populations were observed along the gradient from lesion core to surface regions, with menstrual phase correlating to cellular content in each region. Highlighting the need for more samples to assess cycle synchronization across eutopic and ectopic cells, menstrual cycle timing appeared unsynchronized within lesions. SMCs near lesion borders exhibit impaired contractility and inflammation. Core and surface regions of larger lesions mimicked the basalis and functionalis layers of the eutopic endometrium in their new environment.

Conclusion
Spatial transcriptomics enables analysis of fibrotic tissues, overcoming limitations of single- cell methods. By revealing intra-lesion heterogeneity, this approach refines tissue sampling and illuminates cell population complexity relative to host tissue. Comprehensive lesion analysis advances our understanding of DIE pathophysiology, improves subtype stratification, and identifies potential biomarkers for more precise diagnosis.

Key words
GeoMx spatial transcriptomics, bowel, DIE

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DECONVOLUTION OF BULK ENDOMETRIAL TISSUE IDENTIFIES CELL-TYPE SPECIFIC GENE REGULATION ASSOCIATED WITH ENDOMETRIOSIS

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Country where research was undertaken: Australia

Introduction/Background
Human endometrium is a complex tissue that undergoes cyclical changes in structure and function in response to circulating steroid hormones. Traditional expression analyses in bulk tissue masks cell-type-specific gene regulation, limiting insights into the influence of individual cell-types and genetic regulation on endometrial function in health and disease**.**

Materials and Methods
We investigated the dynamic changes in the cellular and molecular environment of the endometrium using genotype and endometrial RNA-sequencing data from 206 women with (n=143) and without (n=63) endometriosis across different menstrual cycle phases (menstrual(M) n=14; early-proliferative(EP) n=5; mid-proliferative(MP) n=72; late-proliferative(LP) n=22; early-secretory(ES) n=31; mid-secretory(MS) n=41; late-secretory(LS) n=21). Computational deconvolution methods were used to estimate cell-type proportions and gene expression profiles from endometrium RNA-seq, followed by differential expression and expression quantitative trait loci (eQTL) analysis.

Results
Cell-type proportions in the endometrium varied across the menstrual cycle and were altered in women with endometriosis. Proportions of luminal and ciliated epithelia were significantly (FDR<0.05) lower in women with endometriosis during the MS phase. Differential expression analysis between women with and without endometriosis in the MS phase identified 1,301 differentially expressed (DE) genes in luminal epithelia, 1,108 in stromal fibroblasts, 732 in glandular epithelia, 340 in endothelia and 7 in ciliated epithelia. These included genes associated with endometrial receptivity. DE genes were enriched in RNA metabolism and biogenesis pathways that can mediate fundamental mechanisms of cell proliferation and migration. Incorporating genetic data we identified cell-type-specific eQTLs in endometrium that will be integrated with endometriosis genome-wide association data to identify target genes influencing endometriosis pathogenesis.

Conclusion
Our findings suggests that cell type deconvolution can improve our understanding of the role of cell-type-specific gene regulation in endometrium, offering novel insights into the role of individual cell types in fertility and endometriosis.

Key words
Cell-type-specific, endometrium, gene expression

TOP 24 3MT POSTER PRESENTATIONS

TOP 24 3MT POSTER SESSION 1

NEUROPROLIFERATIVE DYSPAREUNIA IN ENDOMETRIOSIS: A PROSPECTIVE VALIDATION STUDY

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Country where research was undertaken:
Canada

Introduction/Background
Neuroproliferative dyspareunia is a proposed pathophysiologic subtype of endometriosis-associated deep dyspareunia related to increased nerve bundle density around endometriotic lesions. Retrospective studies have shown elevated nerve growth factor (NGF) expression in endometriosis to correlate to surrounding nerve bundle density in patients with higher deep dyspareunia severity due to cul-de-sac/uterosacral tenderness[1,2].

Materials and Methods
A prospective endometriosis registry was linked to blinded immunohistochemical (IHC) scoring of protein-gene-product 9.5 (PGP9.5) nerve bundle density around endometriosis, and NGF expression by endometriosis epithelium/stroma. IHC scores were compared (t-test) between a high deep dyspareunia group [deep dyspareunia ≥6/10, and cul-de-sac/uterosacral tenderness during pre-operative pain mapping], and low deep dyspareunia group [deep dyspareunia ≤5/10, and no cul-de-sac/uterosacral tenderness]. In both groups, participants with bladder/pelvic floor tenderness were excluded to rule out other dyspareunia etiologies[3].

Results
This study involved 126 participants with 247 endometriosis tissue samples across all three anatomic subtypes. Significant correlations were found between PGP9.5 nerve bundle density around endometriosis and NGF expression histoscore, specifically in deep endometriosis (epithelium: r = 0.34, $P < 0.001$; stroma: r = 0.27, $P < 0.01$) and superficial endometriosis (epithelium: r = 0.31, $P < 0.05$), but not in ovarian endometriomas. The phenotyped high deep dyspareunia severity group had a significantly higher mean PGP9.5 nerve bundle density (0.59 (SD: 0.80) vs. 0.22 (SD: 0.29), $P = 0.03$) and mean NGF expression histoscore in the stroma (0.55 (SD: 0.40) vs. 0.35 (SD: 0.19), $P = 0.03$), compared to those in the low deep dyspareunia severity group.

Conclusion
The association between PGP9.5 nerve bundle density around endometriosis and NGF expression by endometriosis was prospectively validated in patients with heightened deep dyspareunia related to cul-de-sac/uterosacral tenderness. Therefore, we propose neuroproliferative dyspareunia as a distinct subtype of endometriosis-associated deep dyspareunia in some patients, with implications for personalized care.

Key words
Dyspareunia, neuroproliferation, NGF

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Williams C, Bedaiwy MA, et al. Phenotyping Sexual Pain in Endometriosis Using the Central Sensitization Inventory. J Sex Med. 2020 Apr;17(4):761–70.

CUMULATIVE LIVE BIRTH RATES IN WOMEN WITH ENDOMETRIOSIS UNDERGOING ASSISTED REPRODUCTIVE TECHNOLOGY (ART) TREATMENT

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Countries where research was undertaken:
Australia and New Zealand

Introduction/Background
Endometriosis is involved in about one in five infertility cases, leading many women to pursue ART to achieve pregnancy. This study aimed to estimate cumulative live birth rates (CLBRs) over multiple ART cycles for women with endometriosis-related infertility, either as the sole cause or combined with other infertility factors.

Materials and Methods
A cohort of 79,318 women who initiated autologous ART treatment between 2014-2019 were extracted from the Australian and New Zealand Assisted Reproduction Database (ANZARD) and followed up to two years or to the first treatment-dependant live birth. Conservative and optimal CLBRs were calculated by assuming either zero probability of live birth for women who discontinued treatment (conservative) or the same probability of live birth as those who continued treatment (optimal).

Results
Endometriosis was reported as the sole cause of infertility in 5% of women, while 8% had endometriosis with additional diagnoses (endometriosis-plus), and 87% had other causes or unexplained infertility. Depending on assumptions made regarding patients who discontinued treatment, the CLBR by the six complete cycles ranged from 64% (conservative) to 83% (optimal) for women with only endometriosis, 54.3% to 68.7% for those with endometriosis- plus, and 57.3% to 76.5% for women without endometriosis. The live birth rate was 6% higher in the endometriosis-only group compared to women without endometriosis (aRR: 1.06; 95% CI: 1.04-1.08), but 5% lower in the endometriosis-plus group (aRR: 0.95; 95% CI: 0.93-0.97). Pregnancy loss was also 46% higher in the endometriosis-plus group compared to women without endometriosis (aRR: 1.46; 95% CI: 1.35-1.59).

Conclusion
Women diagnosed solely with endometriosis have higher chances of ART success than those with endometriosis plus another cause of infertility, and those with other causes of infertility. These results are reassuring for patients with endometriosis and aid in counselling regarding ART success rates.

Key words
Endometriosis, cumulative livebirth

PAIN AND PARTICIPATION: HOW MENSTRUAL SYMPTOMS AFFECT ADOLESCENTS' INVOLVEMENT IN SPORTS AND EXTRACURRICULARS

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Country where research was undertaken:
Australia

Introduction/Background
The relationship between menstrual pain and physical activity is complex. While physical activity can help alleviate menstrual pain, severe symptoms, such as dysmenorrhea, often lead individuals to avoid exercise[1, 2]. The Longitudinal Study of Teenagers with Endometriosis, Period, and Pelvic Pain (LongSTEPPP) examined this association and its impact on sports participation.

Methods:
The LongSTEPPP study recruited adolescents aged 10 to 18 who sought medical care for menstrual or pelvic pain. Participants responded to questions about their pain levels (scores on a scale of 1-10), other symptoms and their involvement in sports and other extracurricular activities. Baseline data from these responses were analysed to explore connections between menstrual pain and

activity participation.

Results
At baseline, 239 adolescents (mean age 15.4 years, SD = 1.8) were recruited. Of the 191 who completed the activity questionnaire, 138 (72.3%) reported regular participation in sports, with up to seven different activities mentioned. Due to pain, 21% of participants reported 'almost always' missing extracurricular activities, such as sports or music, while 33.5% missed them 'often'. Pain was the primary reason (77%), followed by dizziness/nausea (65.4%) and heavy bleeding (52%). Focusing on sports, 45.6% reported often missing at least one regular activity. Higher average pain scores correlated with more frequent absences (mean difference 1.5, 95% CI 0.7-2.4, p<0.001), whilst worst pain scores showed no association (mean difference -0.9, 95% CI -1.9-0.1). Those with lower average pain were more likely to "never" miss sports.

Conclusion
Menstrual pain and associated symptoms disrupt adolescents' lives, causing missed physical and extracurricular activities. Impact of average pain on activities highlights the importance of managing pain across the menstrual cycle. Research focusing on menstrual and pelvic pain, and other symptoms is crucial to reduce absenteeism and improve overall adolescent well- being.

Key words
Pain, adolescents, physical activity

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GLOBAL SPECTRUM OF CLINICAL SYMPTOMS IN ENDOMETRIOSIS: A SCOPING REVIEW

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Country where research was undertaken:
South Africa

Introduction/Background
Endometriosis affects an estimated 10-15% of reproductive-aged women up to and 50% of women with infertility. With no cure and prolonged diagnostic delays, understanding symptomatology is crucial for early detection. This scoping review aims to identify the range of clinical symptoms reported in patients with endometriosis globally.

Materials and Methods
Following the Joanna Briggs Institute (JBI) framework and the PRISMA-ScR guidelines, we reviewed literature published in English over the past 20 years. Searches were conducted in PubMed and Scopus. A two-step screening process was employed, starting with titles and abstracts, followed by full-text reviews by two independent reviewers. The review considered various study designs, including randomized and non-randomized controlled trials, cross- sectional studies, case reports and observational studies. Relevant systematic reviews were also included.

Results
Out of 1286 screened articles, 92 articles met the inclusion criteria. The distribution of studies revealed a higher representation of high-income population groups with lower income groups poorly represented in literature. The results highlight the predominance of case reports (45) and cross-sectional studies (18) in the current literature on endometriosis, reflecting a strong focus on describing individual cases and snapshot prevalence data. Gastrointestinal symptoms, although varied, were commonly reported. The most frequently reported symptoms were dysmenorrhea, dyspareunia and dysmenorrhoea. In addition, the review identified significant variability in symptom prevalence across different regions, emphasizing the impact of cultural, environmental, and healthcare factors on symptom recognition and reporting.

Conclusion
The results underscore the complex and multifaceted nature of endometriosis symptoms, which can vary widely among individuals and populations. The concentration of research efforts in high-income countries suggests a potential disparity in research focus and funding, which may limit the generalizability of findings to diverse populations.

Key words
Endometriosis, pelvic pain, dysmenorrhoea

THE ROLE OF CYTOKINE-CYTOKINE RECEPTOR INTERACTIONS IN ENDOMETRIOMA-RELATED INFERTILITY FROM IN VIVO TRANSCRIPTOMIC ANALYSIS

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Country where research was undertaken:
Hong Kong

Introduction/Background
Ovarian endometrioma (OMA) is a common complication of endometriosis, frequently resulting in infertility. Understanding the molecular mechanisms underlying OMA-related infertility and its impact on ovarian function is essential for developing effective treatments to enhance reproductive outcomes. Addressing these mechanisms may lead to targeted therapeutic strategies for affected individuals.

Materials and Methods
Mouse model of ovarian endometrioma (OMA) was established for RNA sequencing to analyze differentially expressed genes (DEGs), pathways, and potential therapeutic targets by comparing ovaries with endometriotic lesions from OMA and control ovaries (n=5 each, P<0.05). Enrichment analysis of DEGs was conducted using KEGG and GO analyses, supplemented by a literature review of gene functions. Validation of the selected targets was performed through western blotting and qRT-PCR.

Results
The OMA mouse model was successfully established and validated morphologically and histologically. RNA sequencing identified significant upregulation of Chemokine Ligand 17 (Cxcl17) and Interleukin-36 (Il1F6) in the OMA group, which are involved in cytokine-cytokine receptor interactions and activate NF-kappa-B and MAPK signalling pathways, leading to inflammatory responses (P < 0.05). To explore the roles of these DEGs during folliculogenesis, oocytes and granulosa cells (GCs) were collected from OMA mice after superovulation. Expression levels of Cxcl17 and Il1F6 were significantly elevated in GCs, while a non-significant upward trend was observed in oocytes.

Conclusion
The upregulation of the cytokine-cytokine receptor signalling pathway may play a significant role in infertility associated with OMA, highlighting potential cytokine-targeted therapies for improving reproductive outcomes in affected individuals in further research.

Key words
Endometrioma, infertility, cytokine

TOP 24 3MT POSTER SESSION 2

ENDOMETRIOSIS AND CARDIOMETABOLIC DISEASE RISK (ENDCAM): A SINGLE-CENTER RETROSPECTIVE STUDY

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Country where research was undertaken:
Australia

Introduction/Background
Emerging evidence suggests a potential relationship between endometriosis and cardiometabolic disease (CAM). CAM diseases are the leading cause of death in women. This study aimed to link health information from hospital records from a single-center to examine the association between endometriosis and CAM.

Materials and Methods
A retrospective analysis of gynaecology admissions, using international classification of disease (ICD) codes, between 2006-2022 was undertaken. Endometriosis and non-endometriosis groups were defined by presence or absence of endometriosis ICD code(s) at admission, respectively. Data were then examined for CAM ICD codes during same study period. Group comparisons were performed using binomial regression reporting relative risks (RR).

Results
Our dataset included n=23,043 (25.1%) with endometriosis and n=68,923 (74.9%) without endometriosis. The endometriosis group were younger (p-value 0.001). Stratifying by age, individuals in the <25yr category with endometriosis had somewhat increased risk of ever receiving a diagnosis of CAM relative to those without endometriosis (RR 1.45, CI 0.87-2.43). The 40-49yr group with endometriosis also demonstrated slightly increased risk of CAM (RR 1.11, CI 0.99-1.24). Conversely, in the 50+yr category, the endometriosis group had reduced risk of CAM (RR 0.78, CI 0.70-0.87). Hypertension alone similarly displayed increased risk in the endometriosis groups for <25yr and 40-49yr categories (RR 1.80, CI 0.97-3.35, and RR 1.19, CI 1.05-1.36, respectively). The 50+yr category pattern was reversed, hypertension was reduced in the endometriosis group (RR 0.79, CI 0.70-0.90).

Conclusion
Our single-center analysis of >90,000 patients supports a relationship between endometriosis and CAM. The association was dependent on age, with opposite patterns observed in younger versus older (50+yr) age groups. Further research is required to better understand the impact of endometriosis on CAM.

Key words
Cardiometabolic disease, hypertension, age

VERY LONG TERM OUTCOMES OF PATIENTS MANAGED FOR COLORECTAL ENDOMETRIOSIS

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Country where research was undertaken:
France

Introduction/Background
Endometriosis affecting the rectum can significantly impact patients' quality of life, with symptoms often persisting despite treatment. Surgical approaches vary, yet their long-term effects on function, recurrence, and fertility remain underexplored.

This study aimed to present functional outcomes, recurrence rates, and pregnancy likelihood in patients undergoing surgery for colorectal endometriosis with a 15-year follow-up.

Materials and Methods
A retrospective comparative study was conducted. All women who underwent surgery for deep endometriosis infiltrating the rectum at the University Hospital of Rouen from January 2005 to January 2010 were included. The final follow-up evaluation was performed 15 years post- surgery. Postoperative digestive symptoms were assessed using three standardized gastrointestinal questionnaires: the Gastrointestinal Quality of Life Index, the Knowles- Eccersley-Scott Symptom Score for constipation, and the Wexner score for anal continence.

Results
Of the 98 patients who had surgery during this period, 38 completed the 15-year follow-up questionnaire. Twenty-two women underwent conservative rectal shaving, one had a full-thickness excision, and 15 underwent colorectal resection; all surgeries were performed laparoscopically. The mean (SD) follow-up was 199 (17) months. Postoperatively, 30 patients received hormonal treatment for a mean (SD) duration of 147 (54) months. Six patients required reoperation for endometriosis, including four for hysterectomy and two for colorectal recurrence. Of the 21 patients who desired pregnancy after surgery, eight achieved pregnancy through assisted reproductive technology, and four conceived spontaneously. The mean (SD) Low Anterior Resection Syndrome (LARS) score was 16 (10), with four patients experiencing minor LARS and one experiencing major LARS. The mean (SD) Gastrointestinal Quality of Life Index (GIQLI) score was 102 (24).

Conclusion
This study provides the first very long-term follow-up data on colorectal endometriosis surgery, suggesting a low risk of recurrence, with sustained symptom relief and stable gastrointestinal function.

Key words
Colorectal endometriosis, functional outcomes, pregnancy

THE MOST IMPACTFUL SYMPTOM: DEVELOPMENT OF A NEW MEASUREMENT INSTRUMENT FOR ENDOMETRIOSIS CLINICAL TRIALS

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Country where research was undertaken:
Australia

Introduction/Background
The 'most bothersome symptom' was included in a core outcome set for endometriosis, yet no patient-reported outcome measure (PROM) exists to assess it.[1] Previous research found the term 'bother' diminishes symptom experiences, with women preferring 'impact'.[2] This study describes the development of a PROM to measure the 'most impactful symptom'.

Materials and Methods
A two-round, international online survey was conducted to identify symptoms for inclusion in the PROM. Participants were asked to identify the symptoms they had experienced, and which symptom impacted them the most. The survey results informed the development of a draft PROM. The measurement instrument was then pilot tested in iterative rounds with people living with endometriosis to ensure its relevance, comprehensiveness, and comprehensibility. Modifications were made in collaboration with expert clinicians and clinical trialists.

Results
A total of 1178 participants completed the surveys, identifying 118 distinct symptoms associated with endometriosis. Of these, 36 were considered to be the most impactful, with pelvic pain (20%), abdominal pain (15%), and cramps (7%) the most common. Based on these findings, 13 symptoms and one free-text item were included in the draft PROM. Thirty-two cognitive interviews using the Three-Step Test-Interview method were undertaken across four rounds to refine the PROM. Feedback was sought from clinicians and trialists after each round to support its face validity. Content was refined and comprehensibility was evaluated. One item was removed, and four were modified. Participants found the PROM easy to complete and that it could comprehensibly evaluate the most impactful symptom for individuals with endometriosis.

Conclusion
A new PROM to be used in future endometriosis clinical trials has been comprehensively developed. It captures the most impactful symptoms of endometriosis, addressing a major gap in the endometriosis core outcome set. Development followed robust methodology, including input from and testing with people with lived experience of endometriosis.

Key words
Patient-reported outcomes, core outcome set, endometriosis

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THE ASSOCIATION BETWEEN ENDOMETRIOSIS AND GYNECOLOGIC CANCERS IN A PROSPECTIVE COHORT STUDY: THE JAPAN NURSES' HEALTH STUDY.

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Country where research was undertaken:
Japan

Purpose:
Women with endometriosis have an increased risk of ovarian cancer. However, the association between endometriosis and endometrial cancer remains controversial. In the previous cross- sectional baseline survey of the Japan Nurses' Health Study (JNHS), we showed that endometriosis is associated with both endometrial and ovarian cancer. This study evaluated whether endometriosis is related to the risk of endometrial, ovarian, and breast cancers in a large prospective cohort.

Methods:
We identified women with endometriosis based on self-reported data from women who indicated they had been diagnosed with endometriosis before baseline. We used a Cox proportional hazard model to assess associations between endometriosis and the risk of endometrial, ovarian, and breast cancers. We adjusted the hazard ratio (HR) for age, body mass index, parity, lactation, smoking, alcohol consumption, and family history of cancer.

Results
The mean age at the baseline was 41.8 years (standard deviation 8.1 years). After a median follow-up of 14.3 years, we identified 41 endometrial, 18 ovarian, and 270 breast cancers among 14,060, 14,474, and 14,578 eligible women, respectively. Endometriosis did not have a statistically significant association with the risk of endometrial cancer (adjusted HR: 1.30; 95% CI 0.31-5.53) HR breast cancer (adjusted HR: 1.00; 95% CI 0.58-1.73). Endometriosis was strongly associated with ovarian cancer risk (adjusted HR: 6.26; 95% CI 1.87-21.0).

Conclusions:
This study demonstrates that women with endometriosis have an increased risk of ovarian cancer, but the association between endometriosis and endometrial cancer requires further investigation that takes into account the exposure period of endometriosis.

MODELING THE TISSUE MICROENVIRONMENT IN ENDOMETRIOSIS: INSIGHTS FROM A MULTI-CELLULAR 3D CO-CULTURE SYSTEM

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Country where research was undertaken:
United States of America

Introduction/Background
In endometriosis, we noted an upregulation of extracellular matrix (ECM) genes such as osteoglycin (OGN) in endometrium and endometriosis lesions via single cell analysis. Currently, no mechanistic studies have fully elucidated their impact regulating the tissue microenvironment (TME).

Materials and Methods
To address this, we developed a multi-cellular 3D co-culture system combining patient-matched epithelial organoids and fibroblasts with modifiable ECM. By incorporating ECM factors such as collagen I (COL1) and OGN, we modeled the TME to investigate differences between healthy vs. endometriosis patients. Measurements include various organoid growth analyses from time course live imaging experiments. Additionally, we characterized cell-cell interactions utilizing a novel single cell spatial imaging technique called STAMP.

Results
We found that the two ECM factors have differential effects in the co-culture model in terms of organoid growth and fibroblast proliferation. Utilizing single cell RNA-seq we have also identified altered transcriptional signatures induced by ECM modulation. Finally, we profiled the stromal-epithelial interaction using Single-Cell Transcriptomics Analysis and Multimodal Profiling through Imaging (STAMP) experiment.

Conclusion
Taken together, our data suggest that we have a perturbable model that can be used to study

the role of ECM proteins in normal tissue and in the pathogenesis of endometriosis.

Key words
Organoid, ECM, single-cell

USING BIOLOGICALLY RELEVANT MODELS TO ELUCIDATE ROLES OF THE ENDOMETRIOTIC INFLAMMATORY MICROENVIRONMENT, A DRIVER OF ENDOMETRIOSIS-ASSOCIATED OVARIAN CLEAR CELL CARCINOMA

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Country where research was undertaken:
Australia

Introduction/Background
Links between endometriosis and elevated ovarian cancer (OC) risk, particularly ovarian clear cell carcinoma (OCCC), have been reported[1,2]. Endometriotic lesions are observed adjacent to tumour tissue[2], suggesting that the endometriotic microenvironment (ME), driven by stromal cells and inflammatory cytokines, may play roles in the pathophysiology and malignancy of endometriosis-associated OCCC.

Materials and Methods
Conditioned media generated from endometrial stromal cells (ESC) was applied to scratch- wound assays of OCCC cells. Three-dimensional (3D) OCCC cell invasion in the presence of ESCs was investigated with the RASTRUM™ bioprinter (Inventia Life Science), utilising hydrogel matrices relevant to OC ME[3] that incorporated adhesion-peptide motifs and the structural glycoprotein fibronectin. Levels of secreted interleukin-6 (IL-6), interleukin-8 (IL- 8) and monocyte-chemoattractant-protein-1 (MCP-1) were assessed in mono- and co-cultures of OCCC and ESCs using enzyme-linked-immunosorbent-assays (ELISAs).

Results
This study aimed to assess the influence of the endometriotic ME on migratory and invasive behaviours that promote the aggressive, treatment-resistant subtype of OCCC. We confirmed that inflammatory cytokines IL-6 and IL-8 were secreted into the media of mono- and co- cultures of OCCC cells and ESCs. Interestingly, ESC conditioned media, when administered to migrating OCCC cells, enhanced the rate of wound closure across 2D migration assays compared to standard culture media. Bioprinted co-culture models showed significantly increased 3D invasion of OCCC cells when in the presence of ESCs *versus* when bioprinted alone. Importantly, to our knowledge, this finding demonstrated for the first time that bioprinted models were able to successfully emulate aspects of the inflammatory endometriotic ME in co-culture with OCCC.

Conclusion
Our data, utilising biologically relevant models, provides an increased understanding of the role of the inflammation-enriched endometriotic ME in the malignant behaviours of OCCC, potentially unveiling therapeutic opportunities for endometriosis-associated OCs. Notably, these findings may also illuminate mechanisms driving the malignant transformation of endometriosis into OC, revealing avenues for future research.

Key words
Endometriosis-associated ovarian cancers, 3D bio-printing, chemokines

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SURGERY FOR ENDOMETRIOSIS ASSOCIATED PAIN- IS IT REALLY EFFECTIVE?

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Country where research was undertaken:
Israel

Introduction/Background
While surgery is frequently used to manage endometriosis associated pain (EAP), there is scarce data on the effectiveness of surgery for treatment of EAP in women with superficial peritoneal endometriosis (SPE). Hence, we aimed to evaluate whether surgery improves pain symptoms of women with SPE.

Materials and Methods
We conducted a retrospective study including women who underwent surgery for suspected SPE in a tertiary medical center between 2019-2024. Included were women aged 16-45 years with EAP symptoms and negative pre-surgical imaging for deep or ovarian lesions. Pre-surgical demographic and clinical characteristics were compared between women with SPE at surgery and women with laparoscopy negative for endometriosis (LNE). We then compared pain reduction between groups and according to various demographic and clinical factors.

Results
Included were 156 women: 62 with LNE and 94 with surgically proven SPE who underwent excisional surgery. Groups were comparable in age, body mass index (BMI), smoking status, and pain-related comorbidities. There were also no significant differences between groups in pre-surgical dysmenorrhea, non-menstrual pelvic pain, dysuria, dyschezia, dyspareunia, or gastrointestinal symptoms. While EAP symptoms improved 6–12 weeks post-surgery for both groups, the improvement was more prominent in the SPE group, as compared to the LNE group (58.7% vs 79.5%, p=0.02). Improvement was especially notable when pelvic adhesions were divided or when endometriosis lesions were removed from the left pelvic sidewall (p=0.04 and p=0.02, respectively). No association was found between age, BMI, presence of pain comorbidities, lesion quantity and presence of adenomyosis and pain improvement.

Conclusion
Pre-surgical symptoms do not predict of SPE. While surgical treatment yielded relatively high rates of pain improvement in women with and without SPE, rates of improvement were higher for women with SPE. Further studies are needed to better delineate factors that may influence success rates of surgery for SPE.

Key words
Superficial endometriosis, endometriosis associated pain

CREATION OF MULTICELLULAR ENDOMETRIAL AVATARS FOR ENDOMETRIOSIS

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Country where research was undertaken:
Australia

Introduction/Background
In an era of precision medicine, there is a need for *in-vitro* models that reflect the genetic, cellular and pathophysiological hallmarks of individual patients. The endometrium is a complex reproductive tissue that consists of epithelial and stromal cells and is regulated by menstrual hormones. Endometrial organoids, three-dimensional cultures that have been generated from primary tissue and remain genetically stable, provide a novel platform to investigate reproductive disease. While promising organoids have limitations, they are predominantly derived from epithelial origins lack key environmental clues from the surrounding mesenchyme and systemic influence of circulating hormones.

Materials and Methods
In this study, we developed endometrial organoids, compared these to freshly isolated epithelial cells and modeled the endometrial menstrual cycle using sequential estrogen and progesterone treatments. We subsequently incorporated stromal cells to create complex, dynamic endometrial assembloids

Results
Transcriptomic comparison between the freshly isolated epithelial cells and organoids revealed fresh epithelial cells retained menstrual stage characteristics whereas organoids did not. Hormonal treatment of organoids led to changes in PR, AR, ESR1, and ESR2 expression. Recombination of organoids and stromal cells established a 3D structure of epithelial glands surrounded by stromal cells. The integration of ESC into organoid cultures for the construction of 3D assembloids influenced organoid growth, by reducing the total number and increasing the average size of the organoids. Whole-mount immunofluorescence indicated organoids cultured with ESC had a low expression of Ki67 and SSEA1, with significant gene expression changes.

Conclusion
Taken together, these findings demonstrate that assembloids, when exposed to the appropriate hormonal cues, can effectively recapitulate the endometrial environment. They highlight the crucial role of stromal cell contributions and hormonal influence on epithelial function and endometrial pathology. The creation of multicellular, hormone-matured endometrial avatars brings the promise of personalized medicine one step closer.

Key words
Endometrial organoids, stromal cells, assembloids

DOES THE STATUS OF THE POD SLIDING SIGN AFFECT THE PERFORMANCE OF ULTRASOUND TO PREDICT ENDOMETRIOSIS IN ALL LOCATIONS?

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Country where research was undertaken:
Australia

Introduction/Background
There are no published data on whether the status of the pouch of Douglas (POD) impacts the diagnostic test accuracy of transvaginal ultrasound (TVS) to predict deep endometriosis (DE). We aim to assess whether the ability to predict DE (in all locations) is affected by the presence or absence of POD obliteration.

Materials and Methods
This was a retrospective multi-center study. Patients with possible endometriosis who had complete ultrasound, surgical and histological data were included in final analysis. All lesions with maximal diameter in longest plane ≥ 5 mm in size on TVS, for all locations in accordance with the IDEA methodology (uterosacral ligaments, torus uterinus, rectovaginal septum, rectosigmoid, and bladder) were included. The presence of a positive or negative 'sliding' sign (marker for POD obliteration) was also recorded. We then examined the data to assess the diagnostic accuracy of TVS to predict DE when the POD was predicted to be either non- obliterated or obliterated. Reference standard was histological confirmation of endometriosis. The overall performance of ultrasound to predict DE in all locations was determined using sensitivity, specificity, positive predictive (PPV) and negative predictive values (NPV) as well as the area under the receiver operating curve (AUC). Data were analyzed using SAS version 9.4.

Results
283 patients with a total of 546 deep endometriotic lesions were included. The prevalence of POD non-obliteration and obliteration were 34.28% and 65.72%, respectively. TVS predicted DE (when the sliding sign was either positive (non-obliteration) or negative (obliteration) with a sensitivity, specificity, PPV, NPV and AUC: 94.0%, 20.0%, 87.3%, 36.4%, 0.53 and 90.9%, 29.4%, 79.5%, 51.7%, 0.73, respectively.

Conclusion
The presence of co-existing POD obliteration is associated with an improvement in diagnostic performance of ultrasound to predict DE.

Key words
Deep endometriosis, transvaginal ultrasound, diagnostic accuracy

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CONSTRUCTING A 3D MULTICELLULAR FREE-FORMING SPHEROID MODEL FOR INVESTIGATING INFLAMMATION IN ENDOMETRIOSIS

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Country where research was undertaken: Ireland

Introduction/Background
Developing in-vitro models for endometriosis that capture its complex pathology is crucial. Advanced 3D models, such as multicellular spheroids and organoids, better replicate cell-cell interactions, inflammation, and fibrosis characteristic of the disease. These models enable targeted studies on immune responses, inflammation, and treatment efficacy (Grümmer, 2013; García-Ibañez *et al.*, 2020).

Materials and Methods
Secondary endometriotic cell lines were co-cultured with immune-like cells in a non-adhesive platform, creating a free-forming spheroid environment. Cell interactions within the spheroid structure were monitored through image analysis to assess growth kinetics and timeline establishment over 20 days. Scanning Electron Microscopy (SEM) illustrated surface topography, while ELISA quantified the presents of inflammatory cytokines. Histology and immunohistochemistry, further defined the Spheroids cellular organization as well as immune cell phenotype & lipidomic status throughout the study.

Results
Results show rapid 3D spheroid formation within the first 24 hours. Growth kinetics reveal, from 24 hours to day 4–6, spheroids undergo size changes, then contract or increase in density, indicating a stabilization phase, followed by steady growth. SEM analysis provides a 3D view of the spheroids' unique cellular surface, with extracellular matrix observed as a liquid-like coating, suggesting cellular secretion into the external environment. Histology reveals organized structures resembling ectopic lesions, with stromal cells beneath superficial epithelial cells. Immune cell influence disrupts spheroid integrity, leading to disorganized morphology and foam cell formation, a macrophage adaptation in high inflammation. ELISA confirms increased cytokine levels (IL-6, IL-8, TNF-α). By days 10–14, heightened proliferation and reduced cell adhesion releasing individual cells into the surrounding medium.

Conclusion
3D spheroid modeling of endometriosis is an advancing in-vitro approach for studying disease mechanisms. This study aimed to enhance understanding of early immune interactions with secondary endometriotic cells in a 3D environment, simulating activities post-retrograde menstruation and cellular relocation to the peritoneal cavity (Burney and Giudice, 2012; Gołąbek-Grenda and Olejnik, 2022).

Key words
Endometriosis, 3D-modeling, inflammation

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TOP 24 3MT POSTER SESSION 3

A COHORT STUDY OF THE CLINICAL PRESENTATION, DIAGNOSIS AND MANAGEMENT OF ENDOMETRIOSIS IN WOMEN ATTENDING GENERAL PRACTICE IN AUSTRALIA.

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Country where research was undertaken:
Australia

Introduction/Background
One in seven women have endometriosis in Australia. General Practitioners (GPs) are often the first point of contact in the healthcare system. We examined the presentation, diagnosis and clinical management of endometriosis in Australian general practice.

Materials and Methods
This was an open cohort study using MedicineInsight, an Australian general practice research database. Women aged 14-49 years attending general practices between 2011 and 2022 were included. Electronic health records were searched for individuals with a recorded diagnosis of endometriosis. Diagnosis date, encounter reasons, other diagnoses, investigations, medications and reported endometriosis symptoms were extracted as well as relevant GP requested medical imaging and prescribed medications prior to and after endometriosis diagnosis.

Results
Among the cohort of 1,748,114 active patients, 19,704 (1.1%) had a documented endometriosis diagnosis. The most common symptoms identified were pelvic pain (42.1%), dysmenorrhea (23.0%), and fatigue (20.1%). Median time from first symptom onset to diagnosis was 2.5 years (IQR, 0.9-5.6). The most commonly requested medical imaging was pelvic ultrasound (38.5%). Following endometriosis diagnosis, significant increases were evident in the proportion receiving prescriptions for hormonal agents including the levonorgestrel-IUD (4.5% vs 6.3%, p<0.001), and non-contraceptive progestogens (5.2% vs 7.6 %, p<0.001), whereas a reduction was observed for the oral contraceptive pill (41.8% vs 28.9%, p<0.001). Increases in prescriptions for other medications, including opioids (32.0% vs 36.7%, p<0.001), tricyclic antidepressants (6.4% vs 9.9%, p<0.001), and gabapentinoids (3.2% vs 6.4%, p<0.001) were observed.

Conclusion
This study provides unique insights into the presentation and management of endometriosis in the primary care setting and can be used to inform interventions aimed at improving clinical management of this often-debilitating condition.

Key words
Endometriosis, primary care, management

UNVEILING ENDOMETRIOSIS-SPECIFIC EPIGENETIC BIOMARKERS IN MENSTRUAL BLOOD

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Countries where research was undertaken:
France, Spain

Introduction/Background
Currently, diagnostic delay for endometriosis stands at 7 to 10 years, in part owing to lack of clinically validated biomarkers. Our aim is to develop a non-invasive diagnostic test by analysing the DNA methylation patterns in menstrual blood, which is postulated to contribute to aetiopathogenesis of endometriosis1.

Materials and Methods
Menstrual blood samples (42 total: 23 controls, 19 endometriosis) were collected from two hospitals. Our proprietary protocol was used to analyse DNA methylation. To evaluate protocol robustness, initial sample processing was conducted at two locations and at different post-collection timepoints (0-48 hours). Additionally, samples were divided into three batches for library preparation and sequencing to assess protocol reproducibility. Alignments were performed via Bismark and downstream analysis were performed in R using dmrseq.

Results
Differentially methylated regions (DMRs) identified were located in or around genes linked to growth regulation, tissue differentiation, developmental processes and pro-inflammatory
regulation. The identified DMRs were able to classify controls and endometriosis cases detecting a dysregulated signal in endometriosis. We did not find correlation of these DMRs with sample collection and initial processing location, timepoint of processing or library preparation batch and sequencing, pointing to a high robustness of our menstrual blood processing protocol. We are currently working on building a diagnostic model using machine learning to assess the specificity and sensitivity of the test.

Conclusion
We conclude that endometriosis is associated with specific changes in DNA methylation patterns, with the potential to be used as specific disease biomarkers and to elucidate disease aetiology and pathogenesis.

Key words
DNA methylation, endometriosis, menstrual blood.

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EXPOSURE OF OVARIAN CLEAR CELL CARCINOMA, AN ENDOMETRIOSIS-ASSOCIATED MALIGNANCY, TO ENDOMETRIAL STROMAL CELLS INCREASES INFLAMMATORY CHEMOKINES AND PROMOTES CANCER-ASSOCIATED BEHAVIOURS

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Country where research was undertaken:
Australia

Introduction/Background
People with endometriosis are reported to have a 4.2-fold increased risk of developing epithelial ovarian cancer. This increases to over 11-fold for the ovarian clear cell carcinoma (OCCC) subtype, a cancer characterised by mutation of the AT-rich Interaction Domain-1 (ARID1A) subunit of the SWItch/Sucrose Non-Fermentable (SWI/SNF) chromatin remodelling complex[1].

Materials and Methods
We co-cultured OCCC cells (JHOC-5, RMG-1, OVMANA, OVTOKO) with endometrial stromal (ES) cells (T-HESC, 1458[2]). A CRISPR-engineered ARID1A knockout (KO) isogenic panel in RMG-1 cells exposed to conditioned media (CM) collected from ES cells was analysed. Proliferation and viability were assessed using live-cell imaging and MTS assay, respectively. Cell migration was measured by scratch wound and chemotaxis assays. Cytokines were quantitated using the LEGENDplex™ assay and enzyme-linked immunosorbent assays (ELISAs). Western blotting detected chemokine receptors.

Results
Real-time live cell imaging showed statistically significant increased proliferation in RMG-1 and OVMANA cell lines exposed to CM from ES cells, with similar results seen in cell viability assays. Chemotaxis assays showed increased OCCC cell movement towards ES cell CM. Interestingly, CRISPR-engineered ARID1A KO OCCC cells showed increased cell migration relative to ARID1A wild-type OCCC cells when exposed to CM from ES cells. LEGENDplex™ bead-based flow cytometry assay and specific ELISAs showed increased levels of the secreted chemokines interleukin-6 (IL-6) and IL-8 in co-cultures of OCCC and ES cell lines compared to monocultures. Higher levels of the IL-6 receptor (IL-6Rα) were observed by Western blotting in all OCCC lines compared with ES cells. This was the opposite for IL-8Rα and IL-8Rβ.

Conclusion
Close proximity of OCCC cells to ES cells or their CM promotes increased inflammatory chemokines, cancer cell proliferation and migration. Migration of OCCC cells exposed to ES

CM was increased in ARID1A KO cells *versus* wild-type. Drugs targeting chemokines, and/or receptors, may be considered for treatment of endometriosis-associated ovarian cancer.

Key words
Ovarian clear cell carcinoma, chromatin remodelling, chemokines

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"IN THE WEEDS": NAVIGATING THE COMPLEX CONCERNS, CHALLENGES AND CHOICES ASSOCIATED WITH MEDICINAL CANNABIS CONSUMPTION FOR ENDOMETRIOSIS

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Country where research was undertaken:
Australia

Introduction/Background
People with endometriosis report consuming cannabis, either legally or illicitly, for pain and symptom management. However, it's unclear what the drivers and barriers for legal medical consumption in this population are and if cannabis is being consumed with the knowledge of their medical doctor.

Materials and Methods
An international, cross-sectional, online survey was hosted on Qualtrics. People aged between 18-55 with a medical diagnosis of endometriosis who had previously used cannabis in the past 3-months were eligible. Recruitment was conducted via Endometriosis New Zealand, Endometriosis Australia, Endometriosis UK, World Endometriosis Society and Endometriosis Canada. Questions included rationale for use of cannabis, classification of cannabis use, likelihood of continuing use, reasons for stopping cannabis and disclosure of cannabis use to medical professionals.

Results
Eligible responses were received from 889 respondents spanning 28 countries. Illicit cannabis (56.7%) was the most common access pathway. 99% of respondents reported they will continue to utilize cannabis to manage their endometriosis-based symptoms. Most common motivations for cannabis consumption were inadequate pain control (68.6%) and bothersome side-effects of pharmaceuticals (56.3%). Cannabis was viewed as superior to pharmaceuticals both in terms of effectiveness and side-effect profile. Concerns over addiction to cannabis (15.9%) was substantively less than concern over addiction to pharmaceuticals (43.9%). Respondents utilising illicit cannabis were significantly less likely ($p<0.0001$) to disclose cannabis consumption to medical professionals, which poses clinically relevant concerns around potential drug interactions, withdrawal effects from self-initiated reductions in pharmaceutical medications by consuming cannabis and side effects that can be caused by cannabis.

Conclusion
Whilst medicinal cannabis has been legal across numerous international jurisdictions for many years, data suggests that normalisation of this re-introduced medicine is some time away. The impact of stigma, drug driving laws, and judgement by medical professionals have all been identified as barriers to adoption. Non-disclosure of cannabis consumption to medical professionals poses clinically important risks to patients, specifically drug interactions and side-effects.

Key words
Cannabis, endometriosis, stigma

FIRST LAPAROSCOPY IN AN ADOLESCENT AND YOUNG ADULT FEMALE POPULATION AND ITS ASSOCIATION WITH CHRONIC PELVIC PAIN: A SUB-STUDY.

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Country where research was undertaken:
Australia

Introduction/Background
Chronic pelvic pain (CPP) affects up to 26.6% of women, with limited attention to adolescent and young adults (AYA). Laparoscopy is frequently used for diagnosing and treating endometriosis, despite frequently yielding negative findings in AYAs. This study compares the effectiveness of surgical vs non-surgical treatment for CPP in AYA females.

Materials and Methods
This sub-study is part of a prospective trial involving 50 AYA females (aged 16–25) with CPP, comparing surgical (laparoscopy) and non-surgical management. Participants either self- selected (n=31) or were randomised (n=19) into treatment groups. Both groups received medical treatment as part of routine care. Pain reduction, measured by the Numerical Rating Scale (NRS) after 12-months, was the primary outcome. Secondary outcomes included surgical findings, quality of life, and psychological wellbeing changes assessed through validated questionnaires.

Results
Intra-group analysis showed both groups had significant pain reduction at <12 months follow up, with a clinically and statistically significant (<20%) decrease in the surgical group (-24.06%, p<0.01) and a statistically significant decrease in the non-surgical group (-17.74%, p=0.05). Between-group analysis showed surgical intervention was associated with lower scores in distress (-4.55 vs 15.53, p=0.02), depression (-4.8 vs 20.26, p=0.04) and anger (-40.35 vs -22.53, p=0.04), compared to the non-surgical cohort. Endometriosis was histologically diagnosed in 72% of the surgical cohort. Both approaches showed reductions in pain scores and certain psychological outcomes, providing some of the first comparative data for managing CPP in AYAs.

Conclusion
This study provides insights into the management of CPP in AYA females, demonstrating reduction in pain in both surgical and non-surgical interventions after 12 months. Larger AYA studies with more diverse populations and longer-term follow-up are needed to confirm these findings and support their broader application in clinical practice.

Key words
Chronic Pelvic Pain (CPP), Adolescent and Young Adult (AYA), laparoscopy

TOP 24 3MT POSTER SESSION 4

HUMAN-AI COLLABORATIVE MULTI-MODAL MULTI-RATER LEARNING FOR ENHANCED ENDOMETRIOSIS DIAGNOSIS FROM MAGNETIC RESONANCE IMAGING

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Country where research was undertaken:
Australia

Introduction/Background
Endometriosis affects approximately 11% of individuals assigned female at birth, causing pain and infertility[1]. Accurate diagnosis remains challenging, particularly in assessing Pouch of Douglas (POD) obliteration from magnetic resonance imaging (eMRI), a key indicator. Current methods rely heavily on invasive laparoscopy, resulting in prolonged diagnostic delays and increased healthcare costs.

Materials and Methods
We propose HAICOMM, a novel Human-AI collaborative multi-modal multi-rater learning method that integrates clinician and Artificial Intelligence (AI) predictions for POD obliteration classification in T1/T2 MRI. Using a dedicated dataset with imaging and surgery-based labels, HAICOMM employs multi-rater learning to reduce label noise and multi-modal learning to harness both MRI modalities.

Results
The HAICOMM model demonstrated superior performance compared to an ensemble of clinicians and state-of-the-art noisy-label and multi-rater learning methods, achieving a classification accuracy improvement of 14.29% for POD obliteration. Compared to other baseline models, the HAICOMM model can improve both accuracy and area under the receiver operating characteristic (AUROC) by more than 50%. Combining clinician input with

AI predictions enhanced classification consistency and allowed for clinically significant findings even in cases where individual clinician consensus was low. Results indicate that HAICOMM's integration of multi-rater and multi-modal features could effectively replace invasive procedures in preliminary diagnostics, offering a more accurate, cost-effective alternative.

Conclusion
The HAICOMM method marks a significant advancement in non-invasive endometriosis diagnostics by leveraging collaborative multi-modal, multi-rater AI learning. This approach not only improves the accuracy of POD obliteration classification from MRI but also establishes a framework for enhancing diagnostic precision through human-AI synergy.

Key words
Endometriosis, human-AI Collaboration, multi-rater learning

Reference
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PAIN PHENOTYPES IN ENDOMETRIOSIS AND ASSOCIATION WITH QUALITY OF LIFE: A POPULATION- BASED STUDY USING LATENT CLASS ANALYSIS

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Country where research was undertaken:
Canada

Introduction/Background
Phenotyping is an innovative statistical approach in pain. The objective is to identify phenotypes of endometriosis and investigate their association with demographics, clinical characteristics, comorbidities and pain-related quality of life (QoL).

Materials and Methods
This is a cross-sectional, single-center, population-based study conducted in a referral university center for endometriosis. Patients aged 18–50 years diagnosed with endometriosis were consecutively enrolled between January 2020 and April 2024. Latent class analysis was used to identify pain phenotypes. The three-step approach, involving logistic regression models, was applied to assess the associations between the phenotypes and demographics, clinical characteristics, comorbidities and pain-related QoL.

Results
352 patients were included in the analyses. The optimal model identified two homogeneous phenotypes of patients with endometriosis. The two groups had distinct clinical presentations, one (54% of the participants) with more severe and frequent pain symptoms and poorer quality of life; the other (46% of the participants) with mild and less frequent pain symptoms. The high pain phenotype was associated with previous treatment failure, use of pain killers, a family history of endometriosis, a low annual family income, and pain comorbidities (painful bladder, fibromyalgia, migraines, low back pain, irritable bowel syndrome, anxiety, and depression or mood disorders). Phenotype membership was associated with distinct QoL profiles ($p<0.001$). The mean QoL score was higher in the high pain phenotype (59; 95%CI 56–62) compared to the low pain phenotype (33; 95%CI 29–37).

Conclusion
Patients with endometriosis and pelvic pain can be grouped into two distinct and homogeneous phenotypes. Phenotype membership correlated with QoL and associated with the patients' characteristics. These findings will need to be validated in other populations and may inform the development of more specialized or personalized interventions.

Key words
Endometriosis, phenotype, quality of life

EFFECTS OF ENDOMETRIOSIS ON THREATENED MISCARRIAGE: A DOUBLY ROBUST ANALYSES

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Country where research was undertaken:
Australia

Introduction/Background
Endometriosis is a chronic condition where endometrial-like tissue grows outside the uterus, leading to inflammation, pain, and subfertility. Despite growing interest, the association between endometriosis and miscarriage remains inconclusive. This study aimed to examine the association between endometriosis and miscarriage and whether Medically Assisted Reproduction (MAR) has a mediating effect in the relationship.

Materials and Methods
A population-based retrospective cohort study was conducted among 468,778 eligible women who contributed 912,747 singleton livebirths between 1980 and 2015 in Western Australia. We used probabilistically linked perinatal and hospital separation data from the Midwives Notification System and Hospital Morbidity Data Collection databases. Our exposure of interest (Endometriosis) and all the outcomes were ascertained using ICD-9/10 codes. We used a doubly robust estimator to estimate the effect (*average treatment effect)* of endometriosis on threatened miscarriage.

Results
There were 19,476 singleton livebirths among 8,874 women diagnosed with endometriosis. Using a doubly robust estimator, we found pregnancies in women with endometriosis to be associated with an increased risk of threatened miscarriage (relative risk, 2.16, 95% confidence interval, 1.63 – 2.86)**.** The observed association persisted when stratified by the use of Medically Assisted Reproduction (MAR), with a slightly elevated risk among pregnancies conceived spontaneously (RR, 2.36, 95% CI, 1.63- 3.42). MAR does not modify but mediates the association between endometriosis and miscarriage. Our causal mediation analyses suggest that 34% of the effect of endometriosis on miscarriage was mediated through MAR.

Conclusion
In this large population-based cohort, endometriosis is associated with an increased risk of threatened miscarriage and the effect is mediated through MAR**.** The study paves the way for future research on mechanisms underlying the relationship between endometriosis and threatened miscarriage.

Key words
Endometriosis, miscarriage, medically assisted reproduction

CESAREAN SECTION AND PARITY AS RISK FACTORS FOR RECURRENCE OF ENDOMETRIOSIS

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Country where research was undertaken:
China

Introduction/Background
The recurrence rate of endometriosis after surgery is approximately 20% to 30% within 5 years. Known risk factors for recurrence include the size of endometriotic lesions, the type of surgical intervention and the presence of ovarian cysts at the time of surgery. Endometriosis, an inflammatory condition, shares similarities with inflammation following cesarean section and surgical suction. Previous studies have reported no association of cesarean sections and the initial development of endometriosis. However, whether the previous cesarean section and surgical suction are associated with the recurrence remain unexplored. In this study, we investigated the association of parity, previous cesarean section and surgical suction, and the recurrence of endometriosis.

Materials and Methods
We included 1,400 women diagnosed with endometriosis at our hospital. Data on parity, gravidity, mode of delivery, age at diagnosis, age at previous delivery, and age at previous diagnosis of endometriosis were collected and analysed.

Results
In total, 98 women developed recurrent endometriosis. After adjusting for age, we found that previous cesarean section(s) significantly increased the recurrence of endometriosis by 90% (p=0.006), compared to vaginal delivery. The median duration for

developing recurrent endometriosis following a cesarean section was 7 years (ranging from 1 to 22 years). Additionally, in total of 1400 cases, 975 women previously had a live birth. We found that a previous live birth was associated with an 80% increased risk of recurrence compared to nulliparous women (p=0.001). The median time to onset of endometriosis after live birth(s) was 12 years, ranging from 1 to 32 years. However, previous surgical suction(s) was not associated with the recurrence of endometriosis.

Conclusion
Although endometriosis recurrence after surgery is common, our study suggests that both previous cesarean section and live births significantly increase the risk of recurrence.

Key words
Recurrence, cesarean section, parity

POSTER SESSION 1

THEME: ADENOMYOSIS

CHARACTERIZING THE GENETIC AND BIOLOGICAL DIFFERENCES BETWEEN ENDOMETRIOSIS AND ADENOMYOSIS USING THE UK BIOBANK

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Country where research was undertaken:
United Kingdom

Introduction/Background
Adenomyosis and endometriosis produce similar debilitating symptoms, including dysmenorrhea. However, they differ in the underlying pathology. In endometriosis, endometrial tissue growth occurs outside the uterus, while in adenomyosis, it invades the uterine walls. We aimed to identify genetic signatures in both diseases and evaluate the genetic and biological differences.

Materials and Methods
This study applied combinatorial analytics to 2 case cohorts derived from the UK Biobank, using ICD-10 codes to designate adenomyosis or endometriosis case status. Both case groups were compared against healthy female controls without chronic gynecological disease to identify combinations of SNPs (single nucleotide polymorphisms) that were significantly associated with either adenomyosis or endometriosis. Where distinct genetic differences were found, further investigation was conducted to elucidate the biological mechanisms driving adenomyosis.

Results
Combinatorial analysis of the adenomyosis case-control dataset revealed 171 disease-associated SNP combinations (genetic signatures'), mapping to 22 protein-coding genes. Nine of these genes appeared in both adenomyosis and endometriosis analyses, though in different combinations of SNP signatures. Among them, three genes—*CDH4*, *MPPED2*, and *PPARG*—have also been associated with endometriosis in prior GWAS studies. Genes uniquely linked to adenomyosis in this study have not been identified in previous endometriosis GWAS or non-genomic studies, suggesting novel pathways. Many of these genes are involved in uterine function, particularly through estrogen signaling, and have connections to endometrial cancer, pregnancy, and fertility.

Conclusion
Adenomyosis remains challenging to diagnose. This research provides valuable insights into the genetic risk factors and pathophysiological mechanisms underlying the disease, potentially improving diagnostic and therapeutic approaches in adenomyosis.

Key words
Adenomyosis, genetics, precision medicine

ESTROGEN REGULATES SCRIBBLE LOCALIZATION IN ENDOMETRIAL EPITHELIAL CELLS THROUGH ACYL PROTEIN THIOESTERASE (APT)-MEDIATED S-PALMITOYLATION IN ADENOMYOSIS

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Country where research was undertaken:
China

Introduction/Background
Despite its prevalence and the severity of symptoms, little is known about the pathogenesis and etiology of adenomyosis. Our research is to reveal the effect and mechanism of estrogen on polarity protein

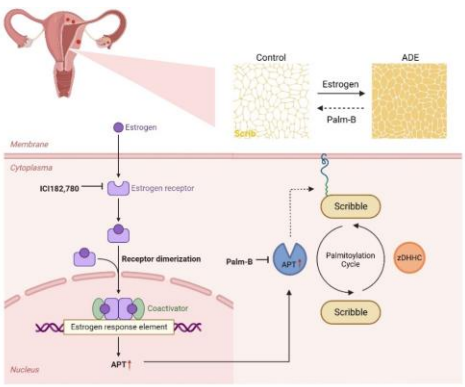
Scribble localization in endometrial epithelial cells

Materials and Methods
Scribble localization in adenomyosis patients and tamoxifen-induced adenomyosis mice was verified using IHC. After treatment with estrogen for 48H, cytoplasmic enrichment of Scribble and the level of palm-Scribble was observed by immunofluorescence, Western blot, and ABE palmitoylation assay. RT-PCR and western blot was conducted for screening and verification of PATs or APTs induced by estrogen. IHC was performed to verify the expression of APT1 and APT2 in adenomyosis patients and their correlation with estrogen production was analyzed by Pearson correlation test.

Results
Scribble translocation from the basolateral membrane to the cytoplasm was easily to be seen in women and mice with adenomyosis (68% vs 27%, 60% vs 10% separately). High estrogen exposure could not only induce partially cytoplasmic translocation of Scribble but also decrease the expression level of palm-Scribble. Instead of PATs, APTs played an important role in regulation of Scribble localization through its S-palmitoylation. Finally, the expression of APT1, APT2 and aromatase P450 in human specimens was all found to be increased dramatically, as well as positive correlations between APT1 or APT2 and aromatase P450.

Conclusion
Estrogen-induced Scribble mislocalization in endometrial epithelial cells through APT-mediated S-palmitoylation might be one of the key mechanisms in the development of adenomyosis, which may provide a new understanding of the pathogenesis of adenomyosis.

Key words
Estrogen, scribble, S-palmitoylation



IMAGES SHOWING ONE REASON WHY THE INCIDENCE OF UTERINE RUPTURE DURING PREGNANCY AFTER ADENOMYOMECTOMY IS HIGHER THAN AFTER MYOMECTOMY

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Country where research was undertaken:
Japan

Introduction/Background
The risk of uterine rupture during pregnancy increases after surgery on the uterine myometrium, such as cesarean section, myomectomy, or adenomyomectomy. The rate of uterine rupture during pregnancy after adenomyomectomy (1-4) has been reported to be several times higher than after myomectomy (5-8). One possible cause is shown in the figure.

Materials and Methods
Two types of T2-weighted magnetic resonance (MR) images are presented. The first type is T2-weighted MR images of the uterus with uterine fibroids or adenomyosis. The second type of T2-weighted MR images presents the normal myometrial areas in the first MRI images in green and the uterine fibroids or adenomyosis areas in black. Complete removal of uterine fibroids or adenomyosis means removing the areas shown in black. The remaining normal myometrium is sutured and repaired.

Results
In the type 2 MR images, most of the normal myometrium (green area) remains after uterine myomectomy. However, after adenomyomectomy, the amount of normal myometrium (green area) appears to be reduced. It is thought that the reduced amount of myometrium will not return to its original total amount. Therefore, pregnancy after adenomyomectomy is more likely to cause uterine contractions and uterine rupture before full term than pregnancy after uterine myomectomy.

Uterine rupture during pregnancy can threaten the baby's life and sometimes the mother's life (8-10). Therefore, close management is considered necessary during pregnancy after adenomyomectomy.

Conclusion
After myomectomy, most of the uterine myometrium remains, however, after adenomyomectomy, the normal myometrium tends to be reduced. Therefore, the risk of uterine rupture during pregnancy after adenomyomectomy is considered higher than after myomectomy, and close management is considered necessary during pregnancy after adenomyomectomy.

Key words
Adenomyomectomy, pregnancy, uterine rupture

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A CASE-CONTROL STUDY OF ENVIRONMENTAL CHEMICAL EXPOSURE AND ADENOMYOSIS RISK

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Country where research was undertaken:
United States of America

Introduction/Background
Adenomyosis, characterized by the presence of endometrial glands and stroma within the myometrium, can confer debilitating symptoms. As estrogen is central to disease pathogenesis, environmental chemicals that are endocrine disruptive may alter adenomyosis risk. Yet, only one study has investigated a single chemical class and adenomyosis risk.

Materials and Methods
Among female enrollees ages 18-59 of an integrated healthcare system in Washington State, cases had incident, pathology-confirmed adenomyosis diagnosed 2001-2006 (n=386). We employed two control groups: randomly selected age-matched enrollees with intact uteri (“population controls”, n=323) and hysterectomy controls (n=233). Data on occupational and non-occupational exposure to chemical groups were collected by in-person interview. We conducted logistic regression to estimate adjusted ORs and 95%

CIs, comparing cases to population and hysterectomy controls.

Results
Our data suggested increased adenomyosis risk with ever exposure to epoxy resins (cases vs. population controls: OR 1.8, 95%CI: 0.9-3.6; hysterectomy controls: OR 1.4, 95%CI: 0.7-2.9) and heavy metals (population controls: OR 1.5, 95%CI: 0.8-2.7; hysterectomy controls: OR 2.0, 95%CI: 1.0-4.1). Our data also suggested twice the risk of adenomyosis with lead exposure (population controls: OR 2.2, 95%CI: 0.8-6.3; hysterectomy controls: OR 2.0, 95%CI: 0.6-6.1); lead exposure mostly occurred from non-occupational sources (paint, home renovation, soldering, and stain glass work). The association with mercury exposure was inconsistent (cases vs. population controls: OR 1.1, 95%CI: 0.5-2.3; hysterectomy controls: OR 1.7, 95%CI: 0.7- 4.5). No association was observed with solvent exposure; results were inconclusive for exposure to herbicides, insecticides, fungicides, and rodenticides given few exposed participants.

Conclusion
Results from our case-control study suggest that exposure to epoxy resins and heavy metals, particularly lead, are associated with increased adenomyosis risk. Given the exploratory nature of our analysis, further research is warranted to investigate environmental risk factors for adenomyosis to inform prevention efforts.

Key words
Adenomyosis, environmental, epidemiology

A RARE CASE OF TYPE IIB UTERINE MALFORMATION WITH PATHOLOGICAL RUDIMENTARY HORN: SETTLING THE ASSOCIATED ADENOMYOSIS WITH FERTILITY PRESERVATION

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Country where research was undertaken:
China

We demonstrated a pain relieved and fertile preserved approach for the treatment of a patient diagnosed with type IIb uterine malformation, whose rudimentary horn developed into a diffuse adenomyosis foci.

Introduction/Background
While endometriosis is commonly seen in patients with uterine malformation, the development of adenomyosis is rare. The long term periodic bleeding inside the obstructive rudimentary horn with functional endometrium may help the development of adenomyosis. Early diagnosis of such a uterine malformation is quite necessary to prevent such severe complications.

Materials and Methods
Transvaginal ultrasonography, magnetic resonance imaging, and laparoscopic resection of rudimentary horn with adenomyosis, endometrioma and superficial endometriosis. Chromopertubation was also performed to assess tubal competency. Laparoscopic resection was performed to relief pain and preserve fertility.

Results
A 29-year-old nulliparous patient presented with severe dysmenorrhea, menorrhagia and an infertility history for nearly 10 years. Her dysmenorrhea has been worsening in recent two years, and she has a strong desire of giving birth. She was diagnosed with the diagnosis of type IIb uterine malformation with associated adenomyosis. We finally performed laparoscopy resection for the patient. During the follow up, her dysmenorrhea resolved. She was considering embryo transfer.

Conclusion
We reported a rare case of type IIb uterine malformation with adenomyosis in the rudimentary horn, with superficial endometriosis lesions and ovarian endometrioma. The laparoscopic resection of the pathological rudimentary horn is possible after careful adhesiolysis without cutting the uterine artery to relief clinical symptoms, restore normal pelvic anatomy, and preserve future fertility.

Key words
Rudimentary uterine horn, adenomyosis, fertility preservation

PERINATAL OUTCOMES WERE ASSOCIATED WITH THE POSITIONAL RELATIONSHIP BETWEEN PLACENTA AND ADENOMYOTIC LESION IN PREGNANT PATIENTS WITH ADENOMYOSIS

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Country where research was undertaken:
China

Introduction/Background
The adverse perinatal outcome caused by adenomyosis has been widely concerned recently, but little attention has been paid to whether the positional relationship between placenta and adenomyotic lesion influences the maternal and perinatal outcomes.

Materials and Methods
A total of 653 women with adenomyosis who were pregnant greater than 20 weeks gestation and delivered between January 2010 and December 2023 were recruited. The positional relationships between placenta and adenomyotic lesions were determined. The patients were divided into two subgroups: group I, placenta located above the adenomyotic lesion; and group II, placenta located far away from the lesion. The clinical data were retrospectively analyzed.

Results
We found a higher rate of diffuse adenomyosis (67.34% vs. 41.96%, p = 0.01), coexisting endometriosis (33.85% vs. 14.63%, p = 0.002), preterm delivery (32.97% vs.13.32%, p < 0.001) and placenta malposition (20.74% vs. 7.19%, p = 0.002) in group I compared to group II. Compared with group II, group I had lower birth weight (p = 0.02). After adjustment using multiple logistic regression analysis, maternal adverse outcome was only correlated with age (p = 0.02). Neonatal adverse outcomes were closely correlated with group I (p = 0.004), including pregnancy induced hypertension (p = 0.01), placenta malposition (p = 0.02), placental abruption (p = 0.003), and scarred uterus (p = 0.02).

Conclusion
The positional relationships between the placenta and adenomyotic lesions were graphically presented. Placental position near or above adenomyosis lesions might correlate to the adverse
perinatal outcomes of pregnant women with adenomyosis and thereby deserve more attention.

Key words
Perinatal outcome, placenta, adenomyotic lesion

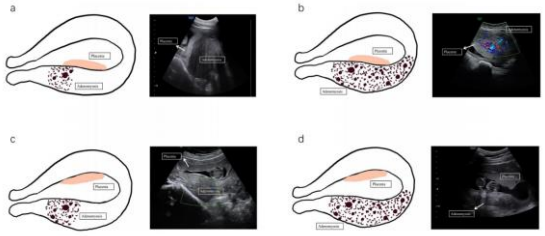

Fig. 2. The diagram of the positional relationships between placenta and adenomyotic lesion. Group I: the placenta was located on the adenomyotic lesion (as shown in (a,b)). Group II: the placenta was far away from the adenomyotic lesion (c,d).

COX2 UPREGULATION IN ADENOMYOSIS LEADS TO ABNORMAL ENDOMETRIAL CELL SENESCENCE AND IMPAIRS DECIDUALIZATION

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Country where research was undertaken:
China

Introduction/Background
Adenomyosis is often associated with infertility. COX2 contributes to the decidualization of endometrial stromal cells (ESCs) and can induce cell senescence through PGE2 production. Our research has demonstrated that COX2 is upregulated in the endometrium of patients with adenomyosis. Therefore, we aim to investigate whether COX2 upregulation can impair the physiological process of decidualization in adenomyosis.

Materials and Methods
Human specimens were collected during surgery with consent of patients. Human Endometrial Stromal Cell line (hESCs) were used to investigate the effects of COX2 overexpression on cell senescence and decidualization. The mouse adenomyosis models were constructed by neonatal Tamoxifen exposure. Specimens were examined by RT-PCR, western blotting, SA-β-Gal staining and immunofluorescence. Nonsteroidal anti-inflammatory drugs (NSAIDs) were given along with PGE2 in cells, and were fed to mouse models orally.

Results
The higher level of COX2/PGE2 expression and cell senescence in ESCs was confirmed in

human specimens of adenomyosis, compared with the control group. Exogenous high-dose PGE2 caused senescence in ESCs, which showed features of decidualization at an early time, well ahead of hormone-induced decidualization. The overexpression of COX2 demonstrated the same effect on ESCs, and these incidences could be reversed by using NSAIDs. In mouse models, we observed a higher level of COX2/PGE2 expression in the adenomyosis group, with deficiency in conceiving and greater chance of abortion. Bioinformatics further revealed crucial disturbance in gene expressions concerning endometrium receptivity. Application of NSAIDs saved these mice from infertility and adverse pregnancy outcomes.

Conclusion
COX2 is overexpressed in the endometrium of patients with adenomyosis. The overexpression of COX2/PGE2 can induce excessive ESCs senescence, leading to premature decidualization and a shortened window of implantation. This results in implantation failure. NSAIDs, commonly used for managing dysmenorrhea pain, have the potential to reverse negative effects of COX2/PGE2 on decidualization.

Key words
Adenomyosis, PGE2, decidualization

THEME: ALLIED HEALTH, COMPLEMENTARY AND ALTERNATIVE MANAGEMENT

THE EFFECTIVENESS OF A MODIFIED TRADITIONAL CHINESE MEDICINE FORMULATION (GUI ZHI FU LING WAN) FOR THE TREATMENT OF ENDOMETRIOSIS

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[2]Medical Research Institute of New Zealand, Wellington, New Zealand
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Countries where research was undertaken:
Australia and New Zealand

Introduction/Background
Gui Zhi Fu Ling Wan is traditionally used for pelvic pain by traditional Chinese medicine (TCM) practitioners but most evidence is pre-clinical or in animal models. This study aimed to evaluate the efficacy of a modified version of Gui Zhi Fu Ling Wan (mGZFLW) on endometriosis pain and symptoms.

Materials and Methods
A randomised, double-blind, placebo-controlled trial was conducted on 92 adult participants with a diagnosis of endometriosis. Participants were randomly allocated in a 1:1 ratio into active or placebo. Both groups received 6 capsules per day for 3 months, with one month of follow-up. The primary outcome was pelvic pain severity at the end of trial. Secondary outcomes include adverse events, quality of life (EHP-30 and EQ5D), rescue analgesic usage (days per month) and fatigue (FSS).

Results
351 participants were screened for eligibility and 92 satisfied the eligibility criteria, underwent randomization, and were enrolled in the trial. a total of 90 participants completed baseline (mGZFLW = 45, Placebo = 45) and were included in the Intention to treat (ITT) analysis, with of 65 participants included in the per protocol analysis. At the end of the study there was no difference in pelvic pain severity between mGZFLW and placebo (MD 0.08 (-0.42 to 0.58), p=0.76), adverse events (RR 0.88 (0.60 to 1.29), p=0.50), EHP-30 overall score (MD -0.54 (-7.63 to 6.56), p=0.88), EQ5D-VAS (MD 0.80 (-8.32 to 9.93), p=0.86), analgesic usage (MD 0.30 (-0.25 to 0.85), p=0.28) or fatigue (MD 0.25 (-4.81 to 5.32), p=0.92).

Conclusion
The results of the current study do not demonstrate any difference in any clinical outcome measure when comparing 3 months of treatment with mGZFLW to 3 months of a matched placebo in either the intention to treat, or per protocol group.

Key words
Herbal medicine, Chinese medicine, endometriosis

THE ENDOCHILL TRIAL: EVALUATING MEDITATION, BREATHWORK, AND COLD THERAPY AS A NOVEL INTERVENTION FOR ENDOMETRIOSIS-ASSOCIATED PAIN

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Country where research was undertaken:
Australia

Introduction/Background
Current treatments for endometriosis-associated pain do not always improve symptoms. Here, we propose a novel intervention combining meditation, breathwork, and cold therapy to reduce pain in women with endometriosis. This method has previously shown to improve pain symptoms in other inflammatory conditions by modifying autonomic nervous and immune system functions.

Materials and Methods
A single-case experimental design trial involving 32 participants with endometriosis-associated pain was undertaken in three phases: Baseline (1-6 weeks), Intervention (12 weeks), and Follow-up (8 weeks). The Intervention phase required weekly practice of a meditation, breathwork, and cold therapy program. Participants recorded pain and other endometriosis symptoms daily. At four timepoints, participants also completed questionnaires on fatigue, sleepiness, and negative emotions. Blood samples were obtained to evaluate corresponding autonomic nervous and immune system parameters.

Results
This pilot study is currently recruiting participants. Preliminary data comparing self-reported pain and other endometriosis symptoms, autonomic nervous system activity, and immune system function between the Baseline and Intervention phases will be presented.

Conclusion
Based on these preliminary data, the safety, feasibility, and effectiveness of the proposed intervention for endometriosis-associated pain will be discussed.

Key words
Endometriosis-associated pain, autonomic nervous system, systemic inflammation

PELVIC FLOOR MUSCLE CONTRACTION-PLUS-RELAXATION VERSUS RELAXATION-ONLY WITH MINDFULNESS FOR WOMEN WITH ENDOMETRIOSIS-ASSOCIATED PELVIC PAIN: A PILOT RANDOMISED CONTROLLED TRIAL

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Country where research was undertaken:
Australia

Introduction/Background
Pelvic floor muscle (PFM) exercise is commonly prescribed to women with endometriosis-associated pelvic pain (EAPP),[1] but the feasibility and effects of PFM exercise protocols are unknown. This study aimed to evaluate the feasibility of PFM protocols and mindfulness in women with EAPP, and changes in pelvic pain and PFM morphometry.

Materials and Methods
This was a pilot randomised controlled trial. Participants underwent an 8-week hybrid intervention (face-to-face and telehealth consultations) that included either PFM contraction-plus-relaxation [PFMC+R] or PFM relaxation-only [PFMR] with mindfulness. The primary outcome was feasibility, specifically retention rate. The secondary outcomes were EAPP symptoms assessed by validated pain questionnaires and PFM morphometry measured by transperineal ultrasound imaging at baseline and after completion of the intervention by an assessor who was blinded to group allocation.

Results
Ninety-five women were assessed for eligibility, of which 45 participants with EAPP (recruitment rate 47%) were randomly assigned to either the PFMC+R group (n=23) or the PFMR group (n=22). The PFMC+R group had higher retention (89%) and attendance (86%) rates compared to the PFMR group (63% retention, 63% attendance). The PFMC+R group demonstrated a significantly lower intensity of general pelvic pain (mean difference [MD]=-2.80, 95% confidence interval [CI] -4.22, -1.45) and dyspareunia (MD=-2.43, 95%CI-3.90, -

1.03) compared to the PFMR group. Additionally, the PFMC+R group had larger anorectal angle (MD=3.61, 95%CI 2.52, 9.48) and anterior-posterior diameter of levator hiatus measurements (MD=0.34, 95%CI 0.14, 0.63) at rest, suggesting a lower PFM resting tone and greater PFM relaxation compared to the PFMR group.

Conclusion
The PFMC+R protocol indicated stronger feasibility than the PFMR protocol and demonstrated greater improvements in EAPP symptoms and PFM morphometry. Physiotherapists may consider incorporating a hybrid intervention program that combines PFMC+R with mindfulness for women with EAPP. Further research with a larger sample size is required to test clinical effectiveness.

Key words
Endometriosis, pelvic pain, pelvic floor muscle

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EFFICACY AND SAFETY OF A CHINESE HERBAL EXTRACT IN ALLEVIATING ENDOMETRIOSIS RELATED SYMPTOMS

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Country where research was undertaken:
Israel

Introduction/Background
Chinese Herbal Medicine (CHM) is frequently employed in the management of gynecological conditions. In patients with endometriosis, CHM may help alleviate symptoms by modulating hormonal and inflammatory responses. In this study, we evaluated the effects of PFD6160, a specialized herbal formula derived from CHM, on patients experiencing endometriosis related symptoms.

Materials and Methods
We performed a four month double-blinded, placebo-controlled, randomized clinical trial for patients with endometriosis related symptoms. Patients received 800 mg capsules of the PFD6160 formula or placebo capsules daily according to body weight. Participants maintained an electronic daily diary and filled questionnaires. Primary efficacy endpoints were improvement in pain symptoms measured by total number of pain-free days (PFD) and overall pain intensity per month. Quality of life (QOL) was evaluated using the EHP-30 questionnaire.

Results
Forty one patients completed the study. There was a significant increase in PFD in the study group compared to the control group for most pain parameters, including lower abdominal pain (p=.007), pelvic pain (p=.004), pain during bowel movements (p=.012), pain during sexual intercourse (p=.007), and other types of pain (p=.038). Weighted overall pain scores revealed significant reductions in back pain (p=.034), thigh pain (p=.029), and lower abdominal pain (p=.028). EHP-30 questionnaire results demonstrated significant improvements in quality of life for the study group across all parameters ($p<0.05$). No significant side effects were recorded during the study period. This comprehensive enhancement in quality of life metrics suggests a broad positive impact of the intervention on patients' overall well-being.

Conclusion
This study addresses limitations in previous research which lacked placebo controls and suffered from incomplete data showing CHM's significant impact in reducing endometriosis related symptoms with fewer adverse effects than standard therapies alone. These promising results pave the way for a scientifically supported, complementary approach that could revolutionize endometriosis treatment.

Key words
CHM, endometriosis, pain

THEME: BEHAVIOURAL HEALTH, MEDICINE AND PSYCHOSOCIAL CONSIDERATIONS

LEVERAGING HEALTH PSYCHOLOGY TO COMBAT PATIENT BARRIERS TO DIAGNOSIS

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Country where research was undertaken:
United States of America

Introduction/Background
The disease perceptions and knowledge of individuals at risk of endometriosis have been understudied as to their impact on health-seeking or diagnosis-promoting behaviors. The Commonsense Model of Illness (CSM; Leventhal et al., 2016) is used to understand lay psychological perceptions of diseases, and how they relate to care-seeking and coping behavior.

Materials and Methods
In the first of a two-part study, undiagnosed individuals with endometriosis-consistent symptoms (a combination of recent survey-based symptomology criteria; Chapron et al., 2022; Fauconnier et al., 2021; Goldstein & Cohen, 2023) were identified. The second study assessed endometriosis disease perceptions (CSM items; Broadbent et al., 2006) and knowledge/awareness (Shah et al., 2010). Outcomes measured were information seeking, coping mechanisms (Brief COPE; Carver, 1997), and intentions to seek care for endometriosis.

Results
Descriptive analysis showed this sample demonstrated adequate endometriosis knowledge and awareness, contrary to expectations based on awareness efforts often cited as needed for future patients. Whether disease perceptions predicted outcomes was examined using hierarchical linear regression modeling, controlling for significant covariates identified in preliminary analyses. Regression analysis found endometriosis disease perceptions explained between 19.6% and 48% of the variance in health outcomes. Of note, perceiving endometriosis with higher concern and perceiving higher personal and treatment control over endometriosis predicted higher care-seeking intentions, greater willingness to learn one's risk, and higher use of coping strategies. Results deem disease perceptions as worthy of inclusion in future investigations of the psychological components entangled in the delay to an endometriosis diagnosis.

Conclusion
Findings suggest individuals that may be at risk of endometriosis are knowledgeable and aware of the disease. Campaigns to promote patient behavior that leads to speedier diagnosis (e.g., seeking care) may profit from targeting problematic disease perceptions identified in this work, including concern and control beliefs.

Key words
Perceptions, lay beliefs

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FIVE YEARS PRACTICE AND ACHIEVEMENTS TO PROMOTE OC FOR DYSMENORRHEA IN THE REMOTE NORTHERN AREA OF OKINAWA JAPAN

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Country where research was undertaken:
Japan

Introduction/Background
In Japan taking OC for dysmenorrhea is not common. Especially in the remote northern area of Okinawa, where people strongly believed that dysmenorrhea is to be endured. The objective of this study is clarify that five years practices and achievements to promote OC for dysmenorrhea in the rural region.

Materials and Methods
I started to educate both local people and medical care providers such as pharmacists, nurses, and counselors in the area in 2019 by workshops, lectures, articles in local newspapers and YouTube. To investigate the prevalence of OC, 34 pharmacies in the area were asked to provide the number of prescriptions of 4 kinds of OC indicated to dysmenorrhea in Japan from 2018 to 2023.

Results
When I started practice at the area, medical care providers didn't understand effectiveness of OC. Also patients hesitated to take OC, because most women believed that dysmenorrhea should be endured. It was hard to change the mind of people who trapped by 'Patience is a virtue' and 'status quo bias', a psychological tendency to hesitate OC. After 5 years I started education, surprisingly the annual number of OC prescriptions in 2018 and 2023 increased 24-fold from 27 to 659 sheets in the area. It was thought that continuous education might have overcome the status quo bias.

Conclusion
In order to deliver appropriate medical care to rural areas, it was necessary to work together with medical care providers in the area and to educate local people continuously through every possible means.

Key words
Dysmenorrhea, status quo bias, Okinawa Japan

DAMNED IF YOU DO, DAMNED IF YOU DON'T? LEGAL CONSEQUENCES OF AUSTRALIAN ENDOMETRIOSIS PATIENTS NOT DISCLOSING CANNABIS USE TO INSURERS

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Country where research was undertaken:
Australia

Introduction/Background
Australians with endometriosis use cannabis based medicinal products (CBMPs) to manage their condition, reporting reductions in use of other pharmaceuticals[1,2,3]. Lower rates of systematic disclosure of risk factors in life insurance settings, particularly of smoked tobacco, impacts premiums, contracts and claims outcomes, but less is known about cannabis[4].

Materials and Methods
A cross-sectional survey was conducted between October-December 2022. Recruitment occurred via social media and email seeking those aged 18 or older; had a diagnosis of endometriosis from a doctor; were residents of Australia or New Zealand; and had consumed either illicit cannabis or a legal CBMP that was prescribed by a health practitioner, after 1 November 2016, to manage endometriosis and pain related symptoms.

Results
The effects of cannabis in 192 Australians with endometriosis were improved: sleep by 69.1%

(SD 35), ability to do activities of daily living 52.4% (SD 40.7), enhanced appetite / food consumption 46.5% (SD 44.6), and capacity to work 43.3% (SD 42.5). Substantial reductions in nicotine, alcohol, opioid and non-opioid pain relief, hormones, neuroleptics and other treatments were reported. In those who had side effects, nearly all advised they'll continue to use cannabis as they didn't find them particularly bothersome. The results suggest improved 'insurability' in those with the disease using cannabis, but only 38 (19.8%) respondents had life insurance, 41 (21.4%) owned total & permanent disability insurance, 11 (5.7%) maintained trauma cover and 33 (17.2%) held income protection, and significant discrimination and disclosure legal risks surrounding cannabis and life insurances emerged.

Conclusion
The study found that life insurance companies need to update and modernise their underwriting guidelines to reflect improvements in health outcomes from cannabis use in people with endometriosis. Further, non-disclosure and underinsurance were identified as significant, with limited actuarial or statistical data on cannabis use as an anodyne in endometriosis disease available to insurance medicine decision makers.

Key words
Endometriosis, insurance, cannabis

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RANDOMISED CONTROLLED PILOT TRIAL OF THE *ENDOSMS* TEXT MESSAGE INTERVENTION FOR INDIVIDUALS WITH ENDOMETRIOSIS: FEASIBILITY, USER ACCEPTABILITY AND SHORT-TERM EFFICACY

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Country where research was undertaken:
Australia

Introduction/Background
EndoSMS is a low cost, highly accessible text message intervention designed to provide psychological and informational support for people with endometriosis. The aim of this two-arm pilot randomized controlled trial (RCT) with Waitlist control was to assess user acceptability, feasibility and short-term (3-month) efficacy of the *EndoSMS* text message intervention.

Materials and Methods
Participants recruited from Australian endometriosis online communities were randomized to the intervention (*EndoSMS*) or control condition after baseline survey completion (*EndoSMS* *n*=139, Waitlist *n*=135). At 3-months, user acceptability was assessed via mixed methods (quantitative survey; qualitative written commentary), and efficacy was assessed via self-reported health-related quality of life (Endometriosis Health Profile-30 Emotional wellbeing subscale; EHP-30) and emotional health (Depression, Anxiety and Stress Scales-21: DASS21). Feasibility data included uptake, attrition, and text message delivery analytics.

Results
Participants indicated satisfactory acceptability (mean = 4.02/5) and rated the number (80.9 %) and language (94.5 %) of *EndoSMS* messages as being 'just right'. Qualitative themes reflected: A shared 'battle': Feeling less isolated and alone; Being kind to yourself: A focus on self-care, self-compassion and active coping; Keeping endometriosis at the forefront: Helpful or stressful?; and the need

for greater Tailoring of text messages. Feasibility was indicated by: a very high conversion rate (99.1 %), low study attrition (14.2 %), few messaging opt-outs (0.02 %), and a high message delivery rate (99.8 %). Linear mixed models analysis indicated significant improved emotional health (DASS21 depression, p =.049) and emotional wellbeing (p =.037) at 3-months for individuals receiving hormone treatments. No other main effects were evident.

Conclusion
The findings of this pilot RCT indicate that *EndoSMS* text messaging is a highly acceptable and feasible means of supporting emotional wellbeing of people with endometriosis. These data also highlighted the need for greater personalisation of the text message content that can be addressed in future developments of this intervention.

Key words
Text message intervention, acceptability, feasibility

THEME: BIOLOGICAL MECHANISMS

FACTORS SECRETED FROM NORMAL HUMAN PLACENTAE REDUCED THE PROLIFERATION OF ENDOMETRIOTIC CELL

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Country where research was undertaken:
China

Introduction
Endometriosis is characterised by the growth of abnormal endometrial tissue outside the uterus. The cause remains unknown and currently no preventive ways have been established. The human placenta is a tumour-like organ in its growth and invasion. However, unlike tumour, placental invasion is well regulated during pregnancy. Increasing evidence suggests that this regulation is, at least in part, due to factors released from the placenta. Therefore, in this study, we investigated whether factors secreted from placenta can inhibit the growth of endometriotic cells.

Materials and Methods
Normal human placental tissues were collected from 1st trimester after surgical suctions. After washing, placental explants were cultured in media for 16 hours, and media were then collected, and centrifuged at 2000×g to remove debris. Endometriotic cell line, 12Z cells were seeded until confluent, and were cultured with placental conditioned media for 24 and 48 hours. The cell proliferation was then measured using Alamar Blue and CCK8 assays.

Results
The Alamar Blue assay showed a 30% or 50% reduction in proliferation of 12Z cells following 24 hours or 48 hours of culturing with placental conditioned media compared to controls. In addition, the CCK8 assay showed a 60% or 70% reduction of proliferation following 24 hours or 48 hours of treatment, compared to controls.

Conclusions
Although specific factors from the placenta contributing to the reduced proliferation of endometriotic cells were not identified in this study, extracellular vesicles may play an important role. Strong evidence suggests that placental extracellular vesicles carry regulatory RNAs, such as miRNA-519d, which are involved in cell proliferation and migration.

Key words
Placenta, proliferation, endometriotic cells

IN SILICO STUDY OF ENDOMETRIUM REVEALS THE ROLE OF COMPLEMENT-COAGULATION CROSS-TALK IN ENDOMETRIOSIS AND HIGHLIGHTS THE POTENTIAL OF JAK INHIBITORS.

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Country where research was undertaken:
Poland

Introduction/Background
Despite its high prevalence, the aetiology and pathogenesis of endometriosis remain poorly understood. Lack of knowledge on the key processes that drive this condition hinders its early detection. Understanding the main pathways involved in endometriosis

development is necessary for the successful biomarker discovery and improved therapy outcomes.

Materials and Methods
We performed network meta-analysis on GEO datasets containing 114 ectopic endometrium samples (EL), 138 eutopic endometrium samples from women with endometriosis (EEM) and 79 eutopic endometrium samples from women without endometriosis (EH). Gene ontology and enrichment analysis was done in DAVID, Metascape and Cytoscape and drug repurposing investigation was done in cMap. Endometrial epithelial 12z cells were treated with various concentrations of Tofacitinib and Ruxolitinib and their proliferation was monitored over 6 days.

Results
Network meta-analysis revealed that eutopic endometrium from patients with (EEM) and without endometriosis (EH) differed in the upregulation of *CCL21* and downregulation of *BIRC3, CEL* and *LEFTY1* genes ($p < 0.05$ and $|log2FC| > 0.5$). Transcriptomic profile of lesions (EL) was significantly different from that of eutopic endometrium and showed increased expression of complement (*C1q*, *C2*, *C3* and *C7*) and serpin superfamily genes. Gene ontology analysis highlighted inflammation, angiogenesis and ECM interaction as key events occurring in endometriosis and showed strong enrichment in complement and coagulation cascade.

Drug repurposing indicated that the candidates most likely to reverse the endometriosis transcriptomic profile were cyclin-dependent kinase (CDK), JAK and topoisomerase inhibitors (tau score>95%). 10uM Tofacitinib and 20uM Ruxolitinib significantly inhibited 12z cells growth at 72h post treatment ($n=5$, $p<0.05$).

Conclusion
Here we highlight pathogenetic mechanisms that are critical for lesion formation regardless of endometriosis subtypes and patients' characteristics. We propose an interplay between complement and coagulation pathway, mast cells, ECM remodeling and JAK/STAT3 pathway in endometriosis. We underscore the significance of C3 and propose JAK inhibitors for potential treatment.

Key words
Complement, coagulation, JAK-inhibitors

RE-EVALUATING ESTROGEN RECEPTORS ERα AND ERβ EXPRESSION IN ENDOMETRIOSIS UNDERSCORES THE PROMINENT ROLE OF ERα

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Country where research was undertaken:
France

Introduction/Background
Endometriosis (EM) is a highly estrogen-dependent chronic inflammatory disease with great heterogeneity, manifested by different types of lesions. Several studies have suggested that the estrogen receptor ERβ might play an active role in the development of EM lesions. However, the presence of ERβ in lesions was challenged, due to a lack of specificity of commonly used antibodies.

Materials and Methods
We took advantage of our large bank of tissue microarrays (TMAs) containing samples from endometrium and matched lesions. Using both RNAScope® and immunohistochemistry, we mapped the expression of both receptors ERα and ERβ, including expression of progesterone receptor (PR) and androgen receptor (AR) in endometrial tissues of EM women throughout the menstrual cycle. Endometrial and matched lesions-derived organoids were also generated and stimulated with 17β-estradiol to better challenge the impact of estrogen signaling in the pathology.

Results
This precise characterization of matched tissues clearly and consistently demonstrated the expression of ERα in EM lesions, contrasting with undetectable levels of ERβ including endometriomas. Although ERα expression is highly heterogeneous and varies throughout the menstrual cycle, comparisons of ERα expression in both superficial and deep lesions with matched eutopic endometrium

revealed that stromal cells in superficial and deep lesions exhibited lower ERα expression compared to matched eutopic endometrium. Some variations of PR and AR are also observed in deep lesions. Analyses of estrogen signaling in endometrial organoids compared to matched endometriotic-derived organoids enabled the study of specific estrogen response in lesions.

Conclusion
Overall our findings show that ERα is the only form of ER receptor expressed in EM lesions, highlighting that ERα is the primary target to design therapeutic strategies.

This work was funded by Region-Occitanie-Graine-ENDOTREAT, Endofrance association, INSERM and Urosphere.

Key words
Estrogen receptor ERα, hormone signaling, organoids

ASSESSMENT OF THE FERROPTOSIS REGULATORS: GLUTATHIONE PEROXIDASE 4, ACYL-COENZYME A SYNTHETASE, AND TRANSFERRIN RECEPTOR 1 IN PATIENT-DERIVED ENDOMETRIOSIS TISSUE

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Country where research was undertaken: Germany

Introduction/Background
Ferroptosis, an iron-dependent form of non-apoptotic cell death, plays a pivotal role in various diseases and is gaining considerable attention in the realm of endometriosis. Considering the classical pathomechanism theories, we hypothesized that ferroptosis, potentially driven by increased iron content at ectopic sites, may contribute to the progression of endometriosis.

Materials and Methods
The study included women aged 19 to 39. Inclusion criteria for the case group were laparoscopic and histological confirmation of endometriosis in women who underwent surgery 2021-2022 at the Department-of-Gynecology-and-Obstetrics at the University-Hospital in Muenster, Germany. Exclusion criteria were ages under 18 or over 50 years and concurrent diagnosis of malignancies. The surgically obtained tissue samples were immediately fixed in 10% neutral-buffered formalin and embedded in paraffin according to the standard procedures.

Results
Our study revealed a significant downregulation of GPX4 in stromal cells of endometriosis patients
($M = 59.7\% \pm 42.4$ versus $90.0\% \pm 17.5$ in the control group, $t(54) = -2.90$, $p = 0.005$). This finding aligned with slightly, but not significantly, higher iron levels detected in the blood of endometriosis patients, using hemoglobin as an indirect predictor (Hb 12.8 (12.2–13.5) g/dL versus 12.5 (12.2–13.4) g/dL in the control group; $t(54) = -0.897$, $p = 0.374$). Interestingly, there was no concurrent upregulation of TfR1 ($M = 0.7 \pm 1.2$ versus 0.2 ± 0.4 for EM, $t(54) = 2.552$, $p = 0.014$), responsible for iron uptake into cells. Our findings provide support for the involvement of ferroptosis in the context of endometriosis.

Conclusion
Progression of endometriosis reveals a complex interplay involving ferroptosis, disrupted iron metabolism, and intricate inflammatory responses.

The downregulation of GPX4 in stromal cells, along with elevated systemic iron levels and the complex regulation of iron transporters in patients with EM, suggests a potential link between ferroptosis and the disease's pathomechanism.

Key words
Endometriosis, ferroptosis, biomarkers

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G3BP2 MODULATES PUFA OXIDATION TO PROTECT ENDOMETRIAL STROMAL CELLS FROM REACTIVE OXYGEN SPECIES (ROS)

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Country where research was undertaken:
China

Introduction/Background
Endometriosis is an estrogen-dependent disease characterized by the presence of endometrial-like tissue outside the uterus, leading to significant reproductive health issues. The disease is often associated with oxidative stress and a microenvironment rich in reactive oxygen species (ROS). Our research focuses on the role of G3BP2, a protein whose elevated expression in ectopic lesions may contribute to the pathogenesis of endometriosis.

Materials and Methods
To explore the function of G3BP2 in endometriosis, we utilized endometrium-specific knockout mice in conjunction with a murine model of endometriosis. We performed RNA sequencing analysis comparing G3BP2 knockout and wild-type (WT) lesions to identify differentially expressed genes. Additionally, we conducted in vitro studies by knocking down G3BP2 in endometrial stromal cells (ESCs) and performed metabolomics analysis to elucidate the metabolic pathways involved.

Results
Our findings reveal that G3BP2 is essential for ectopic lesion growth, as its knockout resulted in reduced lesion number, size, and weight. RNA sequencing and gene ontology analysis indicated significant involvement in lipid metabolism and immune functions. Notably, G3BP2 was found to regulate the expression of PPARA and SLC47A1, enhancing PUFA oxidation and providing protection against ROS in ESCs.

Conclusion
This study establishes G3BP2 as a critical regulator of ectopic endometrial lesion growth in endometriosis. By modulating lipid metabolism through PPARA, G3BP2 promotes PUFA oxidation, thereby protecting endometrial stromal cells from the detrimental effects of oxidative stress. Our research highlights G3BP2 as a potential therapeutic target in managing endometriosis.

Key words
Endometriosis, G3BP2, lipid metabolism, Reactive Oxygen Species (ROS)

THE ROLE OF PERITONEAL FLUID EXTRACELLULAR VESICLES IN ESTABLISHING ENDOMETRIOSIS

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Country where research was undertaken:
New Zealand

Introduction/Background
The role of extracellular vesicles (EVs) in the development of endometriosis is an underexplored area. EVs are nano-sized particles released by all cell types containing various cargo important for intercellular communication. This study aimed to elucidate whether peritoneal fluid (PF) EVs encouraged endometriosis-associated cellular behaviours.

Materials and Methods
PF saline washes were collected from consenting patients at the beginning of endometriosis excision surgery. Three methods were compared for PF-EV isolation: ultracentrifugation (UC), size exclusion chromatography (SEC), and nanofiltration using an S20 device. PF-EVs were then pooled into samples representing Mild or Severe endometriosis and used to assess their effects on cellular viability, proliferation, collagen adhesion and soft-agar colony formation of endometrial cells *in vitro*.

Results
SEC resulted in the highest particle yield ($5.04 \times 10^8 – 2.15 \times 10^{10}$ particles/mL) and lowest concentration of co-isolated proteins (45.3 – 172.5 µg/mL) compared to UC ($9.15 \times 10^7 – 1.74 \times 10^{10}$ particles/mL; 44.0 – 599.6 µg/mL) and S20 ($4.85 \times 10^8 – 1.33 \times 10^{10}$ particles/mL; 432.9 – 1723.1 µg/mL). SEC was used to isolate PF-EVs from PF washes of participants

with varying endometriosis severities (four Mild, four Severe). The highest dose (3.5 x 10^4 particles/cell) of PF-EVs did not affect cellular viability nor proliferation of endometrial cells. However, PF-EVs increased cell adhesion compared to controls, with Mild PF-EVs having more of an effect than Severe PF-EVs. PF-EVs also decreased the number, but increased the size of colonies formed.

Conclusion
PF-EVs may play a role in allowing retrogradely-menstruated endometrial tissue to adhere to ectopic locations and form large colonies – essential first steps in the establishment of endometriotic lesions. Understanding the factors involved will allow the identification of targets for the development of more effective endometriosis treatments.

Key words
Peritoneal extracellular vesicles

THEME: CLINICAL MANAGEMENT

COMPARISON OF ANTI-MÜLLERIAN HORMONE (AMH) LEVELS IN NON-SURGICAL ENDOMETRIOSIS BASED ON AGE SPECIFIC NOMOGRAMS IN TURKEY

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Country where research was undertaken:
Turkey

Introduction/Background
Our aim was to determine age-specific serum AMH levels in non-surgical endometriosis patients and to compare these values with age-specific reproductive nomograms in a Turkish cohort.

Materials and Methods
In this retrospective, cross-sectional study, the medical records of 22,542 patients with serum AMH levels were analyzed. A nomogram was generated by modeling AMH levels against age, using the best-fit model. AMH plasma levels from 808 patients with non-surgical endometriosis were subsequently compared across percentile ranks within this nomogram.

Results
Histogram analysis indicated that AMH levels peaked at age 21, with a marked decline observed by 32.5 years (AUC: 0.762 [0.728-0.797]; sensitivity: 67.3%; specificity: 72.6%) in the non-surgical endometriosis group. In both the general patient cohort and non-surgical endometriosis patients, serum AMH levels showed a significant negative correlation with age (ρ = -0.562 and ρ = -0.478, respectively; $p < 0.001$). A comparison of median AMH levels revealed significantly lower values in non-surgical endometriosis patients (z = -7.334; $p < 0.001$). Age alone accounted for 22.8% of the variation in AMH levels among non-surgical endometriosis patients (Y=-0.022x age+ 1.177).

Conclusion
This study presents a detailed analysis of age-related AMH plasma levels, revealing a statistically significant negative association with age, which may have racial or environmental differences. Notably, serum AMH levels were lower in the non-surgical endometriosis group compared to age-matched nomograms.

Key words
Anti-mullerian hormone, nomogram, endometriosis

INTERVENTIONAL RADIOLOGY MANAGEMENT OF ABDOMINAL WALL ENDOMETRIOSIS (AWE): SYSTEMIC REVIEW AND META-ANALYSIS

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Country where research was undertaken:
Saudia Arabia

Introduction/Background
Abdominal wall endometriosis (AWE) is rare and linked to previous cesarean sections. Its prevalence may rise with increasing cesarean rates [1-3]. While surgical excision is the standard treatment [4], our research compares two nonsurgical options: Cryoablation and high-intensity focused ultrasound (HIFU), which could expand treatment options for AWE.

Materials and Methods
A meta-analysis using Review Manager 5.4 assessed changes in pain scores, lesion sizes, and recurrence rates. The mean difference method evaluated pain and lesion size differences, with a random effects model and I^2 to assess heterogeneity. A P-value of 0.05 or less indicated statistical significance.

Results
A total of 13 full articles were included in the analysis, with a total of 473 patients. The HIFU technique was applied in 9 articles, and Cryoablation was used in 4 articles. The meta-analysis demonstrated a significant decrease ($P < 0.01$) in pain scores and lesion size post-cryoablation Vs HIFU. For pain score, Cryoablation showed a reduction of 6.76 (95% CI: 5.89-7.63, $P < 0.01$), compared to HIFU reduction of 4.43 (95% CI: 4.06-4.80, $P < 0.01$). Regarding lesion size post-intervention, Cryoablation lesion size reduction: 52.98 (95% CI: 11.39-94.58, $I^2 = 100\%$), and HIFU 5.82 (95% CI: -2.32-13.97, $I^2 = 88\%$). HIFU had a lower recurrence rate by 5% (95% CI: 3-9%, $I^2 = 0\%$) compared to Cryoablation recurrence: 13% (95% CI: 7-26%, $I^2 = 51\%$) ($P > 0.05$).

Conclusion
Cryoablation was more effective than HIFU in reducing pain and shrinking lesions of AWE, but its high variability suggests results may vary by patient. HIFU had a lower recurrence rate and consistent results. A long-term randomized controlled trial over 5 years is needed to compare HIFU and Cryoablation effectiveness.

Key words
Abdominal wall endometriosis AWE, HIFU, Cryoablation.

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IMPLICATIONS OF THE EVOLUTION OF SONOGRAPHIC FEATURES IN ENDOMETRIOSIS-ASSOCIATED OVARIAN CANCERS

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Country where research was undertaken:
Taiwan

Introduction/Background
Patients with ovarian endometriosis are at risk for endometriosis-associated ovarian cancers (EAOC), such as endometrioid adenocarcinoma and ovarian clear cell carcinoma (OCCC). Due to the low prevalence and limited evidence regarding screening schedules, the progression interval from a benign ovarian lesion to an EAOC remains poorly understood[1,2].

Materials and Methods
Serial sonograms of patients with EAOCs were retrospectively analyzed from the point of cancer diagnosis back to the earliest available exam. Risk scores from the International Ovarian Tumor Analysis (IOTA) simple rules and the institution-specific model were recorded[3]. To enable comparisons across different time points and patients, the scores were standardized as risk ratios, defined as the individual risk score of a patient divided by the risk score from their earliest available exam.

Results
One hundred ninety-eight exams from 26 patients were analyzed over a median follow-up of 34.1 months. Compared to baseline, the risk ratio from the IOTA simple rule model was significantly elevated only within 6 months of cancer diagnosis, while the institution-specific model showed elevation during months 30–35,

24–29, 18–23, and within 6 months. To facilitate early detection of EAOC, patients were categorized by FIGO 2009 stages: IA-IC1 and IC2-IIIC. CA-125 levels differed significantly between groups, at 34.9 versus 136.4 U/mL (p = 0.026). However, using the receiver operating characteristic curve, neither the IOTA simple rule model (AUC = 0.59, 95% C.I. 0.37–0.77) nor the institution-specific model (AUC = 0.47, 95% C.I. 0.27–0.67) effectively discriminated between stages.

Conclusion
There may be a progression interval during which an ovarian cyst develops into an EAOC. To improve early detection, further research is needed to explore clinical assessments beyond the features of the IOTA simple rules risk assessment model and the institution-specific model in larger cohorts.

Key words
Ovarian neoplasms, endometriosis

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FERTILITY PROTECTING MANAGEMENT OF ENDOMETRIOMA IN ADOLESCENT AND YOUNG GIRLS

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Country where research was undertaken:
Bangladesh

Introduction/Background
Endometrioma, >4 cm needs surgery in the form of cystectomy or ablation. Endometrioma itself and cystectomy reduce ovarian reserve (OR). The study was aimed to avoid cystectomy and use sclerotherapy for management of endometrioma in adolescent and young girls to relieve symptoms, prevent the recurrence of cysts and save ovarian reserve.

Materials and Methods
This prospective study was conducted in Infertility Care and Research Centre, Dhaka, Bangladesh, between July 2021 and September 2024. Twenty adolescent and young girls with endometrioma were selected for the procedure. Endometriomas ≥5 cm were aspirated either vaginally or laparoscopically, followed by sclerotherapy with 95% ethanol. Subsequently participants were put on dineogest. AMH level was measured preoperatively and 3 months and 6 months after the procedure. A p-value of <0.05 was considered as significant

Results
The age range of the patients was 17-25 years with a mean value of 19.15±2.6 years. Thirteen patients had unilateral cysts measuring 6 -10 cm with a mean of 7.85±1.6 cm, and 7 patients had bilateral cysts, 4-11 cm with a mean of 7.57 ±2.5 cm in the right ovary and 4-9 cm with a mean of 6.43±2cm in left ovary. Pre-intervention mean AMH level was 2.64±0.47ng/ml, and 3 and 6 months after intervention mean AMH level was 2.48±.45 and 2.38±.46 ng/ml respectively. Declining of AMH level was not significant, p-value was 0.27 and 0.08 after 3 months and 6 months respectively

Conclusion
Surgical excision of endometriomas have detrimental effects on ovarian reserve (OR), which compromise future fertility. To protect fertility potential of adolescent and young girls, cyst aspiration and sclerotherapy followed by continuous medical suppressive therapy can avoid cystectomy, surgery-induced follicular loss and recurrence of the cyst.

Key words
Endometrioma, Sclerotherapy, OR

MEDICAL MANAGEMENT IN ENDOMETRIOSIS: DOES CLASS OF MEDICATION PREDICT COMPLIANCE RATES AT 12- AND 24-MONTHS AFTER BEGINNING TREATMENT?

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Country where research was undertaken:
Australia

Introduction/Background
Medical management of endometriosis by hormonal, analgesic and anti-neuropathic medication is a common treatment for managing symptoms. The aim of this study was to investigate compliance rates for medical treatments and reasons for non-compliance at 12- and 24-months after beginning treatment.

Materials and Methods
Data collected through the National Endometriosis Clinical and Scientific Trials (NECST) Registry were interrogated. A statistical analysis plan has been tested on a cohort of participants at 6-months using the Clopper Pearson exact method to find 95% confidence intervals whilst testing between-group differences using a generalized linear mixed model. This same data analysis plan will be adopted at both the 12- and 24-month periods to compare compliance rates between hormonal, analgesic and anti-neuropathic medications.

Results
At 6-months, 162 participants have an overall medical compliance rate of 80.3% (95% CI [75.9, 84.3]). Between groups, variability was observed with analgesics having the highest compliance - 94.3% (95% CI [87.2, 98.1]), hormonal 76.1%, (95% CI [70, 81.6]) and anti-neuropathics 75.4%, (95% CI [62.6, 85.5]). There was a statistically significant difference when comparing analgesics to both other groups (p<0.01 for both comparisons), however no significant difference was observed between hormonal and anti-neuropathic medications. Of the 54 non-compliant participants, the most common reason was side effects/adverse effects (53.8%) followed by symptoms not improving (17.5%), worsening (5%) or improving (1.3%). Currently, follow-up data has been collected on 446 and 265 participants at the 12- and 24-month periods, respectively, and will be presented.

Conclusion
At 6-months, medical compliance is dependent upon medication prescription, with analgesics significantly more likely to result in continued use. The findings from this large cohort study will be discussed to provide a critical examination into the current landscape of the medical management of endometriosis.

Key words
Endometriosis, medical management

ASSESSING THE EFFECT OF ANTI-INFLAMMATORY DIETS ON ENDOMETRIOSIS AND CHRONIC PELVIC PAIN

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Country where research was undertaken:
Australia

Introduction/Background
Endometriosis is the leading cause of chronic pelvic pain (CPP), affecting 10% of reproductive-aged women worldwide (1). Current therapeutics have limited efficacy (2). However, emerging evidence suggests anti-inflammatory diets may help mitigate symptoms of pain and inflammation (3). This umbrella review evaluates the effect anti-inflammatory diets on endometriosis and CPP in women of reproductive age.

Materials/Methods
A systematic search of PubMed, Embase, Medline (Ovid), and Cochrane Library was conducted to identify systematic reviews of interventional and observational studies. Eligible studies included women of reproductive age with endometriosis or other

conditions characterised by CPP, anti-inflammatory dietary interventions or supplements, pain scores assessed by the visual analogue scale (VAS), or inflammatory biomarkers. Quality of included studies was appraised using AMSTAR 2

Results
A total of 6 systematic reviews were included. Dietary interventions including vitamin E + C, vitamin B1, polyunsaturated fatty acids (PUFAs), diindolylmethane (DIM), palmitoylethanolamide (PEA) + alpha lipoic acid (ALA), Garlic, fatty acids, low FODMAP and gluten-free diets significantly reduced endometriosis and CPP-related pain symptoms. Interventions that significantly reduced inflammation included, a high antioxidant diet, vitamin D, vitamin E + C and vitamin E. The quality of included reviews was of low to critically low quality due to numerous critical and non-critical flaws in the methodology. Only one of the included systematic reviews conducted a meta-analysis.

Conclusion
Anti-inflammatory dietary patterns effectively reduced inflammation and pain symptoms in endometriosis and CPP. However, the quality of this evidence was low. Additionally, most studies focused on dietary supplements rather than patterns and did not investigate inflammatory biomarkers. Higher-quality research is needed to confirm these findings and optimise endometriosis management worldwide.

Key words
Endometriosis, inflammation, diet

DYDROGESTERONE FOR TREATMENT OF CHRONIC PELVIC PAIN ASSOCIATED WITH ENDOMETRIOSIS AND REPRODUCTIVE OUTCOMES: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Country where research was undertaken:
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Introduction
Endometriosis affects the quality of life of women mainly due to chronic pelvic pain. Although hormonal treatments are effective in managing pain, they may limit reproductive desires. Dydrogesterone, has been suggested as a therapeutic option for managing pain without contraceptive effects, making a alternative for patients who wish to conceive.

Materials and Methods
Conduct a systematic review and meta-analysis of the existing scientific literature in the main available databases about the use of dydrogesterone in patients with endometriosis to control pelvic pain symptoms and the pregnancy rates during the treatment, evaluating if it is beneficial for patients with pelvic pain due to endometriosis with desire of pregnancy.

Parte inferior do formulário

The project was registered at PROSPERO and was conduct by the PRISMA statement. The data was compiled and meta-analysis was conducted.

Results
This systematic review included all analytical studies on dydrogesterone in endometriotic patients that reported clinical improvements in chronic pelvic pain and/or perinatal outcomes. Initially, 523 studies were identified; after excluding 323 duplicates, 200 articles underwent title and abstract review, resulting in 7 studies included in the review. These consisted of 4 prospective cohorts, 2 case-control studies, and 1 interventional study. Six studies analyzed dydrogesterone's effect on chronic pelvic pain, two examined dysmenorrhea, and three assessed pregnancy rates. Meta-analysis showed an 81% improvement rate in chronic pelvic pain with cyclic dydrogesterone use and 89% with continuous use. Regarding pregnancy rates, a meta-analysis indicated a 17% prevalence of pregnancy in the three studies evaluated.

Conclusion
The results demonstrate a significative prevalence (81 and 89%) of improvement on pelvic pain with the use of dydrogesterone treatment (cyclical or continuous) respectively in women with endometriosis and a success in achieving pregnancy in 17% of patients during or after its use.

Key words
Endometriosis, dydrogesterone, pregnancy

CLINICAL TRIAL: EFFECT OF A 28-DAY LOW FODMAP DIET ON GASTROINTESTINAL SYMPTOMS ASSOCIATED WITH ENDOMETRIOSIS (ENDOFOD) – A RANDOMISED, CONTROLLED CROSS-OVER FEEDING STUDY

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Country where research was undertaken:
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Introduction/Background
Gastrointestinal symptoms affect the majority of women with endometriosis(1-3), but existing treatments fail to target these symptoms(4, 5) and diet therapies are poorly defined(6). Preliminary data from non-randomised studies suggest the low FODMAP diet (LFD) may relieve gastrointestinal symptoms related to endometriosis(7, 8).

Materials and Methods
This single-blinded randomised, controlled, cross-over, feeding trial, randomised women with endometriosis and poorly controlled gastrointestinal symptoms to a LFD (<5 g/d FODMAPs) or control diet (20 g/d), both modelled on Australian Dietary Guidelines, before a 28-day washout and cross-over to the alternate diet. The primary outcome was proportion of responders, defined by the change in overall gastrointestinal symptoms on a 100-mm visual analogue scale. Secondary outcomes included individual gastrointestinal symptoms, quality-of-life (QOL) and psychological status.

Results
233 participants were screened, 193 were excluded for ineligibility, 35 were randomised and 25 completed the study. Mean age was 31 (95% CI 29, 33) years. 21 (60%) responded to the LFD compared with 9 (26%) to the control diet (p=0.008), relative risk of responding to the LFD 0.26, 0.09, 0.71; p=0.015. End of intervention overall gastrointestinal symptom scores were 35 (21, 42) mm on the LFD versus 58 (55, 65) mm on the control diet (p<0.001). These changes were accompanied by improvements in abdominal pain (<0.001), bloating (<0.001), stool form (<0.001) and QOL when measured in relation to gastrointestinal symptoms (0.004) and symptoms of endometriosis (<0.001). No overall effects on perceived stress, anxiety or depression were observed.

Conclusion
A LFD reduces gastrointestinal symptom severity in patients with endometriosis, and these changes are accompanied by a normalisation in stool form and improvements in QOL. While further studies are needed to confirm long-term benefits, these findings support the role of diet therapy in the management in endometriosis-related gastrointestinal symptoms.

Key words
Diet, nutrition, endometriosis

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ENDOMETRIOMA AND DERMOID CYST AS COLLISION TUMORS OF THE OVARY: A CASE SERIES AND LITERATURE REVIEW

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Country where research was undertaken:
Turkey

Introduction
The presence of different types of ovarian cysts in the same patient is referred to as 'collision tumors,' and the management of these tumors can be quite complex. In this study, we aimed to present 18 new patients who were diagnosed with endometrioma and dermoid cyst as collision tumors and to highlight the characteristics of these cases with the reported cases in the literature.

Materials and Methods
A total of 18 cases were identified, all of whom had been surgically treated in the Department of Obstetrics and Gynecology at five different hospitals in Turkey since 2005, with pathology results available. A literature search in the PubMed/Medline and Google Scholar databases for the association between endometrioma and dermoid cysts revealed 37 cases. The characteristics of these cases were analyzed.

Results
In the 18 newly reported cases, the mean age was 34.83 ± 8.70 years, and 10 of the cases were nulliparous. Seven patients presented with pelvic pain, three with primary infertility, and one case had incidental cysts detected. Four patients had received preoperative hormonal therapy, and nine patients had a desire for future fertility. The mean diameter of dermoid cysts was 46.88 ± 12.75 mm and endometriomas was 52.83 ± 24.71 mm. Both cysts were located in the right ovary in 10 patients, the left ovary in 7, and bilaterally in 1 patient. Postoperatively, only one patient became spontaneously pregnant, while no pregnancy occurred in the remaining cases.

Conclusion
Although tissue diagnosis is crucial for excluding malignancy and for follow-up, it is equally important to preserve the existing ovarian reserve in these patients. Recognizing the presence of collision tumors can help us utilize radiological methods more effectively and adopt a more proactive approach, considering the future fertility and quality of life of these patients.

Key words
Endometrioma, dermoid cyst, fertility

EVALUATION OF OVARIAN RESERVE AFTER ROBOTIC SINGLE-SITE OVARIAN CYSTECTOMY USING CHANGES IN ANTI-MÜLLERIAN HORMONE LEVELS: COMPARISON OF HISTORICAL LAPAROSCOPIC COHORTS

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Country where research was undertaken:
South Korea

Objective
Serum anti-müllerian hormone (AMH) is regarded as a useful marker in predicting for ovarian functional reserve. The aim of this study was to investigate the impact on the ovarian reserve after robotic single-site ovarian cystectomy.

Materials and Methods
About 130 patients who underwent robotic single-site ovarian cystectomy for benign ovarian tumor from 2020 to 2024 were analyzed retrospectively. The AMH levels were measured by enzyme immunoassay preoperatively and at 6 or 9 months after surgery. The difference and ratio of AMH levels were compared to the historical laparoscopic cohorts from published studies.

Results
The AMH levels were decreased at 6 or 9 months after surgery in all patients 9 (ratio of AMH levels between preoperative and 6 or 9 months, 0.53 ± 0.22 ng/mL). Considering age, total operation time, tumor histology, tumor size, and tumor bilaterality, both preoperative basal and postoperative AMH levels in

bilateral endometrioma group were significantly lower than the unilateral endometrioma group ($p = 0.022$ and $p < 0.001$, respectively). In addition, the decrease of AMH level after surgery in bilateral endometrioma in this study was less compared to the historical laparoscopic cohorts.

Conclusion
Robotic single-site ovarian cystectomy could be considered for preserving ovarian function in patients with bilateral ovarian endometrioma.

Key words
Anti-Müllerian hormone, benign ovarian cyst, ovarian reserve, robotic surgical procedures, evaluation of ovarian reserve after robotic single-site ovarian cystectomy using changes in anti-müllerian hormone levels: comparison of historical laparoscopic cohorts

DO WE NEED PLACEBO-CONTROLLED STUDIES TO ASSESS MEDICAL TREATMENTS OF PAIN ASSOCIATED WITH ENDOMETRIOSIS?

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Country where research was undertaken:
France

Introduction/Background
Primary treatment for endometriosis associated pain is amenorrhea induced by hormonal therapy. New drugs have to be assessed clinically, studies currently compare those with placebos. This approach may be questioned as we do have effective treatments. This work was undertaken to study results of placebo-controlled studies of medical treatment.

Materials and Methods
A systematic review and meta-analysis was carried out following the PRISMA checklist and registered in the PROSPERO.

PubMed, Embase and Cochrane Library databases were used for computerized strategy. Studies from inception to November 2024 were searched. *-The MeSH terms used were “endometriosis” AND “placebo” AND “randomized controlled trial” NOT “animals not humans”.

Results
The search yielded 933 articles; after eliminating duplicates 606 were selected, among which 171 studied hormonal treatments were included in the present study. All studies show a benefit in favour of hormonal treatment. All the treatments inducing amenorrhea are more effective than placebo. These included GnRh analogues, estrogen-progestin and progestin-only contraceptives, Dienogest and GnRh receptor antagonists. Data collection is nearing completion, full statistical studies are underway and will be presented at the conference.

Conclusion
All placebo-controlled studies have confirmed the efficacy of hormonally-induced amenorrhea in the treatment of pain associated with endometriosis, calling into question the ethical acceptability of this type of study in the evaluation of new drugs that induce amenorrhea.

Key words
Endometriosis, review, hormonal treatment

NEUROMODULATORY PHARMACOTHERAPY FOR CHRONIC PELVIC PAIN: SYSTEMATIC REVIEW AND META-ANALYSIS PROTOCOL

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Country where research was undertaken:
Australia

Introduction/Background
Chronic pelvic pain (CPP) is a common and disabling condition affecting up to 25% of females worldwide. Neuromodulatory medicines (eg., antidepressants, anticonvulsants) are recommended in clinical guidelines for the treatment of CPP. However,

the efficacy and safety of these medicines in CPP is unclear.

Materials and Methods
We searched five databases for randomised controlled trials (RCTs) that evaluated the efficacy and safety of neuromodulatory medicines compared to placebo in females with CPP. The primary outcomes were pain intensity and adverse events (AEs) following treatment. The secondary outcomes were pain impact, health-related quality-of-life, depressive symptoms, sexual function, sleep and tolerability of the intervention. Two reviewers independently screened studies, extracted data, and assessed risk of bias and certainty of the evidence. PROSPERO: CRD42024564134

Results
Eight placebo-controlled RCTs of 592 CPP participants (with or without endometriosis) were analysed. At immediate-term (≤4 weeks), there was no clear evidence that lidocaine (mean difference (MD), -5.0, 95% confidence interval (CI) -14.7 to 24.7, n=25; very low certainty) or diazepam (MD, 10.7, 95% CI -1.2 to 22.6, n=49; very low certainty), reduced pain intensity. At short-term (≥5 to ≤13 weeks), gabapentin probably reduced pain slightly (MD, -5.5, 95% CI -10.8 to -0.1, n=320, moderate certainty), but there was no clear evidence that sertraline reduced pain (MD, -0.0, 95% CI -19.6 to 19.6, n=25, very low certainty). Risk of AEs were uncertain for all medicines but gabapentin may increase risk of serious AEs (risk ratio (RR), 3.57, 95% CI 1.19 to 10.68, n=527, low certainty).

Conclusion
There is considerable uncertainty about the efficacy and safety of neuromodulatory medicines for CPP. Gabapentin may reduce short-term pain compared to placebo, but may be associated with increased risk of serious adverse events. There is a pressing need for large, high-quality studies to evaluate the efficacy of neuromodulatory medicines for CPP.

Key words
Pelvic pain, neuromodulatory medicines, randomised controlled trials

DEVELOPMENT OF COMPREHENSIVE, PRAGMATIC E-TRAINING FOR PRACTITIONERS TO BE CONFIDENT AND COMPETENT IN MANAGING WOMEN WITH PERSISTENT PELVIC PAIN (PPP).

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Country where research was undertaken:
Australia

Introduction/Background
PPP affects 25% of women[1], who report lack of validation, arduous diagnostic journeys and perceived lack of medical support.[2] Yet General Practitioners (GPs) and gynaecologists report low confidence in understanding and management of PPP[3]. Best practice is a multi-disciplinary (MD) approach[4]. GPs are best placed to lead this team once upskilled.

Materials and Methods
Consumer surveys identified a need for upskilling GPs in PPP mechanisms and treatment [5] aligned with national healthcare strategies and GPs' requests for clear treatment pathways.[6] In response, a 15.5-hour online course was developed by a Women's Health GP, Pelvic Health Physiotherapist, and learning specialist, collaborating with PPP patients and MD experts. The pragmatic, structured, engaging course incorporates knowledge assessments to embed learning. It received approval from key medical colleges and endorsements from EndoZone and QENDO.

Results
A self-paced e-learning course was launched in March 2024.

The course included lived-experience patient stories, structured and comprehensive teaching modules; history taking, communication (validation, empathy, inclusive language and cultural context), assessing pain drivers, pain science education, trauma informed pelvic floor examination, appropriate investigations and limitations, cyclical management and non-pharmacological, pharmacological, psychosocial treatment

strategies, from the perspective of the MDT.

Feedback describes course as “engaging”, “comprehensive”, “informative”, “excellent, highly relevant learning activity”.

Preliminary data reveals, participants are currently ‘often’ treating patients with PPP (92.5%), 79% feel overwhelmed, and 75% consider patients with PPP as hard to manage (n=53). On completion, 90% improved scores on ability to manage PPP and 100% agree they can confidently manage a patient with a holistic care plan (n=10).

Conclusion
Preliminary data demonstrates a comprehensive e-course improves confidence and competence in GP holistic management of PPP.

Key Words
Endometriosis, pain, GP

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THEME: DIAGNOSIS OF ENDOMETRIOSIS

PATIENTS WITH DEEP ENDOMETRIOSIS EXPERIENCE A PROLONGED DIAGNOSTIC DELAY: AN OBSERVATIONAL STUDY

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Country where research was undertaken:
Denmark

Introduction/Background
A diagnostic delay of 4-11 years is often reported for endometriosis(1,2). An association between diagnostic delay and advanced endometriosis has been suggested but remains debated (3).

We aimed to evaluate the diagnostic delay in a Danish endometriosis cohort and explore its association with deep endometriosis affecting nearby organs.

Materials and Methods
This observational cohort study included 129 patients, primarily operated for moderate to severe endometriosis, with data collected from questionnaires and surgical findings at the time of inclusion. Patients were categorized into two groups: those with deep endometriosis affecting the vagina, intestine, rectovaginal septum, or bladder (eVIRB), and those without (non-eVIRB). The diagnostic delay, defined as years from first symptom until diagnosis, was calculated from questionnaire responses and related to intraoperative findings and symptoms.

Results
The median diagnostic delay was 5 years. However, the eVIRB (n=75) experienced a significantly longer median diagnostic delay of 9 years when compared with non-eVIRB (n=54), who had a median delay of 2 years ($p=0.005$). The OR of having eVIRB was 5-fold increased if the diagnostic delay exceeded 5 years (95% CI 2.18-11.61, $p<0.001$). The eVIRB patients reported a significantly earlier onset of endometriosis symptoms. Both groups reported numerous pain symptoms, with a significant difference observed only in responses regarding severe period cramps requiring bed rest and use of painkillers. The eVIRB group had used hormones significantly

longer and had taken painkillers more regularly due to pelvic pain.

Conclusion
Our study identified a significant association between advanced endometriosis and prolonged diagnostic delay, even after adjusting for years of hormonal use and age at surgery. Future research should focus on strategies to enable earlier diagnosis in patients with advanced endometriosis, given the potential for severe complications associated with delayed detection.

Key words
Diagnostic delay, deep endometriosis

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UTEROSACRAL LIGAMENT ASSESSMENT SKILL ACQUISITION: ASSESSING LEARNING CURVES IN IDENTIFYING UTEROSACRAL LIGAMENTS AND ENDOMETRIOSIS ON ULTRASOUND

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Country where research was undertaken:
Canada

Introduction/Background
Accurate identification of uterosacral ligaments (USL) and associated pathology, such as endometriosis, is essential for effective diagnosis, counseling, and management. Many Minimally Invasive Gynecologic Surgery (MIGS) fellows lack formal training in advanced gynecologic ultrasound and rates of ultrasound skill acquisition varies[1,2]. Understanding their learning curves in identifying USLs on ultrasound may inform future competency-based training programs.

Materials and Methods
In this retrospective observational study, 3 first- and second-year MIGS fellows (T1, T2, T3) without formal advanced gynecologic ultrasound training performed transvaginal ultrasounds as part of standard clinical practice after independent review of educational materials on USL identification. Each fellow identified USLs and pathology if present with real-time comparison to an expert standard scan. Data were analyzed using a conservative Learning Curve Cumulative Sum (LC-CUSUM) analysis (H=7, failure rate H0/P0=0.2, Ha/P1=0.05, K=0.5, with adjusted baselines).

Results
Overall, trainees T1 and T2 surpassed the competency threshold, though their improvement was gradual. T1 required more scans than T2 to reach threshold but maintained competency afterward. T3 consistently struggled to meet the threshold.

In the left USL assessment, T1 and T2's scores rose steadily above the threshold, while T3 remained below competency. In the right USL assessment, T1 and T2 maintained scores well above the threshold, whereas T3 lagged significantly. These results highlight performance variability, with T1 and T2 achieving competency, and T3 requiring additional support.

USL endometriosis prevalence was 46.5% (73/157) for the right USL and 43.3% (68/157) for the left USL.

Conclusion
This study demonstrates that some trainees may achieve competency under conservative conditions, while others may require additional support. Notably, cumulatively improving accuracy with additional scans suggests capacity for progressive USL assessment improvement. These findings suggest individualized training strategies could be beneficial to ensure competency in USL assessment across all trainees.

Key words
Ultrasound, uterosacral ligaments

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DOES THE SIZE OF BLADDER ENDOMETRIOSIS LESIONS AND THE STATUS OF POD ON ULTRASOUND AFFECT PREDICTION OF DISEASE?

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Country where research was undertaken:
Australia

Introduction/Background
The aim of this study was to evaluate the effect of the increasing size of bladder deep endometriosis (DE) lesions and the status of the pouch of Douglas (POD) on transvaginal ultrasound (TVS) to predict disease these locations.

Materials and Methods
This was a retrospective multi-center study. Patients with possible endometriosis in the bladder who had complete ultrasound, surgical and histological data were included in final analysis. All bladder with maximal diameter in longest plane ≥ 5 mm, ≥ 10 mm, ≥ 15 mm, ≥ 20 mm, ≥ 25 mm, ≥ 30 mm on TVS were included. The presence of a positive or negative 'sliding' sign (marker for POD obliteration) was also recorded. We then examined the data to assess the performance of TVS to predict bladder DE when the POD was predicted to be either non-obliterated or obliterated. Reference standard was histological confirmation of endometriosis. The overall performance of ultrasound to predict DE in the bladder were determined using the area under the receiver operating curve (AUC). Data were analyzed using SAS version 9.4.

Results
23 lesions for bladder were identified. The AUCs for prediction of bladder without and with POD obliteration were 0.44 and 0.90, respectively. As DE lesion size on ultrasound increases for bladder, specificity and positive predictive value (PPV) increase but sensitivity decreases if POD was obliterated.

Conclusion
POD obliteration is associated with improved diagnostic performance of ultrasound in predicting bladder DE.

Key words
Deep endometriosis, ultrasound, lesion size

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THE IMPORTANCE OF DIAGNOSTIC LAPAROSCOPY IN ABDOMINAL WALL ENDOMETRIOSIS (AWE): A CASE SERIES

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Country where research was undertaken: Taiwan

Introduction/Background
For patients with prior Cesarean sections, the development of abdominal wall endometriosis (AWE), while rare, can cause discomfort and cyclic lower abdominal pain. This case series examines our approach to diagnosing and managing AWE using laparoscopy, focusing on the surgical findings and the unique challenges encountered.

Materials and Methods
We retrospectively reviewed medical records of patients who underwent surgery for AWE at our institution between January 2014 and August 2024. Inclusion criteria were a history of Cesarean section and cyclic lower abdominal wall pain lasting 1-14 years post-surgery. A total of 18 patients with suspected AWE were identified. All underwent mini-laparotomy and diagnostic laparoscopy for diagnosis and excision. Data collected included demographics, surgical findings, and postoperative outcomes.

Results
Among the 18 patients, 3 (16.7%) were presented with concomitant pelvic endometriosis, suggesting a possible association between AWE and pelvic endometriosis. Furthermore, 3 patients (16.7%) required mesh repair by a general surgeon due to fascial defects created during

AWE lesion excision. This highlights the potential for complications (incisional hernia) and the need for multidisciplinary collaboration in AWE management. In one challenging case (5.6%), the AWE lesion was not readily identifiable through the abdominal wall incision. Diagnostic laparoscopy allowed for visualization and complete excision of the lesion from the peritoneal side. In the post operative 3 months following up ,all patient reported complete lower cyclic pain disappeared.

Conclusion
Given the variable presentation of AWE, individualized treatment strategies are paramount. A thorough preoperative assessment, combined with a comprehensive surgical approach that may include laparoscopy, is critical for effective management. Further investigation is warranted to better understand the pathogenesis and long-term implications of AWE.

Key words
Abdominal wall endometriosis

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MORE THAN JUST A SCORE: EVALUATING THE EXPERIENCE OF THE PERIOD IMPACT AND PAIN ASSESSMENT (PIPPA) WEBSITE IN YOUNG PEOPLE

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Country where research was undertaken:
Australia

Introduction/Background
The PIPPA tool is the only validated screening tool for menstrual symptom impact in young people, and people with endometriosis score significantly higher than those without. The PIPPA website includes the screening tool but also other resources to improve help-seeking behaviour and self-management, however the usability has not been tested.

Materials and Methods
Qualitative think-aloud interviews will be used to collect audio-visual data about how young people aged 17-25 years navigate and experience the PIPPA website. 6-18 new participants will be recruited in rounds to meet an iterative process of testing and website changes until minimal new navigational and user issues are identified. An inductive content analysis will be used with reporting to follow the Cognitive Interviewing Reporting Framework (CIRF) checklist.

Results
Results will include data on the experience of navigating the PIPPA website including tracked pathways, identified user issues, the iterative process of website improvements and user appetite for web-based PIPPA self-screening, website downloads and menstrual information.

Conclusion
This study will provide information on how young people prefer to self-screen with PIPPA and consume information regarding menstrual management. The outcomes from this study will not only be incorporated into an updated PIPPA site but will also provide vital information relevant to all web-based health delivery platforms.

Key words
Impact, menstruation, young people

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REPURPOSING POSITRON EMISSION TOMOGRAPHY (PET) IMAGING FOR DIAGNOSIS AND SURVEILLANCE OF ENDOMETRIOSIS (REPETE): AN EXPLORATION OF POSSIBLE ENDOMETRIOSIS PET MARKERS

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Country where research was undertaken: Australia

Introduction/Background
The objective of this study was to establish if positron emission tomography (PET) imaging could be repurposed for the non-invasive diagnosis and surveillance of endometriosis. We aimed to explore the expression of several plausible endometriosis markers in lesions, endometrium and myometrium (including adenomyosis) for already existing PET tracers.

Materials and Methods
Immunohistochemistry (IHC) against estrogen receptor alpha (ERα), androgen receptor (AR), fibroblast activation protein (FAP), collagen type 1 (COL1A1) and prostate-specific membrane antigen (PMSA) were undertaken, n=5; eutopic endometrium with/without endometriosis, (menstrual, proliferative, secretory, hormone-treated), myometrium (proliferative, secretory, hormone-treated), adenomyosis (hormone-free, hormone-treated) and superficial, deep and endometrioma lesions (menstrual, proliferative, secretory, hormone-treated). CD10 and H&E slides were also used for basic morphology. Slides were analysed for sub-cellular and tissue-specific staining, and intensity of staining.

Results
ERα was observed to be nuclear, and highly expressed in myometrium and endometrium. It was also abundant in adenomyosis and superficial/deep/endometrioma lesions (ERα+ 80-100% glands and stroma). AR, like ERα, was predominantly nuclear. AR was found to be endometriotic lesion-specific, in that surrounding tissues were negative, but overall staining intensity was low. AR was also positive (weak) in myometrium and adenomyosis regions. COL1A1 and PSMA both showed minimal (or absent) staining in lesions, but were positive in surrounding healthy tissue of lesions. PMSA was strongest in myometrial musculature, including blood vessel walls. FAP was largely associated only with staining for red blood cells, and was overall not specific to lesions.

Conclusion
Four markers, AR, FAP, COL1A1 and PMSA, were overall non-specific to lesions and / or demonstrated weak expression. In comparison, ERα, was more abundant in endometriotic lesions and adenomyosis. Therefore, the PET tracer ^{18}F-16α-17β-fluoroestradiol (^{18}F-FES), which binds to ERα, warrants further exploration in the setting of endometriosis.

Key words
PET imaging, diagnosis, immunohistochemistry

ENDOMETRIOSIS IN AFRICAN WOMEN: FINDINGS FROM A COHORT OF REPRODUCTIVE AGE WOMEN ATTENDING AN ENDOMETRIOSIS ULTRASOUND TRAINING PROGRAM.

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Country where research was undertaken:
Kenya

Introduction and Background
Transvaginal ultrasound (TVUS) is the recommended tool for non-invasive diagnosis of endometriosis. Our study seeks to demonstrate its utility in the diagnosis of endometriosis among a cohort of reproductive age women attending a capacity building program in endometriosis ultrasound in sub–Saharan Africa.

Materials and Methods
A capacity-building workshop for reproductive health care practitioners on endometriosis ultrasound was conducted in Kenya. The 3 day workshop included theoretical and practical training, utilizing pelvic phantoms and live scanning sessions. Women with clinical symptoms of endometriosis were recruited via social media and invited to attend. An inclusion and exclusion criteria were used to identify women for invitation. Data were collected from 34 participants who underwent TVUS during the live scanning sessions. Demographic data and ultrasound findings were recorded and analysed.

Results
The mean age of participants was 29 years, with 73.5% being nulliparous. All participants reported severe dysmenorrhea, and 85.3% experienced non-cyclical pelvic pain. TVUS findings revealed adenomyosis in 86% and deep endometriosis in 54% of participants. Of these, 20.6% had endometriomas, 38% had non-bowel deep endometriosis, and 23.5% had bowel deep endometriosis. Participants with a history of prior surgery for endometriosis were significantly more likely to have higher-stage disease, particularly bowel endometriosis.

Conclusions
TVUS is a useful tool in the diagnostic pathway for endometriosis in sub-Saharan Africa. The high prevalence of significant endometriosis-related pathologies despite prior surgeries highlights the need for continuing training. Social media recruitment was effective in the region, indicating growing recognition of endometriosis symptoms among young African women.

UNDERSTANDING ENDOMETRIOSIS DIAGNOSIS: UTILISING PATIENT LIVED EXPERIENCES FOR HEALTH SYSTEM INSIGHTS, AND IDENTIFYING INTERVENTION OPPORTUNITIES FOR IMPROVED DIAGNOSIS ACCESSIBILITY

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Country where research was undertaken:
Australia

Introduction/Background
6.4 years to gain an endometriosis diagnosis[1], a well referenced statistic in Australia. However, in order to assess the potential impact a diagnosis-aide intervention may have on patient diagnosis accessibility improvement, the researchers needed to further understand the current health system. Utilizing the lived experience of patients to do so.

Materials and Methods
A cross-sectional online survey of individuals recently diagnosed with endometriosis. The researchers aimed for data achieved to be representative of the Australian population, inclusive of minority and vulnerable population groups.

Survey questions focused on patient reported diagnosis modalities; time to diagnosis; instances with health services providers; accessibility of health services; and appropriateness of health service care.

Logistic regression was used to explore the factors associated with different diagnosis

modalities.

Results
Researchers we are to compare the lived experiences of those with differing diagnosis modalities, allowing for a discussion on the improvements to be made in health systems based on diagnosis pathways.

Researchers were also able to compare the lived experiences of those with differing social determinants of health, assisting in the identification of opportunities differing diagnosis modalities had in 'closing the gap' of health equity.

Conclusion
In order to assess any intervention for potential improvement in patient experiences, researchers must take on a systems-thinking approach. Understanding the lived experience of patients will greatly aide health policy makers; health service providers; and technology developers, in the implementation of interventions that truly make beneficial impact.

Key words
Diagnosis; systems-thinking; accessibility.

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DOES THE SIZE OF RECTOSIGMOID ENDOMETRIOSIS LESIONS AND THE STATUS OF POD ON ULTRASOUND AFFECT PREDICTION OF DISEASE?

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Country where research was undertaken:
Australia

Introduction/Background
The aim of this study was to evaluate the effect of the increasing size of rectosigmoid deep endometriosis (DE) lesions and the status of the pouch of Douglas (POD) on transvaginal ultrasound (TVS) to predict disease these locations.

Materials and Methods
This was a retrospective multi-center study. Patients with possible endometriosis in the rectosigmoid who had complete ultrasound, surgical and histological data were included in final analysis. All bowel with maximal diameter in longest plane ≥ 5 mm, ≥ 10 mm, ≥ 15 mm, ≥ 20 mm, ≥ 25 mm, ≥ 30 mm on TVS were included. The presence of a positive or negative 'sliding' sign (marker for POD obliteration) was also recorded. We then examined the data to assess the performance of TVS to predict rectosigmoid DE when the POD was predicted to be either non-obliterated or obliterated. Reference standard was histological confirmation of endometriosis. The overall performance of ultrasound to predict DE in the rectosigmoid were determined using the area under the receiver operating curve (AUC). Data were analyzed using SAS version 9.4.

Results
190 lesions for rectosigmoid were identified. The AUCs for prediction of rectosigmoid without and with POD obliteration were 0.58 and 0.60, respectively. As DE lesion size on ultrasound increases for rectosigmoid specificity and PPV increase but sensitivity decreases.

Conclusion
POD obliteration is associated with improved diagnostic performance of ultrasound in predicting rectosigmoid DE.

Key words
Deep endometriosis, Lesion's size, bowel endometriosis.

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CAN IMAGING DETERMINE THE PREVALENCE OF ENDOMETRIOSIS IN AN ASYMPTOMATIC POPULATION, AND IS IT A FEASIBLE SCREENING TOOL?

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Country where research was undertaken:
Australia

Introduction/Background
Endometriosis diagnosis takes on average 6.4 years, with time delay negatively impacting quality of life and fertility. When collecting control scans for development of our diagnostic tool, with ethics we asked a cohort of asymptomatic people to undergo a magnetic resonance imaging (MRI) scan and an endometriosis transvaginal ultrasound (eTVUS).

Materials and Methods
To increase the data required to train algorithms for diagnosing endometriosis using imaging, we recruited and screened women aged 18-45 with informed consent, as healthy controls, asymptomatic for endometriosis. We offered an MRI scan and specialist transvaginal ultrasound scan (TVUS). Radiology and sonography endometriosis experts confirmed all findings. If incidental pathology was found, a full Radiologist report was sent to the participant's general practitioner, and the women counselled by either their GP or gynaecologist.

Results
Since May 2024, we had 81 women volunteer to be part of this ethically approved cohort. After screening through RedCap we found 65 women were eligible, with another 16 meeting our exclusion criteria. Twelve women declined an eTVUS, only having an MRI. Of the 40

asymptomatic participants who volunteered, 4 had endometriosis, and 2 had adenomyosis. At this stage, one has gone onto fertility preservation treatment, one has chosen not to have treatment, and all have been reviewed by gynaecologist.

Conclusion
This unexpected finding demonstrates the importance of evaluating the impact of endometriosis scanning in populations without symptoms. This has implications for its use as a screening tool, and for past and future studies that have used asymptomatic controls, where we would anticipate at least 10% to have endometriosis.

Key words
Diagnosis, imaging, study design

THE ASSOCIATION BETWEEN CLINICAL PRESENTATION AND ENDOMETRIOSIS TYPES

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Country where research was undertaken:
Israel

Introduction
Endometriosis exists mainly as three subtypes: superficial endometriosis, deep endometriosis and ovarian endometriosis. Although earlier research indicates that clinical symptoms do not correlate with the severity of anatomical disease, there is currently scarce data on the association between clinical presentation and demographic characteristics and endometriosis subtype.

Materials and Methods
A retrospective study at an endometriosis center of a tertiary medical center, which included women aged 18-50 with endometriosis. Demographic data (age, BMI, smoking, ethnicity, parity, background comorbidities), various endometriosis symptoms (dysmenorrhea, dyspareunia, dysuria, dyschezia, chronic pelvic pain (CPP), chronic fatigue, abdominal bloating, lower back pain) and gastrointestinal symptoms (GIS) were compared between women with superficial endometriosis and deep and ovarian endometriosis.

Results
A total of 248 women were included in the study. Among them, 32.3% (n=80) had surgically-proven superficial endometriosis, and 67.8% (n=168) had deep or ovarian endometriosis, diagnosed by surgery or imaging. Women with superficial endometriosis were younger as compared to women with deep or ovarian endometriosis (31.9±6.8 vs 37.3±6.8 years, p=0.001, respectively). Dyschezia, dyspareunia and CPP were more common among women with deep and ovarian endometriosis, as compared to superficial endometriosis (dyschezia: 77.2% vs 53%, P=0.02; dyspareunia: 54.8% vs 18.8, % p=0.001; CPP: 51.5% vs 16.2%, p=0.001). severe-dysmenorrhea, dysuria and GIS were more common in women with superficial endometriosis, as compared to women with deep and ovarian endometriosis (severe-dysmenorrhea: 81% vs 45.8%, p=0.001; dysuria: 30% vs 11.9%, p= 0.002; GIS: 31.2% vs 13.7%, p=0.01).

Conclusions
As opposed to previous literature, in our cohort, clinical presentation differed between different types of endometriosis with dysmenorrhea, dysuria and gastrointestinal symptoms more common in women with superficial endometriosis and dyschezia, dyspareunia and CPP more common in women with non-superficial endometriosis. Better understanding of clinical presentation may improve diagnostic accuracy.

Key words
Superficial endometriosis, deep endometriosis, ovarian endometriosis.

PREDICTIVE MODEL FOR THE NON-INVASIVE DIAGNOSIS OF ENDOMETRIOSIS FOR PATIENTS RECEIVING CONTRACEPTION BASED ON CLINICAL PARAMETERS

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Country where research was undertaken:
Germany

Introduction/Background
A non-invasive test for endometriosis is still lacking. Are pain symptoms correlated to endometriosis suitable for a clinical prediction model?

Materials and Methods
We conducted a prospective study from 2016 to 2023 including a total of 228 women on contraception with numerous pain symptoms and other parameters. All women filled in two questionnaires and were examined by palpation and transvaginal ultrasound (TVUS). In cases of suspected deep endometriosis magnetic resonance imaging (MRI) was performed. After operation by hysterectomy and/or laparoscopy endometriosis was diagnosed by histological examination.

Results
The most important pain symptoms for the prediction of endometriosis were dysuria, obstipation, dyspareunia, cramping, pulling, pain to the legs/thighs, sum of visual analog scores (VAS) and numbers of significant parameters. The prediction resulted in 91.6% sensitivity, 87.2% specificity and a positive likelihood ratio of 7.1

Conclusion
We could show for the first time that a questionnaire could be used as a non-invasive test for endometriosis with a very high sensitivity and specificity.

Key words
Questionnaire, non-invasive diagnosis, endometriosis

ASSOCIATION OF PAIN SYMPTOMS AND DEMOGRAPHIC CHARACTERISTICS WITH SUPERFICIAL ENDOMETRIOSIS FINDINGS IN LAPAROSCOPY

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Country where research was undertaken:
Israel

Introduction
Limited data exists on the association between demographic and clinical characteristics and the presence or location of surgical proven superficial endometriosis (SPSE). Therefore, we aimed to compare pain symptoms and demographic data between women with and without SPSE. We also assessed the relationship between specific symptoms and lesion sites.

Methods
A retrospective study of women aged 18-43 who underwent laparoscopic surgery for investigation of pelvic pain and/or infertility was conducted. Women with pre-surgical imaging indicating endometriosis and those with ovarian or deep lesions at surgery were excluded. Pain symptoms (dysmenorrhea, dyspareunia, dysuria, dyschezia and chronic pelvic pain), infertility and demographic data (age, BMI, parity, smoking) were compared between women with and without SPSE. We then assessed the correlation between these variables and specific lesion locations.

Results
A total of 161 women who underwent surgery between 2019-2022 were included in the study. Of them, 60.2% (n=97) had SPSE and 39.8% (n=64) were not found to have endometriosis lesions at surgery. Severe dysmenorrhea was more common in women without endometriosis compared to those with SPSE (98% vs 87%, p=0.003). Although highly prevalent in both women with and without SPSE, mild to moderate dysmenorrhea or dyspareunia was less common in women with endometriosis (98.4% vs 90.7 %, p=0.05). Demographic characteristics did not differ between groups. While no specific correlations were found between specific pain symptoms and lesion location, women with pelvic sidewall lesions, had lower rates of infertility as compared to other lesion locations (18.3% vs 38% p=0.03).

Conclusions
Our cohort suggests that in women with negative imaging before surgery, pain symptoms do not predict the presence or location of endometriosis lesions. Further research is needed to examine whether clinical characteristics could enhance the pre-

surgical diagnosis of SPSE.

Key words
Superficial endometriosis (SPSE**),** dysmenorrhea, dyspareunia

THEME: DIGITAL HEALTH AND ARTIFICIAL INTELLIGENCE

THE ENDOMETRIOSIS LONGITUDINAL FERTILITY STUDY (ELFS): 36MONTHS' EXPERIENCE WITH THE ELFS APP FOR LONGITUDINAL FERTILITY DATA COLLECTION

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Countries where research was undertaken:
Australia and Israel

Background:
Endometriosis is associated with reduced pregnancy rates. At present, the effect of surgery on the fertility of women with moderate/severe endometriosis remains unanswered. Mobile phone Apps are a novel research tool with important potential benefits in longitudinal data collection. Optimal use of these tools requires ongoing assessment and consumer input.

Methods:
The Endometriosis Longitudinal Fertility Study (ELFS) is a prospective cohort study aiming to measure and compare monthly fertility outcomes in women with evidence of moderate/severe endometriosis. Following baseline questionnaire completion, participants install the ELFS App – a purpose-built data collection tool – to their mobile phone and receive longitudinal cyclical surveys initiated by in-build logic. Participants have the option to use an alternative A new version of the ELFS App is being deployed in November 2024 aimed to improve participant and researcher functionality.

Results
Following 36months of recruitment, 229 patients had enrolled in ELFS and 180 participants have begun using the study App. 1,425 cycle questionnaires have been prompted, with 1,296(91%) being completed. Twenty-six participants(11.3%) have failed to complete a single App questionnaire after baseline. 107(46.3%) have completed all App-initiated cyclical questionnaires (median(IQR), 6(2,11) cycles). The App re-design was prompted by an unreconcilable coding error, preventing some operating systems from accessing or saving App data. Qualitative and quantitative assessment of App usage and App experience are planned for 3months following the transition to the new ELFS App.

Conclusions:
The purpose-built ELFS App is facilitating timely cyclical data collection, with superior response rates compared with prior longitudinal questionnaire-based studies in fertility. However, technology limitations and programming errors have necessitated App redesign. Long-term ELFS App use will be monitored as its functionality and participant acceptance is integral to study success.

Key words
Digital health**,** endometriosis**,** fertility

USING ARTIFICIAL INTELLIGENCE FOR DETECTING POUCH OF DOUGLAS OBLITERATION AND RECTAL NODULES THROUGH MAGNETIC RESONANCE IMAGING AND TRANSVAGINAL ULTRASOUND

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Country where research was undertaken:
Australia

Introduction/Background
Endometriosis transvaginal ultrasound (eTVUS) and Magnetic resonance imaging (eMRI) and are complementary imaging modalities for diagnosing endometriosis[1]. The IMAGENDO® project developed a multi-modal multi-label Artificial Intelligence (AI) approach to combine eMRI and eTVUS. This method enables automatic detection of Pouch of Douglas (POD) obliteration and rectal nodules using either modality.

Materials and Methods
We developed a novel deep learning (DL) model based on mutual knowledge distillation to detect both endometriosis signs from either eMRI or eTVUS. The DL model was pretrained on 8,984 unlabeled female pelvic MRIs and then fine-tuned with 171 labelled endometriosis MRIs (63 with POD obliteration, 11 with rectal nodules), 749 TVUS videos showing the uterine 'sliding sign' (103 with POD obliteration), and 519 TVUS videos demonstrating the rectal area (35 with rectal nodules).

Results
To ensure a consistent positive-negative distribution in both training and testing sets while improving model generalization, we employed stratified 5-fold cross-validation. We report the mean and standard deviation (SD) of the area under the receiver operating characteristic curve (AUROC) across the five folds. Our DL model achieved an average AUROC of 84.81% (SD 0.0587) in detecting two endometriosis signs across two imaging modalities. Specifically, with eMRI, it reached an AUROC of 77.04% (SD 0.0921) for POD obliteration and 89.77% (SD 0.0849) for rectal nodules. For TVUS, it achieved an AUROC of 91.77% (SD 0.0437) for POD obliteration and 81.27% (SD 0.0688) for rectal nodules. Notably, our model processes each testing eMRI or eTVUS in just 0.018 seconds, demonstrating its clinical application potential.

Conclusion
Our AI model can effectively and efficiently detect POD obliteration and rectal nodule signs from either eTVUS or eMRI data. This is the first clinically translatable method achieving fully automated diagnosis of multiple endometriosis signs from either eMRI or eTVUS, enabling faster, non-surgical diagnosis for endometriosis.

Key words
Artificial intelligence, pouch of douglas obliteration, rectal nodule,

Reference
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EXPLORING THE DIGITAL NEEDS OF THE AUSTRALIAN ENDOMETRIOSIS COMMUNITY FOR THE CO-CREATION OF ENDOZONE: A DIGITAL PLATFORM FOR ENDOMETRIOSIS MANAGEMENT

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Country where research was undertaken:
Australia

Introduction
Endometriosis associated symptoms are highly heterogeneous and are often normalised due to stigma and poor awareness. This study aims to understand information needs of those living with endometriosis to develop Endozone, a reliable online information resource.

Materials and methods
Semi-structured focus groups were conducted across Australia. Participants were included if they were: (i) aged > 16 years, (ii) Australian residents, (iii) experiencing symptoms suggestive of endometriosis or (iv) supported someone with endometriosis. Participants were divided into three groups: (i) those aged ≥ 16-18 years, (ii) those aged ≥ 19 years, and (iii) supporters (parents and partners aged ≥ 18 years). Data was analysed using Braun and Clarke's approach to reflexive thematic analysis (1).

Results
Thirty-six people participated in eight focus group discussions conducted across Australia between March-May 2020. One focus group was conducted face-to-face, while the remaining were conducted online using Zoom due to COVID-19 lockdown restrictions. Three main themes were identified: participants' need for: (i) a central hub of endometriosis information that provided evidenced-based endometriosis related information, addressed normalisation of period pain, included resources for different users like young people, parents and partners and helped to navigate the healthcare system, (ii) holistic strategies for symptom management to support physical and psychological wellbeing, and (iii) supporting the digital user experience.

Conclusions
This is a novel study which assessed the digital needs of the Australian endometriosis community which contributed to the co-creation of EndoZone, a digital platform for endometriosis. Participants expressed that evidence-based information will assist in improving endometriosis knowledge which can empower them to seek timely medical attention and self-manage symptoms.

Key words
Digital health; qualitative research; improving awareness

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TOXIC CLUES: A KNOWLEDGE MINING APPROACH TO CONNECT ENVIRONMENTAL POLLUTANTS TO ENDOMETRIOSIS PROGRESSION.

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Country where research was undertaken:
France

Introduction/Background
Unraveling the link between chemicals, metabolic modulations and endometriosis requires combining metabolic data with health-impacting mechanisms. We propose a framework to analyze vast knowledge bases using data mining and reasoning algorithms to advance human-machine collaboration in toxicology: simplifying results interpretation, optimizing hypothesis generation and assisting literature search.

Materials and Methods
We built a knowledge network linking concepts and compounds associated with endometriosis, derived from FORUM - a large-scale knowledge base containing over 9 billion relations between chemical compounds and biomedical concepts, automatically inferred from the literature. FORUM aims to elucidate metabolic signatures through associated concepts and pathways. We also integrated Adverse Outcome Pathway (AOPs) into the network, facilitating the association of chemical compounds with the contaminants' modes of action, using recent advancements in controlled vocabularies.

Results
We extracted an endometriosis-focused network containing 295 concepts and 3,785 compounds, and applied filters to target specific classes of organochlorine pollutants. To achieve this, we developed a pipeline that crawls a massive knowledge base, extracting relevant information related to an adverse outcome and/or experimental results, such as disrupted signaling pathways. Requiring minimal computational skills, this tool enables researchers to build a private local knowledge base, combining their own experimental data and hypotheses with public scientific knowledge. Leveraging metabolomics experimental data, knowledge graph mining techniques unveil Key Events that intricately link pollutants to the pathophysiology of endometriosis. This framework also enhances the visualization and exploration of complex data, helping researchers to uncover hidden patterns and connections in the disease mechanisms using machine learning

algorithms.

Conclusion
This resource alleviates the burden of literature searches by offering visual exploration of relevant knowledge, supported by recommendation systems and smart filtering, condensing the information in the literature. This will enable identification of compound-concept relationships, simplifying hypothesis generation and AOP building, deepening our understanding of pollutants mixtures' role in endometriosis.

Key words
Pollutant exposures, metabolism, knowledge mining

LEVERAGING AN ARTIFICIAL INTELLIGENCE LARGE-LANGUAGE MODEL AND REDDIT DATA FOR INSIGHTS INTO ENDOMETRIOSIS TREATMENT

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Country where research was undertaken:
United States of America

Introduction/Background
Endometriosis patients' experiences and perspectives are imperative to understand.[1] Exploring public real-world data provides an opportunity for greater insights. Leveraging an artificial intelligence [AI] large-language model [LLM], we analyzed large-scale Reddit data from thousands of individuals to gain insight into endometriosis care and treatment.

Materials and Methods
We used OpenAI and Reddit application-program-interfaces [APIs], and openai[2] and praw[3] Python packages to quantify posts and comments within the "r/endometriosis" and "r/ENDO" subreddits as of October 2024. We used the GPT4 model and engineered prompts to analyze and summarize themes with respect to endometriosis care and treatment from all content within the endometriosis-theme subreddits.

Results
Endometriosis-themed subreddits contained in total 1,986 posts and 79,993 comments (4,321,905 words) from 17,049 users (02/07/2018–10/31/2024). Code runtime 16m:56s. Themes regarding endometriosis treatment identified by the GPT4 model included:

"-Patients with chronic pain often face emotional distress and medical gaslighting, leading to frustration with healthcare.
-Surgical treatments like excision surgery and laparoscopies offer mixed outcomes, with some experiencing relief and others facing complications or inaccessibility due to costs.
-Non-medication interventions, such as diets and physical therapy, are tried but lack consensus on effectiveness.
-Many patients resist the suggestion of pregnancy as a treatment, preferring pain-focused solutions.
-Quality of care varies widely, with some patients praising their specialists and others reporting neglect and difficulty finding knowledgeable professionals."

Conclusion
Leveraging LLMs and large-scale real-world data, such as 6.5 years of Reddit content submitted by approximately 17 thousand individuals, can provide within minutes data-driven insights into known issues and under-realized concerns regarding endometriosis treatment. These insights can, in turn, highlight endometriosis patient care aspects to further investigate and prioritize.

Key words
Endometriosis, artificial intelligence, large language model

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CO-DESIGNING A HOLISTIC DIGITAL ENDOMETRIOSIS SURGERY OPTIMISATION PROGRAM

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Country where research was undertaken:
Australia

Introduction/Background
Endometriosis surgery is a pivotal, yet distressing time often marked by uncertainty, anxiety and lack of preparation. Many feel isolated, without guidance on physical, nutritional or psychological readiness. Digital interventions offer the potential to streamline this journey, foster peer connection and support better surgical outcomes, though research remains limited.

Materials and Methods
We conducted two hybrid (in-person and online) 90-minute co-design sessions with individuals who have undergone endometriosis surgery and consulted individually with gynaecologists and holistic care experts. Sessions were analysed using the Jobs-to-Be-Done framework.

Early program versions were iteratively refined through fortnightly co-design sessions over two months. The first version was released on App Stores and piloted with ten gynaecologists. User interviews provided feedback, leading to further refinements and improvements for future iterations of the program.

Results
Ten individuals with lived experience participated in two co-design sessions. Input was also received from two gynaecologists, two physiotherapists, two dietitians, two psychologists, one yoga and mindfulness instructor, one Pilates instructor and one endometriosis nurse.

Key pre-surgery needs included understanding procedural expectations, managing anxiety, physical and mental preparation, and organising logistics. Post-surgery needs focused on managing pain, ensuring proper care, effective communication with healthcare providers, monitoring recovery, regaining strength and receiving emotional support.

Fortnightly co-design sessions refined the program's layout, messaging, accessibility, and user experience, emphasising peer support and ensuring a seamless journey.

This collaborative process enabled the rapid release of the program on both Google Play and the Apple App Store, allowing for further pilot testing to enhance the program's effectiveness.

Conclusion
This study highlights the potential of a digitally delivered endometriosis surgery optimisation program to address critical pre and post-surgery needs such as preparation, recovery and emotional support. Collaborative co-design ensured a user-centred approach, leading to a pilot-ready digital-health app. Findings provide a foundation for future research and broader program implementation.

Key words
App, digital health.

THEME: EPIDEMIOLOGY, CO-MORBIDITIES AND RISK FACTOR(S)

UNSUPERVISED CLUSTERING OF ENDOMETRIOSIS PATIENTS USING ELECTRONIC HEALTH RECORDS

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Country where research was undertaken:
United States of America

Introduction/Background
Electronic health record (EHR) databases contain a wealth of information on large populations and can be used to characterize patients experiencing complex diseases at a clinical level [1]. We applied unsupervised clustering to endometriosis patients from two large EHRs to identify patient groups and reveal patterns of associated diagnoses.

Materials and Methods
Leveraging the Observational Medical Outcomes Partnership (OMOP) schema [2], we selected patients using conditions descended from "endometriosis" in the standard concept hierarchy and identified clusters by applying the Leiden algorithm [3] to a binary matrix of their diagnoses. We

computed odds ratios for comorbidities within each cluster and determined exclusive and significantly enriched conditions via hypergeometric tests. All analyses were performed using both the full set of diagnoses and only pre-endometriosis diagnoses.

Results
We identified a total of 19,059 and 24,453 endometriosis patients across our respective EHR databases. Clustering analysis revealed 21 and 26 groups of endometriosis patients across the two databases when considering all conditions, and 31 and 41 groups of patients when considering pre-endometriosis conditions, respectively. Many of these clusters can be assigned themes based on the conditions exclusively enriched in each. We found clusters characterized by comorbidities related to various pregnancy complications, Crohn's disease, and renal disorders. Moreover, we found that many clusters from one database had enriched conditions that overlapped with those found in clusters from the other database, such as with conditions related to pregnancy or cancer, indicating similar patterns of comorbidity across the two separate patient populations.

Conclusion
Our findings uncover distinct comorbidity patterns among endometriosis patients, with consistent clusters observed across two separate large EHR databases. This clustering approach provides insights into disease associations, offering potential pathways for personalized management and improved understanding of endometriosis-related health risks.

Key words
Electronic health records, clustering, comorbidity

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POSTMENOPAUSAL HORMONES AND RISK OF ENDOMETRIOSIS DIAGNOSED AFTER MENOPAUSE: A PROSPECTIVE COHORT STUDY

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Country where research was undertaken:
United States of America

Introduction/Background
Hormones are prescribed for management of peri-and postmenopausal symptom relief. Case reports document links between hormone use and recurrence of endometriosis as well as first diagnosed endometriosis after menopause. Furthermore, case reports document regression of postmenopausal endometriotic lesions with cessation of hormone treatment in the postmenopausal period.

Materials and Methods
This prospective study utilized data from participants in the Nurses' Health Study II after menopause. Participants enrolled in 1989, and menopause status, hormone use after menopause(PMH), PMH formulation and duration, were updated biennially through 2019. We utilized multivariable Cox regression models to calculate risk of surgically-confirmed endometriosis after menopause with PMH status, formulation and duration of use. We also evaluated these associations stratified by body mass index (BMI), cigarette smoking, nulliparity, and age at menopause.

Results
Among 79,454 postmenopausal women never diagnosed with endometriosis before menopause, 853 incident cases of endometriosis diagnosed after menopause were reported. Compared to participants who never used PMH, risk of postmenopausal endometriosis was greater among women with current PMH use (hazard ratio(HR)=1.72; 95%

confidence interval(CI)=1.41-2.09) and with use of PMH for ≥72 months (HR=1.76; CI=1.38-2.23; p-trend=0.0004) adjusting for age, calendar time, race/ethnicity, BMI, smoking, alcohol use, age at menarche and menopause, parity, and health screening. Greater risk of postmenopausal endometriosis diagnosis was found with oral conjugated estrogen (HR=2.00; CI=1.62-2.47) and with estrogen + testosterone (HR=2.05; CI=0.99-4.28), but not for progesterone alone (HR=1.05; CI=0.54-2.03) or for estrogen + progesterone (HR=1.04; 0.82-1.33) formulations. No differences in these associations were found by BMI, smoking, nulliparity, or age at menopause.

Conclusion
Given the estrogen-dependent nature of endometriosis and influence of progesterone, PMH use may impact recurrence or *de novo* endometriosis after menopause. General practitioners and gynecologists should be aware that endometriosis can be present after menopause and should be considered in PMH decision making and symptom monitoring.

Key words
Menopause, hormone use, laparoscopically confirmed endometriosis

HOSPITALISATIONS AND LENGTH OF STAYS IN WOMEN WITH ENDOMETRIOSIS: A DATA LINKAGE PROSPECTIVE COHORT STUDY

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Country where research was undertaken:
Australia

Introduction/Background
Women with endometriosis experience more hospitalisations than those without. However, no longitudinal study has examined readmission rates or lengths of stay before and after diagnosis. We assessed all-cause hospital admissions and lengths of stay among women with and without endometriosis, before versus after diagnosis.

Materials and Methods
This study included 13501 women of reproductive age, born in 1973-78. The Australian Longitudinal Study on Women's Health survey data linked to administrative health records was used to identify women with endometriosis. Hospital admission rates and length of stays were examined using hospital records of patients admitted up to 2022. Analysis was conducted using mixed-effects zero-inflated negative binomial models.

Results
Women with endometriosis were more likely to be admitted to hospitals than those without the condition, with an adjusted incidence rate ratio (IRR) of 2.11 (95% CI: 1.83 – 2.43) for admissions per year. However, they had shorter hospital stays (IRR: 0.90; 0.81 – 0.99) for days per year and were more often discharged on the same day (odds ratio: 1.27; 1.20 – 1.33). Post-diagnosis, women experienced more hospitalisations and more days in hospital compared to their pre-diagnosis (IRR: 1.52; 1.22 – 1.88) and (IRR: 1.81; 1.53 – 2.14), respectively. Consistent findings were found for women with surgically confirmed or clinically suspected endometriosis.

Conclusions
The higher number of hospitalisations among women with endometriosis, compared to those without, highlights the substantial burden of the condition on healthcare utilisation. The persistent frequent hospitalisations and longer stays post-diagnosis indicate recurrent endometriosis, posing significant management challenges.

Key words
Endometriosis, hospitalisation, length of stay

ENDOMETRIOSIS HOSPITALISATIONS AND EMERGENCY DEPARTMENT PRESENTATIONS IN AUSTRALIA: WHAT WE KNOW FROM NATIONAL ADMINISTRATIVE HEALTH SERVICE DATA

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Country where research was undertaken:
Australia

Introduction/Background
Hospitals and emergency departments (EDs)

play a key role in treating endometriosis. As a historically under-recognised condition, awareness of endometriosis appears to be increasing, leading to increased diagnoses among women born more recently[7]. This study aims to improve understanding of hospitalisations and ED presentations for endometriosis in Australia.

Materials and Methods
This study used administrative health service data to explore endometriosis-related hospitalisations and emergency department presentations. Data were sourced from the National Hospital Morbidity Database (2011–12 to 2021–22) and the National Non-admitted Patient Emergency Department Care Database (2018–19 to 2021–22). Endometriosis-related hospitalisations and ED presentations were identified as those with a principal and/or additional diagnosis of endometriosis. Results were disaggregated by demographic, geographic and service characteristics.

Results
There were 40,500 endometriosis-related hospitalisations in 2021–22. Most were partly or fully funded by private health insurance (58%).

The rate of endometriosis-related hospitalisations:

- increased by 24% between 2011–12 and 2021–22, from 250 to 310 per 100,000 females. This was greater than the 9% increase in female hospitalisations over this period.
- doubled among females aged 20–24 in the past decade, from 330 to 660 hospitalisations per 100,000 females.
- was lower among First Nations people, and for people living in lower socioeconomic areas and remote areas of Australia.

There were over 3,600 endometriosis-related ED presentations in 2021–22; a rate of 28 presentations per 100,000 females.

For the Congress, data will be updated to the latest available year (2022–23).

Conclusion
Effective population monitoring of endometriosis requires comprehensive and accurate data. Growth in endometriosis-related hospitalisations over the last decade highlights the importance of tertiary care for endometriosis. Variation across population groups warrants further investigation about whether this represents unequal disease burden or service access, or appropriate diversity of care.

Key words
Endometriosis, hospitalisation, data

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COMORBIDITY PROFILES IN WOMEN WITH ENDOMETRIOSIS IN THE COMPARE - ENDOMETRIOSIS COHORT

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Country where research was undertaken:
France

Introduction/Background
Endometriosis is associated with an increased risk of various chronic diseases, including autoimmune, atopic, psychiatric, and pain-related conditions. Although many studies have examined the links between endometriosis and individual diseases, very few have focused on associations with multiple comorbidities. Our study aimed to identify comorbidity profiles in women with endometriosis.

Materials and Methods
ComPaRe-Endometriosis is a prospective e-cohort initiated in 2018 and following over 10,000 women with endometriosis. Participants self-reported their chronic conditions at baseline from a list of 87 diseases. We conducted a cross-sectional study and used hierarchical clustering to identify baseline comorbidity profiles, and we described the socioeconomic, lifestyle, disease, and patient characteristics associated

with each profile.

Results
Among 10,761 participants, 64.2% reported only endometriosis, while 35.8% reported at least one comorbidity (1 comorbidity: 52.7%, 2: 22.9%, 3: 10.2%, 4: 5.4%, 5+: 8.8%). We identified seven clusters of participants: Cluster 1 (n=8,656) included endometriosis patients with less comorbidities; Cluster 2 (n=693) included mostly those with chronic pain (44.3%), irritable bowel syndrome (40.4%), and/or fibromyalgia (33.3%); Cluster 3 (n=193) those with depression (99.5%) and/or anxiety (14.0%); Cluster 4 (n=532) those with asthma (57.9%), allergies (36.5%), and/or chronic skin diseases (30.6%); Cluster 5 (n=185) those with ovarian cysts/polycystic ovary syndrome (100%); Cluster 6 (n=299) those with thyroid diseases (100%); and Cluster 7 (n=203) those with migraine (100%).

Conclusion
This study identified distinct comorbidity profiles in women with endometriosis, underscoring the diversity of health profiles associated with this condition. These findings highlight the need for multidisciplinary care addressing the complex interactions between endometriosis and multiple physiological systems, offering new perspectives for improving disease management and guiding future research.

Key words
Comorbidities, clustering, epidemiology

ROLE OF POLYGENIC RISK, FAMILY HISTORY, AND COMORBIDITIES IN ENDOMETRIOSIS: IMPLICATIONS FOR RISK ASSESSMENT AND DISEASE PREVALENCE

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Country where research was undertaken:
Australia

Introduction/Background
Endometriosis is a multifactorial disease influenced by genetic and environmental factors, with known associations to comorbid conditions. Despite advances in understanding genetic risk factors, the relationship between genetic risk, family history and comorbidity burden over the life course remains poorly understood.

Materials and Methods
Using genetic, survey and health record data from the Genetic Variants, Early Life Exposures, and Longitudinal Endometriosis Symptoms (GELLES) study (240 cases, 1170 controls), a sub-study of the Australian Longitudinal Study on Women's Health, and UK Biobank (UKB)(5,432 cases, 92,344 controls) we tested associations between endometriosis polygenic risk score (PRS) and family history of endometriosis, and between PRS and comorbidity burden, respectively. Interactive effects of PRS with prevalent comorbidities (eg. uterine fibroids; dysmenorrhoea) were also tested.

Results
Women with a PRS in the top 10% were 3.4-3.8x more likely to be diagnosed with endometriosis than those in the bottom 10%. Women with a family history of endometriosis were 4.2x more likely to be diagnosed than those without. Models including both family history and PRS gave a better fit compared with those with family history or PRS alone. PRS explained only 2% of the effect of family history and family history only 6% of the effect of PRS. Women with endometriosis had a higher comorbidity burden than those without. Comorbidity burden was positively correlated with PRS in women without endometriosis but negatively correlated in women with the disease. Additive interactions between PRS and uterine fibroids were also observed, enhancing disease prevalence.

Conclusion
Family history and PRS are largely independent but complementary in assessing inherited risk. PRS can identify early risk in individuals without family history, while both measures improve risk stratification. Furthermore, interactions between genetic risk and comorbidity burden influence disease prevalence, highlighting complex relationships that may offer insights into underlying mechanisms.

Key words
Family history, comorbidity, genetic risk

ASSOCIATION BETWEEN ENDOMETRIOSIS AND CONGENITAL UTERINE MALFORMATIONS: A SINGLE-CENTER RETROSPECTIVE STUDY

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Country where research was undertaken:
Switzerland

Introduction/Background
The aim of our study is to evaluate the prevalence of CUAs in women with endometriosis and to identify specific characteristics in women with both CUAs and endometriosis in a large cohort of patients.

Materials and Methods
This is a retrospective single-center observational study conducted between January 2006 and June 2021. All women included in this study underwent a preoperative 2D ultrasound by an experienced sonographer. In cases of suspected intrauterine pathology, bleeding disorders, or infertility, an additional hysteroscopy was performed.

Results
Out of 1566 women with histologically confirmed endometriosis, 93 were diagnosed with CUAs (5.9%). The most frequent malformations were U1c (arcuate uterus) (41/93, 44.1%), U2a (partial septate uterus) (19/93, 20.4%), U3b (complete bicorporeal uterus) (17/93, 18.3%) and U3a (partial bicorporeal uterus) (10/93, 10.8%). Women with both CUAs and endometriosis were more frequently diagnosed with endometriosis rASRM stage IV (p=0.017) and presence of dysmenorrhea (p=0.019) in comparison to women with endometriosis and a morphologically normal uterus.

Conclusion
According to our findings, the prevalence of CUAs in women with endometriosis does not appear to be higher than in the general population. However, women with CUAs and endometriosis are more likely to suffer from severe endometriosis (rASRM stage IV) and dysmenorrhea compared to endometriosis patients without CUA.

Key words
Endometriosis, congenital uterine anomaly

WHAT IS THE PREVALENCE OF PELVIC FLOOR TENSION MYALGIA AND PELVIC FLOOR MYALGIA IN PATIENTS PRESENTING WITH ENDOMETRIOSIS?

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Country where research was undertaken:
Australia

Introduction/Background
Pelvic floor tension myalgia (PFTM), a pain syndrome arising from increased pelvic floor muscle tone and associated with pelvic floor myalgia (PFM) is a component of chronic pelvic pain (CPP). It is estimated to be common in people with endometriosis, yet the prevalence of PFM/PFTM in this population remains unknown.

Materials and Methods
This retrospective cohort study utilised data recorded on the National Endometriosis Clinical and Scientific Trials (NECST) registry, that collects information from people living with endometriosis, and endometriosis-like symptoms. In patients attending a private gynaecological practice for treatment of endometriosis, PFM/PFTM was assessed at the first clinical visit by the treating gynaecologist. Information regarding associated symptoms was obtained from the registry.

Results
Among 200 patients (mean age 35.9± 9.3), 94.5% were diagnosed with endometriosis. The combined prevalence of PFM/PFTM was 72.5% (95% CI 65.8% - 78.6%). In patients with PFM/PFTM, there was a significant association with dyspareunia ($\chi^2 = 11.854$, p = 0.001) with higher odds of both cyclical dyspareunia (odds ratio [OR], 3.80; 95% confidence interval [CI], 1.73 – 8.39) and non-cyclical dyspareunia (OR 4.56; 95% CI 2.13 – 9.74). Other associated symptoms included cyclical headaches ($\chi^2 = 5.856$, p = 0.016; OR 4.50; 95% CI 1.21 – 16.74) and straining during bowel movements ($\chi^2 = 5.911$, p = 0.015; OR 2.32; 95% CI 1.17 – 4.60).

Logistic regression identified non-cyclical dyspareunia (Exp (B) of 3.496 (95% CI = 1.444 – 8.465, p = 0.006) as a significant predictor of PFM/PFTM.

Conclusion
The prevalence of PFM/PFTM is high at 72.5% in patients diagnosed with endometriosis, highlighting the importance of performing pelvic floor examination in this cohort, particularly if patients report the symptom of non-cyclical dyspareunia. Improved awareness and diagnosis of PFM/PFTM will enhance management and expand non-surgical interventions for patients with endometriosis.

Key words
Pelvic floor tension myalgia, pelvic floor myalgia, chronic pelvic pain

WHAT IS THE BURDEN OF DISEASE OF ENDOMETRIOSIS? DEVELOPING A MARKOV MODEL TO ESTIMATE REGIONAL AND NATIONAL DISEASE BURDEN

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Country where research was undertaken:
Germany

Introduction/Background
Endometriosis is a common, chronic gynecological condition affecting women of reproductive age, with prevalence estimates in literature ranging from 1% to 15%. Accurate data on incidence and prevalence remain limited, especially in low- and middle-income countries, complicating assessments of the global disease burden and associated healthcare needs.

Materials and Methods
A comprehensive Markov model was developed to calculate Disability-Adjusted Life Years (DALYs) over 35 years. The model applies a standardized prevalence rate across reproductive ages and integrates detailed transition probabilities between pain stages (no pain, mild, moderate, severe) to assess endometriosis progression. To simulate disease progression, key risk factors such as BMI, menstrual cycle length, parity, and age at menarche were incorporated, utilizing data from Germany, Indonesia, and Nigeria for diverse population insights.

Results
Risk factors such as lower BMI, shorter menstrual cycles, early menarche, and low parity increase the burden, while a BMI ≥ 30 has a protective effect. The global burden is quantified at 600.05 Years Lived with Disability (YLD)/DALYs per 100,000, with a lifetime incidence of ~21% among women of reproductive age, peaking at ages 15-24, decreasing after 45. Progression from mild to severe pain highlights the chronic nature of endometriosis. Diagnostic delays, especially in low- and middle-income countries, contribute to underdiagnosis and potential underestimation of the disease burden. Regional differences are influenced by demographic variations, such as age distribution and reproductive health practices. Countries with younger populations/ higher fertility rates may experience a higher prevalence of endometriosis among younger age groups, intensifying the disease burden in those demographics.

Conclusion
This study highlights the limitations of existing data on endometriosis and the need for ongoing research. The model presented offers a stable framework for assessing disease impact across diverse populations and risk factors, providing a solid foundation for future studies to expand and adapt as more precise data become available.

Key words
Endometriosis, disease burden, Markov model

THEME: EXPERIMENTAL MOMDELS OF ENDOMETRIOSIS

EVALUATION OF THE MIGRATORY POTENTIAL AND TROPISM OF MENSTRUAL FLOW-DERIVED MESENCHYMAL STEM CELLS IN ENDOMETRIOSIS

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Country where research was undertaken:
Brazil

Introduction/Background
Given that (I) endometrial mesenchymal stem cells (eMSCs) and menstrual flow cells (MenSCs) are linked to endometriosis[1]; (II) eMSCs migrate *in vitro* preferentially to ectopic over eutopic endometrial cells[2]; and (III) our unpublished data show fewer MenSCs in women with endometriosis, we hypothesize that MenSCs are recruited to endometriotic lesions.

Materials and Methods
MenSCs from women with (E-MenSCs) and without (NE-MenSCs) endometriosis and eutopic and ectopic (deep infiltrating lesions) endometrium samples were obtained with ethical approval. Migration experiments were carried out with E-MenSC (n=7) and NE-MenSC (n=8) using a medium with fetal bovine serum (FBS) as an attractant. For tropism, an FBS-free medium was conditioned with eutopic and ectopic endometrial (n=5, paired) tissue for 24 hours, and MenSC migration assays utilized these secretomes as attractants.

Results
The migratory potential of MenSCs in healthy and endometriosis is similar when exposed to the same stimuli (p = 0.8322). However, our preliminary results indicate a higher migratory potential of MenSCs for the secretome of ectopic compared to eutopic endometrial tissue, regardless of the origin of the cells (NE-MenSC and E-MenSC).

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Conclusion
We showed a similar migration of healthy and endometriosis MenSCs under a common stimulus. However, incorporating components of the endometriotic niche is crucial to understanding MenSC migration in endometriosis. The preferential tropism for endometriotic lesion secretomes underscores the importance of the microenvironment over cellular alterations in MenSCs.

Key words
Endometriosis, MenSC, migration.

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PHOSPHORYLATION AND PROTEOLYTIC CLEAVAGE PROFILES OF PROTEINS IN INTRACELLULAR SIGNALLING PATHWAYS OF MENSTRUAL BLOOD-DERIVED MESENCHYMAL STEM CELLS IN ENDOMETRIOSIS

L Lorenzi[1], N Siqueira Arruda[1], G Aguiar Ferreira[1], I Pavan Silva[1], A Lagazzi Cressoni[1], R Ferriani[1], J Rosa e Silva[1,2], **O Poli-Neto**[1,2], J Meola[1,2]

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Country where research was undertaken:
Brazil

Introduction/Background
Endometrial (eMSCs) and menstrual stem cells (MenSCs) contribute to endometriosis development due to high proliferation and differentiation potential[1]. Altered protein and transcript expression in endometriosis MenSCs[2] suggest functional changes in signalling pathways. We hypothesize that MenSCs in endometriosis have altered intracellular signalling activation compared to controls.

Materials and Methods
This case-control study analyzed MenSCs from women with endometriosis (n=8) and controls (n=8) with ethical approval. Cells were assessed using the PathScan® Array Kit for key signalling protein activation in a standard culture medium. Endometriosis MenSCs (n=4) were further evaluated by Western Blot for BAD activation before and after exposure to an endometriotic lesion-conditioned medium. The significance level was set at α = 0.05.

Results
Our functional analysis did not show alterations in key intracellular signalling molecules (ERK1/ERK2, STAT1, STAT3, AKT1, AMPK alpha, RPS6, mTOR, HSP27, BAD, P70S6K, PRAS40, p53, p38, SAPK/JNK, PARP, Caspase 3 and GSK3β) in endometriosis MenSCs under standard culture conditions, before reaching the peritoneal cavity. However, our preliminary results suggest that their contact with the secretome of deep endometriotic lesions may inhibit the apoptosis pathway mediated by BAD. Supported by FAPESP2023/09461-2.

Conclusion
Our analysis did not provide evidence that MenSCs have intrinsic molecular alterations predisposing to endometriosis, but their signalling pathways may be modulated by exposure to the endometriotic niche. This suggests that MenSCs reaching the pelvic cavity via retrograde menstruation are altered by existing endometriotic lesions, contributing to disease maintenance.

Key words
Endometriosis, MenSC, signalling.

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OVULATION DRIVES THE DEVELOPMENT OF ENDOMETRIOSIS: THE ROLE OF IGF SIGNALING FROM FOLLICULAR FLUID

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Country where research was undertaken:
Taiwan

Introduction/Background
Sampson's retrograde menstruation theory links endometrial deposits to endometriosis, supported by endocrine, immune, and inflammatory factors. Our research suggests IGF-axis proteins in ovulatory follicular fluid (FF) may promote endometrial deposit ectopic growth in the peritoneum.

Materials and Methods
Analysis of IGF-axis protein levels in FF and peritoneal fluid from clinical samples. Establishment of an ovulation-related endometriosis mouse model. In vitro and ex vivo experimental using IGF-axis related inhibitors, IVF-FF, endometriosis cell lines and mouse uterus.

Results
In ex vivo and spheroid culture systems, FF-IGF signaling increased stemness, suspension survival and clonal expansion, whereas IGF-1R inhibition significantly attenuated these effects. In two mouse syngeneic transplantation experiments, we demonstrated that superovulation increased endometriosis lesion formation in recipient mice. In addition, intraperitoneal injection of human FF

increased lesion number and weight, whereas co-injection with an IGF-1R inhibitor induced necrosis in the lesions and reduced the number of large, non-necrotic lesions.

Conclusion
This is the first discovery that ovulation is an essential driver for the development of endometriosis, and IGF signaling from the FF is mainly responsible for the drive.

Key words
Endometriosis, follicular fluid, IGF axis proteins

HISTONE DEACETYLASE 10 EXPRESSION IS ENHANCED IN ENDOMETRIOSIS AND PROMOTES THE PROGRESSION OF ENDOMETRIOSIS

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Country where research was undertaken:
Japan

Introduction/Background
We have previously demonstrated that *Histone deacetylase (HDAC)10* expression is upregulated in endometrial cyst stromal cells (ECSCs) compared to normal endometrial stromal cells (NESCs). In this study, we investigated the roles of HDAC10 in the pathogenesis of endometriosis.

Materials and Methods
ECSCs were isolated from surgically resected endometriotic cysts. HDAC10 inhibitors (10μM) were added to cultured ECSCs to examine their effects on cell proliferation, apoptosis and cell cycle. Then, target molecules of HDAC10 inhibitors were identified by using new generation RNA sequencing analysis.

Results
HDAC10 inhibitors inhibited cell proliferation, promoted apoptosis, and induced cell cycle arrest at G0/G1 phase. Comprehensive genetic analysis with new generation RNA sequencing analysis identified 17,192 upregulated genes. Among them, we extracted *Dachshund homolog 1 (DACH1)* and *Interferon regulatory factor 6 (IRF6)* as the downstream targets of HDAC10 by using Gene Ontology analysis and RT-qPCR.

Conclusion
Enhanced HDAC10 may promote cell proliferation, apoptosis, and cell cycle arrest in ECSCs by downregulating *DACH1* and *IRF6* expression. HDAC10 inhibitors are promising for the treatment of endometriosis.

Key words
HDAC10, cell proliferation, apoptosis

THEME: FERTILITY AND INFERTILITY IN ENDOMETRIOSIS

PITUITARY SUPPRESSION IN CONJUNCTION WITH ATOSIBAN ADMINISTRATION COULD IMPROVE PREGNANCY OUTCOME OF FROZEN-THAWED EMBRYO TRANSFER IN WOMEN WITH ENDOMETRIOSIS

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Country where research was undertaken:
Taiwan

Introduction/Background
Endometriosis is linked to reduced fertility and suboptimal pregnancy outcomes in assisted reproductive treatments. Pituitary suppression using GnRHa and atosiban administration during frozen embryo transfer (FET) may enhance endometrial receptivity and implantation. This study investigates whether combining these approaches improves pregnancy outcomes in women with endometriosis undergoing FET.

Materials and Methods
This retrospective study (03/2020-10/2023)

included 443 FET cycles from women diagnosed with endometriosis. Diagnosis was confirmed via ultrasound or ovarian cyst aspiration, with or without CA-125 testing. Participants were divided into four groups based on atosiban use on embryo transfer day and GnRHa pretreatment (Group A(-)(-)(n=120); B(-)(+)(n=90); C: (+)(-)(n=88); D: (+)(+)(n=147)). Subgroup analysis with and without preimplantation genetic testing for aneuploidy (PGT-A) was conducted to assess the effectiveness of combining GnRHa pretreatment and atosiban administration.

Results
The mean ages were comparable across all groups (38.5±3.8, 38.4±3.7, 38.2±4.4, 38.6±3.9 for Groups A, B, C, and D, respectively, p>0.05), with no significant differences in BMI, blastocyst transfer rates, or other baseline characteristics. Pituitary suppression or atosiban alone improved clinical pregnancy rates (46.7% and 48.9% vs. 41.6%, p>0.05), but not significant. The combination of GnRHa and atosiban resulted in a significantly higher pregnancy rate (55.8% vs. 41.6%, p=0.02). Early miscarriage rates were similar across groups (29.2%, 26.8%, 23.8%, 21.3%, p>0.05). Although not significant, ongoing pregnancy rates showed an upward trend (30.5%, 34.1%, 38.1%, 43.4%, p>0.05). Subgroup analysis revealed that combining GnRHa and atosiban enhanced implantation rates in PGT-A (50.0% vs. 28.6%, p=0.1) and non-PGT-A cycles (41.3% vs. 27.1%, p=0.004).

Conclusion
GnRHa pretreatment combined with atosiban may improve pregnancy outcomes in FET cycles for women with endometriosis. However, findings are limited by small sample sizes and lack of detailed severity assessment. Larger randomized trials stratifying by endometriosis phenotype and severity are needed to confirm effectiveness and optimize FET strategies.

Key words
Endometriosis, GnRHa pretreatment, atosiban

THE PREVALENCE OF ENDOMETRIOSIS AMONG FERTILITY PATIENTS BEFORE AND AFTER IMPLEMENTATION OF A SIMPLE SCANNING PROTOCOL

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Country where research was undertaken:
Canada

Introduction/Background
Endometriosis is encountered in nearly 50% of biological females experiencing infertility; yet, the diagnosis of endometriosis on ultrasound is missed in 3 out of 4 patients [1]. This study evaluated the prevalence of endometriosis at a Canadian fertility centre before and after routine use of a dynamic ultrasound scanning protocol.

Materials and Methods
A retrospective cohort study design included patients referred for fertility assessment who had an intake ultrasound performed at time of consult. Patient demographics, relevant history, and ultrasound findings were extracted from medical records. Data will be compared across three 6-month time periods: Pre-intervention (July 1-December 31, 2023), Mid-intervention (April 1-September 30, 2024), and Post-intervention (January 1-June 30, 2025). The ultrasound intervention was based on a systematic approach by the International Deep Endometriosis Analysis group [2].

Results
Based on stakeholder feedback, dynamic techniques of uterine sliding sign, ovarian mobility, and site-specific tenderness were incorporated into routine ultrasound for all patients for identifying “soft signs” of endometriosis. Training materials, reporting templates, and workshop content were developed using the Plan-Do-Study-Act cycle with positive feedback from end-users. Implementation of finalized protocol will occur December 2024.

Data extraction for the Pre-intervention phase is complete, and Mid-intervention phase is in-progress. For Pre-intervention, 979 patients were included (mean±stdev Age=34.1±4.8 years, BMI=27.5±6.9kg/m^2). Most patients admit to dysmenorrhea (n=739, 75%) and 91 (9.3%) admit to deep dyspareunia. Only 14 patients (1.4%) had endometriosis indicated as reason for consult. The prevalence of endometriosis on ultrasound Pre-intervention

was 6.6% (n=65/979). We except this rate to increase Mid-intervention, and up to 20% Post-intervention.

Conclusion
The rate of endometriosis in our fertility population is less than observed in the general population (10%)[3], indicating endometriosis is underreported at fertility centres. Implementation of a simple dynamic ultrasound technique will improve detection of endometriosis and help patients access personalized care and timely management.

Key words
Transvaginal ultrasound; fertility assessment; endometriosis diagnosis

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PROGNOSTIC FACTORS OF REPRODUCTIVE OUTCOMES IN WOMEN WITH ENDOMETRIOSIS UNDERGOING ASSISTED REPRODUCTION CYCLES

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Country where research was undertaken:
Brazil

Introduction/Background
Endometriosis is a chronic disease that affect women in reproductive age and may be associated to infertility. The aim of this study was to assess what are the predictive factors of successful reproductive outcomes of infertile women with endometriosis who underwent Assisted Reproduction (AR) treatment between 2016 and 2021.

Materials and Methods
This cross-sectional observational study involved data collection from medical records of endometriosis patients treated with AR between 2016 and 2021, in a tertiary hospital. Only patients with a documented diagnosis of endometriosis in their records were included. The analyzed variables included demographic

characteristics, clinical data and reproductive outcomes. To characterize the clinical profile of the patients, results were presented both qualitatively and quantitatively. Normality testing was applied, with statistical significance set at $p<0.1$.

Results
A total of 252 patients were included. Of these, 68 women (27%) became pregnant, with 41 patients (60%) having live births. The remaining cases resulted in spontaneous abortion (22%), biochemical pregnancy (12%), or other outcomes (6%). Comparing patients with live births to those who did not conceive revealed a higher number of mature oocytes ($p=0.0739$), a greater number of embryos produced ($p=0.0042$), and more embryos transferred ($p=0.0502$).

Conclusion
No demographic or clinical variables differed between women with endometriosis and infertility who became pregnant and those who did not after Assisted Reproduction treatment. The only differences observed were related to reproductive outcomes, with the number of mature oocytes, embryos produced, and embryos transferred being higher in the group that achieved pregnancy.

Key words
Endometriosis; infertility; assisted reproduction

MINIMIZATION OF THE LEAKAGE OF OVARIAN ENDOMETRIOMA USING LACTATED RINGER'S SOLUTION CONTRIBUTES TO AN EARLY NATURAL PREGNANCY FOLLOWING THE SURGERY

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Country where research was undertaken:
Japan

Introduction/Background
Recently, lactated Ringer's solution (LR) has been becoming preferable as a peritoneal lavage rather than normal saline (NS) from the viewpoint of preventing adhesions in removal of endometrioma (EMoma). The purpose of this study is to know the effect of LR as a lavage on pregnancy after surgery.

Materials and Methods
We developed a modified procedure of removal of EMoma; we firstly store LR in the pelvis until half of cyst is submerged. We grab EMoma following aspiration of the content, cut the adhesions between the cyst and the peritoneum, and give ovary appropriate sutures following removal of the cyst wall using vasopressin dissection. We retrospectively examined patient background, the postoperative pregnancy rate and the period until spontaneous pregnancy. For statistics, t-and chi-square test were used.

Results
Twelve cases of ovarian EMomas by laparoscopic surgery in our hospital from January 2020 to March 2023 are eligible for the new procedure, while 49 cases before 2019 for the conventional procedure. Subjects were limited to those who desired to become pregnant after surgery.

There was no difference in patient background between the two groups, but the time to spontaneous pregnancy in the new procedure and conventional groups was 4.3±4.8 and 15.6±13.6 (M), respectively ($p <0.0001$), and the pregnancy rates were 50 and 39 (%), respectively ($p=0.572$), Recurrence rates were 10 and 29 (%), respectively ($p=0.037$). The new procedure resulted in several cases of spontaneous pregnancy after only one postoperative menstrual period, while the conventional method required two years.

Conclusion
Our minimization of the leakage of ovarian endometrioma using LR solution contributes to an early natural pregnancy following the surgery. This method appears to facilitate an early natural pregnancy as early as about four months after surgery, compared to more than a year with conventional methods.

Key words
Lactated Ringer's solution, endometrioma, natural pregnancy

THEME: GENETIC AND -OMICS TECHNOLOGIES

UTILISING CHANGES IN CIRCULATING CELL-FREE DNA DURING MENSTRUATION AS A BIOMARKER FOR ENDOMETRIOSIS

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Country where research was undertaken:
Australia

Introduction/Background
Cell-free DNA (cfDNA) technology has promise and proven application in cancer diagnosis1. Early research demonstrates cfDNA has potential as an early diagnostic marker for endometriosis2,3, which remains a top research priority4. The aim of this study is investigating differences in total- and endometrial-cfDNA in endometriosis patients compared with controls.

Materials and Methods
Participants were recruited from public/private gynaecology clinics and the community. Endometriosis was surgically confirmed following blood collection. Controls were either surgically confirmed not to have endometriosis or had minimal clinical suspicion of endometriosis. Venous blood was collected on day 1-2 of menstruation, and 3-5 days after cessation of menstruation. Total cfDNA was extracted and measured by quantitative polymerase chain reaction (qPCR) of an ALU repetitive element, and endometrial-cfDNA was measured by qPCR targeting FAM101A.

Results
Currently, paired samples have been collected from 5 endometriosis (including peritoneal and deep infiltrating) and 14 control participants. The current overall cohort age range is 24-49 years, with a median age range of 31 years. The endometriosis cohort has an age range of 24-42 years, median 32 years, and the control cohort has an age range of 25-49 years, median 41 years. Main presenting symptoms for surgical management of endometriosis include dysmenorrhea, dyspareunia, infertility and bloating. We aim to have 40 participants with endometriosis and 40 controls for analysis. Utilising 40 pairs of matched samples gives 90% power to detect a 30% increase and >95% power to detect an increase of 35% and over in this biomarker study.

Conclusion
Further analyses are underway assessing whether endometrial-cfDNA in blood increases during menstruation in people with endometriosis compared to controls, with the latter already known to have no changes in cfDNA during menstruation. This data will be informative in understanding the potential of cfDNA for early diagnosis of endometriosis.

Key words
Endometriosis, diagnosis, cell-free DNA

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THE DINUCLEOTIDE (CA) REPEAT POLYMORPHISM OF ESTROGEN RECEPTOR B IN WOMEN IN KOREAN PATIENTS WITH ENDOMETRIOSIS

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Country where research was undertaken:
South Korea

Introduction/Background
The estrogen receptor β (ER β) gene is significant in follicular growth and oocyte development. Polymorphism in the CA repeat region of ER β has been associated with various diseases, but its link to endometriosis remains unexamined. This study aimed to determine the association between ER β CA repeat polymorphism and endometriosis in a Korean population.

Materials and Methods
Conducted in Korea, this study included 507 women diagnosed with endometriosis and 275 controls. The CA repeat polymorphism of ER β was analyzed using fluorescent PCR and gene scan analysis. Allele frequencies were assessed, and genotypes were classified as SS (≤23 repeats), SL, or LL (≥24 repeats).

Results
A total of 15 alleles were identified, with PCR products ranging from 153 to 181 bp (14–28 repeats). Allele distribution in the control group was consistent with findings from similar ethnic studies. No significant differences were observed in genotype distribution between patients (LL: 13.4%) and controls (LL: 9.8%). Subgroup analyses based on endometriosis stage and bilaterality also showed no significant differences.

Conclusions
The dinucleotide (CA) repeat polymorphism of ER β is not associated with endometriosis risk in the Korean population.

THEME: LIVED EXPERIENCES AND QUALITY OF LIFE IN ENDOMETRIOSIS

INSIGHTS FROM FOCUS GROUPS WITH TRANS AND GENDER DIVERSE PEOPLE WITH ENDOMETRIOSIS: STORIES YOU TELL, STORIES YOU DON'T

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Countries where research was undertaken:
Netherlands, Italy, Greece, Germany, Austria, United Kingdom, Switzerland, United States of America, Canada, Australia.

Introduction/Background
Predominantly framed as a "women's disease," current endometriosis research overlooks experiences of transgender and gender diverse (TGD) individuals with endometriosis.

This study aims to explore the real lived and embodied experiences of this community, and to examine the accessibility and competence of healthcare systems for this group.

Materials and Methods
The methodology included two online semi-structured interviews - each aligned with one of the study's aims - conducted across four focus groups, for a total of eight sessions. Fourteen participants representing diverse gender identities, various stages of endometriosis and ages, were recruited online from countries across three continents, forming a heterogeneous group. Thematic analysis identified fifteen codes and seven clusters. The results were organized into themes, following the four embodiment epidemiological notions.

Results
Participants reported that their gender self-perception and endometriosis symptoms were interrelated and mutually influential. Feelings of disconnection and alienation were prevalent among TGD individuals, particularly during significant life events such as menarche. Due to mistrust and experiences of discrimination, many TGD individuals often withhold critical information during medical consultations. TGD people with endometriosis have unique health needs, e.g. how to combine gender-affirming and endometriosis care. They are often more concerned about future employability, and less about subfertility compared to cisgender women.

Conclusion
TGD people with endometriosis have distinctive real lived experiences compared to cisgender women that reflect in unique health needs. The study highlights the need for improved healthcare to mitigate health disparity between TGD and cisgender individuals, and it emphasizes the necessity for further research in this area.

Key words
Transgender; health disparity; qualitative methods.

'ENDO KNOWLEDGE': THE INTERSECTION OF POPULAR CULTURE AND MEDICAL EDUCATION IN UNDERSTANDINGS OF ENDOMETRIOSIS

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Country where research was undertaken:
Australia

Introduction/Background
Historically women's experiences of endometriosis within both medical and sociological research have been marginalised. More recently, work by Seear (2016) and Lupton (2012) underscore the need for more attention to the structural and cultural aspects of endometriosis. In addition, contemporary social media movements such as 'Endo Warriors' have amplified public awareness, generating a new realm of endo knowledges that reflect lived experiences. Nevertheless, other research highlights ongoing biases within medical education (Young et al., 2019 & 2020), which perpetuate misconceptions and often stigmatize sufferers.

This paper reports on a sociological study exploring the cultural politics of endometriosis in Australia, focusing on how knowledge about the disease arises and is formed within both social media and medical education discourses.

Materials and Methods
This study involves two qualitative research methodologies: social media content analysis of current and high-profile social media and popular culture content aimed at publicising and politicising lived experiences of endometriosis to understand how knowledge about the disease arises and is formed within social media in Australia. Qualitative interviews with medical students were conducted to understand how social media knowledge and medical education knowledge intersects in medical students' understandings of endometriosis.

Results
The social media study found specific framings of medical responses to endometriosis, including invisibility (e.g. as an invisible chronic condition), dismissal and stigma. The paper examines the interaction and intersection of popular endometriosis ('Endo') knowledge with information about endometriosis provided in medical education courses. The findings emphasise the need for medical curriculum to incorporate lived experiences to enable students to value this knowledge and foster a more empathetic care for patients with endometriosis.

Conclusion
This research aims to contribute to addressing misconceptions about the disease and integrating lived experiences in new conceptions. Ultimately, the findings will offer insights into how social media knowledge and medical education can better align to improve endometriosis care.

Key words
Sociology, endo knowledge, medical education

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"WHAT I AM SEEKING IS PAIN RELIEF, I AM NOT SEEKING DRUGS": LIVED EXPERIENCES WITH PELVIC PAIN AND ENDOMETRIOSIS.

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Country where research was undertaken:
Australia

Introduction/Background
Persistent pelvic pain (PPP), effects up to 1 in 4 women with significant biopsychosocial and economic impact irrespective of diagnosis. Overlapping conditions, including endometriosis, often involve overlooked muscular contributors to PPP (pelvic floor myalgia), treatable with physiotherapy and Botox. Qualitative research on PPP, endometriosis and pelvic floor myalgia remain limited.

Materials and Methods
The primary objective was to explore the lived experiences of adult women (≥18 years) with PPP (≥6 months) with self-reported endometriosis and/or pelvic floor myalgia, or those without a diagnosis yet. The secondary objective was to examine their diagnostic journey, healthcare access, utilization, barriers, supports, assessment and management. Participants were recruited via snowball sampling from clinics, social media, completing one-on-one, semistructured virtual interviews. Reflexive thematic analysis was used to identify key themes and insights.

Results
Thirty participants were interviewed with a median age of 32.5 years (21-47) and mean duration of PPP of 11.4 years (2-29). Diverse diagnostic groups were represented, including participants with both pelvic floor myalgia and endometriosis (33.3%), pelvic floor myalgia alone (26.7%), endometriosis alone (23.3%) and those who did not have a diagnosis (16.7%). Majority (70%) had an undergraduate degree, living in areas (63.3%) of least disadvantage according to the Index of Relative Socio-economic Disadvantaged (IRSD). Three overarching themes were identified, ‘psychosocial and psychological impacts of the condition’, “psychosocial and psychological impacts of the healthcare journey’ and ‘economic impact of the condition’. Participants described impacts from the invisible costs, non-monetary toll, uncovered healthcare expenses and challenges in diagnostic journey at multiple levels of the healthcare system.

Conclusion
Our data reveal that women experience wide-ranging psychosocial impacts related to their condition itself (PPP) and its associated healthcare, often without tailored and streamlined support. Our findings, highlight the need for person-centered care models that prioritize improved diagnostic experience, access, ongoing psychosocial support, enhancing the lived experience and healthcare journey.

Key words
Persistent pelvic pain, endometriosis, pelvic floor myalgia

COMBINED QUALITATIVE ANALYSIS OF ENDOMETRIOSIS PATIENT AND CLINICIAN EXPERIENCES IN AOTEAROA NEW ZEALAND

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Country where research was undertaken:
New Zealand

Introduction/Background
Endometriosis is a profoundly difficult for patients to experience, and for primary care practitioners to diagnose and manage. The purpose of this project was to holistically analyse and characterise facilitators and barriers of primary endometriosis care from the perspectives of patients, clinicians, and explore potential future solutions from their viewpoint.

Materials and Methods
A mixed methods approach was used to collate information about endometriosis patients (including indigenous, minority, and LGBTQIA+ patients), their supporters, and clinicians including both general practitioners (GPs) and nurses. 111 patients took part in asynchronous, online discussions, 105 supporters and 1157 patients participated in an online survey, 185 GPs and 55 nurses took part in online surveys regarding their view on patient management and nine GPs and six nurses participated in interviews.

Results
These studies indicated that all individuals involved in primary care of people with endometriosis face key barriers including challenging symptom recognition; the rapidly evolving nature of endometriosis management practices; persistence of dismissive attitudes; the lack of effective, accessible endometriosis management options; and the challenges of

navigating care which may include weight-based stigma, racism, tokenism, homophobia, transphobia, and gender-based discrimination.

Patients stated that a key improvement needed was medical practitioner knowledge being up-to-date, while GPs highlighted the challenges associated with remaining up to date with the evolving best practices for a wide range of conditions. Both GPs and nurses highlighted that having nurses with specialist endometriosis roles could be powerful for the streamlining of patient management and care.

Conclusion
Significant barriers still exist that prevent endometriosis patients from accessing the care they need, and for clinicians to provide care for their patients. Engagement with those working in and interacting with our healthcare system is critical for ensuring that developed solutions effectively address the actual, as opposed to perceived, issues.

Key words
Patient experiences, clinician experiences, research priorities

IT'S A JOURNEY. A GRAPHIC MEDICINE EXPLORATION OF ENDOMETRIOSIS AND GENDER DIVERSITY.

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Countries where research was undertaken:
Netherlands, Italy, Greece, Germany, Austria, United Kingdom, Switzerland, United States of America, Canada, Australia.

Introduction/Background
Transgender and gender-diverse (TGD) individuals assigned female at birth (AFAB) are also impacted by endometriosis, which can severely affect their quality of life. This group faces significant barriers to healthcare due to structural discrimination and marginalization. Their experiences are often silenced, and healthcare professionals (HCPs) lack training to adequately diagnose and treat them.

Materials and Methods
This study is based on participatory action research and utilizes principles of graphic medicine, a field combining healthcare and visual storytelling to enhance understanding of medical experiences. TGD individuals with endometriosis were involved in every research phase. Community validation checks were performed systematically and iteratively until consensus was achieved at each stage.

Results
A comprehensive graphic medicine product was developed, incorporating three key components: (1) a biographical narrative of a representative nonbinary transmasculine individual with endometriosis, (2) anonymized quotes from focus groups with TGD individuals, capturing diverse lived experiences, and (3) educational content aimed at HCPs on combining endometriosis treatment with gender-affirming care. Available in English, both online and in hardcopy, the product is currently used for educational, clinical training, and scientific purposes. Feedback from early use suggests its effectiveness in enhancing awareness and understanding among HCPs about endometriosis, gender diversities and their intersections.

Conclusion
Graphic medicine is a valuable tool for bridging healthcare and lived experiences, fostering better understanding and education among HCPs. "It's a Journey." sheds light on the unique challenges faced by TGD individuals with endometriosis, amplifying their voices and addressing the healthcare inequalities experienced by this often-marginalized community.

Key words
Transgender; graphic medicine; participatory action research methods.

DIFFERENCES IN BARRIERS TO AN ENDOMETRIOSIS DIAGNOSIS AMONG LATINA, NON-LATINA BLACK, AND NON-LATINA WHITE ADULT WOMEN: A QUALITATIVE ASSESSMENT

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Country where research was undertaken:
United States of America

Introduction/Background
Most qualitative research on barriers to reaching an endometriosis diagnosis have been conducted among White women[1-3]; however, barriers may differ among racial and ethnic groups. We investigated personal, cultural, societal, and healthcare interaction differences in barriers to reaching an endometriosis diagnosis among Latina, non-Latina Black, and non-Latina White adult women.

Materials and Methods
One-on-one, in-depth interviews were conducted with 4 Latina, 4 non-Latina Black, and 6 non-Latina White women, ages 21-50 years, diagnosed with endometriosis between ages 15-31 (57% were <20 years at diagnosis). Interview questions addressed social and cultural implications of symptoms and healthcare interactions. Interviews were transcribed and analyzed using immersion/crystallization, template organizing style, and thematic analysis approaches. Preliminary themes have been developed and will be expanded and compared among the participant groups.

Results
Preliminary themes reflecting barriers to reaching an endometrioses diagnosis included: (1) incorrect specialist referral for symptoms; (2) feelings of not being heard by healthcare professionals; (3) normalizing reactions of family members to symptoms; and (4) families being unsure of how to address symptoms in the healthcare setting. Most themes were reported across all racial and ethnic groups. However, in preliminary findings, Latina participants were more likely than other groups to report normalizing reactions to symptoms by family members, particularly mothers and aunts. Additionally, one Latina participant reported stigmatization from family members about taking birth control pills for her symptoms due to her young age. Advocacy by family members and participants in seeking appropriate healthcare was a strong driving factor behind reaching an endometriosis diagnosis.

Conclusion
Preliminary themes suggest differences in barriers to an endometriosis diagnosis between racial and ethnic groups, particularly related to what is considered to be “normal” pelvic pain. These results serve as important preliminary data to further our understanding of potential racial and ethnic group differences in reaching an endometriosis diagnosis.

Key words
Qualitative, health disparities, endometriosis diagnosis

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SEXUAL DYSFUNCTION IN WOMEN WITH ENDOMETRIOSIS AND ITS ASSOCIATED FACTORS - A CROSS-SECTIONAL STUDY

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Country where research was undertaken:
Brazil

Introduction/Background
Endometriosis can cause pain, sexual, urinary and evacuation dysfunction. In women there are 3-types of sexual dysfunction: genito-pelvic pain/penetration disorder, sexual interest and arousal disorder and orgasm disorder. We assessed the prevalence of female sexual dysfunction in women with endometriosis and the association with urinary and bowel function.

Materials and Methods
We recruited women with endometriosis, aged

between 18-45, non-virgin, non-pregnant, with no other causes of pain. Patients answered questions about the presence of the 3-types of sexual disorder, urinary and evacuation dysfunction. Pearson's chi-squared test investigated associations between the three types of sexual dysfunction and urinary and bowel symptoms.

Results
Eight-three out of 92 women had sex in the previous 6 months and 100% had sexual dysfunction. Genito-pelvic pain/penetration disorder was the most prevalent (99%), with 60% of women reporting pain during penetration. This was followed by female sexual interest and arousal disorder (88%) and female orgasm disorder (61%). There was an association between the intensity of pain during penetration and the sensation of incomplete evacuation and constipation. There was also an association between the intensity of pain during sexual intercourse and dysuria, polyuria, hardened/dry stools and the sensation of anorectal blockage. Female sexual interest and arousal disorder and orgasm disorder were not associated with urinary or bowel symptoms.

Conclusion
All sexually active women with endometriosis have sexual disorders, with genito-pelvic pain/penetration disorder being the most prevalent. Given the number of women with endometriosis experiencing sexual disorders, there should be more openness/transparency about the issues to enable appropriate management by health professionals, including physiotherapists.

Key words
Psychological; pelvic floor disorders; levator ani.

THE EFFECTS OF GENDER NON-CONFORMITY ON HEALTH-RELATED QUALITY OF LIFE IN PEOPLE WITH ENDOMETRIOSIS.

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Country where research was undertaken:
United Kingdom

Introduction/Background
Endometriosis is often framed as a women's disease, excluding gender non-conforming patients and leading to inadequate care and delayed diagnoses. This study aims to identify HRQoL differences across genders, highlighting how misconceptions may lead healthcare providers to overlook the unique needs of gender non-conforming populations, ultimately worsening patient outcomes.

Materials and Methods
Patients with endometriosis were recruited between 11 March 2021 and 31 July 2022 via social media, support groups, and the British Society of Gynaecological Endoscopy (BSGE)-approved centres. A total of 2,056 individuals aged 16 and above participated in this mixed-method study, which included the Endometriosis Health Profile-5 (EHP-5) and Pelvic Pain Impact Questionnaire (PPIQ). Data from a single interview with a 27-year-old, Caucasian/Māori, non-binary participant was analysed using interpretative phenomenological analysis (IPA).

Results
The average diagnosis time for our sample was 8.2 years, ranging from 3.2 ± 6.6 years in males to 13 ± 6.56 years in gender-fluid participants. 39% of participants across all genders felt victimised due to their gender when seeking care for endometriosis. A one-way ANOVA indicated that gender impacted overall mean PPIQ scores ((F (5, 2008) =10.10) p=<0.0001), showing significantly lower scores for females (*M*=51 ±27.09) compared to gender-fluid ((*M*=71, ±19.10) *p*=<0.05) or non-binary participants ((*M*=72, ±20.08) *p*=<0.0001)). Major themes from the IPA analysis included poor emergency care, navigating mental health, interpersonal relationships, loss of self, dismissal of pain, and navigating physical health.

Conclusion
This study uncovered significant between-group variations in both the EHP-5 and PPIQ scores that underscore the need for tailored and inclusive approaches to care. Identifying IPA themes provides a framework for understanding the multifaceted challenges faced by gnc individuals.

Key words
Endometriosis, gender non-conforming

THE EXPERIENCES OF QUEENSLAND FEMALES OBTAINING AN ENDOMETRIOSIS DIAGNOSIS

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Country where research was undertaken: Australia

Introduction/Background
Queensland is a broad state in Australia with approximately 35% of residents living in regional, rural and remote areas (Australian Bureau of Statistics, 2024). For some Queenslanders, geographical location can create barriers to healthcare. This study explores the difference in experiences of regional and urban Queensland females with an endometriosis diagnosis.

Materials and Methods
An online Qualtrics survey will be conducted in January-March 2025 with Queensland females to explore their experiences and identify the differences and/or similarities between regional and urban females in Queensland in their experiences obtaining an endometriosis diagnosis. The anonymous survey will include demographic questions and the Endometriosis Impact Questionnaire. Eligible participants are females over 18 years of age with an endometriosis diagnosis who reside in Queensland and can speak English.

Results
Preliminary findings of survey data analysis will be shared. Data analysis will use descriptive data, bi-variate and multi-variate methods. Results are anticipated to provide important insight into the unique challenges experienced by Queensland females with endometriosis. An understanding of diagnosis barriers and facilitators can assist with the effective shaping of health service responses for females with endometriosis.

Conclusion
By exploring the experiences and challenges of rural Queensland females accessing an endometriosis diagnosis, this research aligns with the Australian Government National Action Plan for Endometriosis and their call for action for services that are 'appropriate, available and accessible' (Australian Government, 2018).

Key words
Diagnosis, regional, barriers.

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THE PEPPER STUDY: PERCEPTIONS OF PELVIC PAIN & ENDOMETRIOSIS IN DIVERSE COMMUNITIES

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Country where research was undertaken: United Kingdom

Introduction/Background
Endometriosis affects up to 1 in 7 women of childbearing age. White middle-class women with pelvic pain are over-represented in research and clinical settings, while little is known about the experiences of women from other ethnic groups. To our knowledge, there are no publications directly exploring minority perspectives on endometriosis.

Materials and Methods
Community listening workshops facilitated discussion on experiences and understanding of pelvic pain, including endometriosis, as well as reflections on healthcare interactions from the perspective of minority ethnic women. The researchers developed relationships with three existing groups, connecting with community workers who acted as cultural and language interpreters. Notes from the workshops underwent thematic analysis, with triangulation from the research team and group leaders. The findings influenced the development of culturally appropriate information materials for patients.

Results
At the time of submission the PePPER study is ongoing. Further community listening workshops are planned to bring the total number of participants to 100. A common thread in introductory and study discussions was that participants saw the workshops as an

opportunity for their voices to be heard on an important issue.

There are four emerging themes from our preliminary analysis, consistent amongst participants across a range of minority ethnic groups. First, pelvic pain is understood in its cultural context. In many cases this creates normalization of female pain. Second, this is compounded by limited culturally appropriate education and materials on endometriosis, and third, low confidence in healthcare professionals. This leads to a high threshold for seeking medical care and potential for poorer health outcomes.

Conclusion
Despite relative silence in the literature, these workshops demonstrate clear unmet informational and relational needs for minority ethnic women with endometriosis. Co-produced educational materials for women, translated into several languages, were a core study output. However, the disparities highlighted must also be addressed through clinician cultural training and further research.

Key words
Endometriosis; ethnic minorities

WOMEN WITH ENDOMETRIOSIS WANT TO KNOW MORE ABOUT EXERCISE: THE EXERCISE 4 ENDO TRANS-TASMAN QUALITATIVE INTERVIEWS

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Country where research was undertaken:
Australia

Introduction/Background
Endometriosis affects 1 in 7 women and those assigned female at birth. This project aims to understand the perceptions and experiences of women with endometriosis in Australia and New Zealand; to explore their current exercise practices and understand the impacts it has on their endometriosis symptoms.

Materials and Methods
Study participants were ≥18 years and had an endometriosis diagnosis. Participants were recruited via social media and endometriosis-related organisations using an anonymous survey link. Survey respondents had the option to be contacted for a focus group discussion on their views and experiences of exercise. Discussions were recorded and transcribed verbatim. Inductive thematic analysis was performed on the data, whereby emerging themes and sub-themes were extracted.

Results
Following the initial Exercise 4 Endo survey of 424 respondents (results formed the basis of a separate study), 54 Australian and New Zealand women consented to be contacted for participation in a focus group discussion. Of those 54, 24 (44%) participated in a focus group using a semi-structured qualitative interview schedule. Thematic analysis was performed on qualitative interview data using inductive thematic coding to identify emerging themes from the data. Key themes and sub-themes emerging from interview data included: “I exercise even though it hurts me”; Flexible individualised programming is the key to making it achievable; Exercising for many different benefits; and, Support is not only helpful but crucial.

Conclusion
Women with endometriosis choose to exercise because they enjoy it and find it helps them manage their endometriosis symptoms. However, exercise sessions need to be adaptable to suit their individual needs and symptom experiences. More support and exercise-related treatments are needed, such as through tailored programs.

Key words
Endometriosis, exercise, perceptions

STIGMA EXPERIENCES OF BLACK WOMEN WITH ENDOMETRIOSIS IN THE WASHINGTON, DC, METROPOLITAN AREA

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Country where research was undertaken:
United States of America

Introduction/Background
While research on stigma and endometriosis is growing, most of it focuses predominantly on non-Hispanic white populations, with far less research on how stigma informs the

intersection of racism and endometriosis[1-3]. This current pilot study examined stigma experiences among Black women with endometriosis in the Washington, DC, area.

Materials and Methods
An online, anonymous cross-sectional survey was conducted. Inclusion criteria were self-report of physician diagnosis of endometriosis, identifying as Black, African American, Native American or Alaska Native, Pacific Islander and Native Hawaiian, Asian, South Asian, Latino or Hispanic, Arab or Middle Eastern, being at least 18 years, and residing in DC, Maryland or Virginia. Respondents (n=39) provided answers to questions about endometriosis, healthcare experiences, stigma, and depression. Summary statistics of the variables of interest were calculated.

Results
In this population of Black women with endometriosis (n=28), mean stigma scores (scale of 1 (least) to 5(most) were: enacted = 2.0 (SD ±0.9), anticipated= 2.3 (SD ± 1.0), and internalized= 2.5 (SD ± 0.7). non-heterosexual participants had higher overall stigma compared to heterosexual participants, the largest difference in anticipated stigma (3.2 v 1.9) . Participants reporting a healthcare provider made assumptions about their ability based on racial stereotypes, had higher anticipated stigma, compared to those who did not (2.5 v 1.7) as well as those who changed providers due to racial discrimination, compared to those who did not (2.9 v 1.7). Those with moderately severe to severe depression, had greater internalized stigma, compared to those with no to moderate depression (2.7 v 2.2).

Conclusion
Black women with endometriosis in the Washington, DC area, experience stigma that inform their health seeking behaviors. These preliminary data on medical racism and stigma experiences underscore the importance of culturally and historically congruent interventions, informed by intersectional community engaged research. This will increase patient trust and improve health outcomes.

Key words
Stigma, racism, endometriosis

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THE EXPERIENCES OF SOUTH AFRICAN WOMEN WITH ENDOMETRIOSIS: DIAGNOSTIC DELAYS, SYMPTOM BURDEN, AND QUALITY OF LIFE

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Country where research was undertaken:
South Africa

Introduction/Background
Endometriosis, is a debilitating chronic condition, negatively impacting the quality of life (QoL)of women globally. This study provides an in-depth exploration of the experiences of South African women with endometriosis, including diagnostic delays, symptom profiles, and the disease impact on patient quality of life.

Materials and Methods
A cross-sectional study was carried out using the validated EPHECT EPQ questionnaire to capture the minimum clinical phenome in endometriosis cases as outlined by the WERF. The online survey, captured on REDCap (Version12.5.7), was distributed among females over the age of 18 enrolled in an endometriosis support group in South Africa with a diagnosis of endometriosis. Patients with a diagnosis through suspicion, pregnant patients or patients undergoing assisted reproductive cycles were excluded from the study.

Results
Among 570 surveyed women with endometriosis, 76.5% were diagnosed via laparoscopy, and 10.4% through symptoms alone. Delays from symptom onset to diagnosis were common: 43.6% waited 4-10 years, and 23.2% over 10 years. Pain

prompted 93% to seek care, with 85.2% experiencing severe cramps. Pelvic pain averaged 8.5/10 pre-therapy, reducing slightly to 6.5/10 post-therapy. Additional symptoms included lower back pain (80.6%) and radiating leg pain (51.2%). The impact on daily life was profound, severely affecting work (43.1%), home activities (47.2%), and sleep (44.5%). Anxiety (46.8%) and depression (40.1%) were the most frequent reported comorbidities. Despite treatment, 31.2% reported no significant relief of pain, highlighting a critical need for improved management strategies.

Conclusion
The findings reveal that South African women with endometriosis face substantial diagnostic delays, a high symptom burden, and considerable impacts on their quality of life and mental health. This study adds to the global understanding of endometriosis and calls for targeted healthcare initiatives to enhance the lives of those affected.

Key words
Endometriosis, chronic pain, dysmenorrhoea

ARE AUSTRALIAN HEALTHCARE PRACTITIONERS PROVIDING COLLABORATIVE AND TRAUMA-INFORMED PELVIC PAIN CARE? LESSONS FROM LIVED EXPERIENCES.

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Country where research was undertaken:
Australia

Introduction/Background
This study explores healthcare satisfaction and engagement among Australian women and gender diverse individuals (presumed female at birth) with endometriosis and persistent pelvic pain. The study aimed to enhance understanding of access to interdisciplinary and trauma-informed care, with a view to identifying potential enhancers and barriers to evidence-based care.

Materials and Methods
Twenty-six individuals (women: *n=22,* gender-diverse: *n=4*) participated in semi-structured interviews to explore their experiences accessing persistent pelvic pain care. An interpretive phenomenological approach was used to interpret the documented lived experiences, with a whole-of-person lens to understand the physical, psychological, and social needs of individuals with persistent pelvic pain. Reflexive thematic analysis and the four life-worlds of embodiment, spatiality, temporality, and relationality were used to inform understanding of healthcare experiences as perceived by the individual.

Results
Pelvic pain diagnoses included endometriosis, adenomyosis, painful bladder syndrome and vulvodynia, with an average symptom duration of twelve years, with all Australian states represented. Qualitative accounts reflected *Vulnerability* and *Perceived Power Imbalance* associated with the intimate and invasive nature of pelvic investigations and recommended treatments, highlighting a need for *Trauma Informed Care*. The need for *Self-Advocacy Skills* was identified across the course of healthcare engagement and provided a sense of agency and control in healthcare choices. Participants requested a stronger focus on *Individualised Holistic Healthcare*, highlighting unmet allied healthcare needs such as physiotherapy and psychology that were not identified by medical healthcare practitioners. A need for enhanced *Coordinated Care* via GP Care Plans, with proactive rather than reactive engagement of allied healthcare was emphasised.

Conclusion
Recommendations include improving access to individualised holistic healthcare, enhancing coordination and communication among practitioners, and increasing the understanding and implementation of trauma-informed practices. Trauma-informed care may reduce patient vulnerability and perceived power imbalances in pelvic pain healthcare.

Key words
Self-advocacy, holistic healthcare, trauma-informed care

THEME: MODELS OF CARE IN ENDOMETRIOSIS

A PILOT MODEL OF CARE FOR CHRONIC PELVIC PAIN IN GENERAL PRACTICE

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Country where research was undertaken:
Australia

Introduction/Background
Chronic pelvic pain, often linked to endometriosis, depression, anxiety, infertility, and sexual dysfunction, is a complex and underdiagnosed condition that profoundly impacts patients' quality of life. The Garden Family Medical Clinic's pilot program seeks to enhance patient-centred care pathways and expedite treatment.

Materials and Methods
The program includes a comprehensive pre-screening questionnaire (DASS-21 and Central Sensitisation Inventory), a pre-consult telehealth call, a 60-minute GP consultation, and a multidisciplinary care approach with tailored follow-up. Patients may be referred to additional services, including pelvic physiotherapy, pain psychology, and specialised support groups.

Results
This model has improved diagnostic accuracy, particularly for endometriosis, with notable enhancements in patient-reported well-being and satisfaction. Early data shows a decrease in opioid reliance and improved communication among clinicians. Patients report a greater sense of being heard and valued, having sought this level of care for years.

Conclusion
This model offers a promising approach to early diagnosis and targeted treatment for chronic pelvic pain, potentially scalable across primary care settings, improving patient experience and outcomes in complex chronic conditions.

Key words
Chronic pelvic pain, multidisciplinary care, endometriosis

A NURSE-LED MODEL OF ENDOMETRIOSIS CARE COORDINATION

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Country where research was undertaken:
Australia

Introduction/Background
Barriers to accessing specialised endometriosis care contribute to diagnostic delay and difficulty navigating a complex medical system with multiple care providers. Our Centre provides a nurse-led clinic with a self-referral pathway to streamline access and support collaboration with the multidisciplinary team.

Materials and Methods
A chronic-disease management model is applied to care coordination for patients with known or suspected endometriosis and/or pelvic pain. Patients access an endometriosis clinical nurse consultant for individual assessment and ongoing care as required. Patients self-refer or are referred via a member of the multidisciplinary team, the inpatient wards, or emergency department. Virtual care (telehealth) is utilised to deliver the nursing service.

Results
Specialist nurses complete an initial assessment including: menstrual, obstetric, medical and surgical history; imaging; systematic symptom profile; assessment of bowel, bladder and sexual function; social history; functional status; sleep and mood status; interventions trialled to date; hormonal use and tolerance. A care plan is formulated according to patients' goals, priorities, capacity and access. Suggestions for multidisciplinary care providers are given. Assessment findings and recommendations are communicated to their general practitioner and reviewing gynaecologist. Relevant investigations and initial MDT management can therefore be initiated prior to gynaecologist assessment. Ongoing support with the nurse is available and allows provision of emotional support and validation, education, advocacy, and patient empowerment to self-manage. Between March 2022 and September 2024, the nurses conducted 552 initial patient assessments and 446 follow up appointments.

Conclusion
Our nurse-led model supports patients with known or suspected endometriosis to access thorough assessment and ongoing support to manage their disease without the need for a medical referral. This streamlined pathway enhances efficiency of onward care and allows

for the institution of initial management prior to gynaecologist review - reducing delays in accessing care.

Key words
Nursing, telehealth, model-of-care

CONSUMER USE, EXPERIENCE AND SATISFACTION OF CARE COORDINATION: CONEXS STUDY – THE PROTOCOL

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Country where research was undertaken:
Australia

Introduction/ Background
Support for nurse-led chronic pain clinics exist (1), yet evidence is limited for endometriosis. We recently established a nurse-led model of care (NLMOC) (2), which has provided and coordinated personalised care plans for 580 individuals with endometriosis. A protocol was designed to objectively measure the patient experience of the NLMOC.

Materials and Methods
A group of clinician/academic researchers designed a protocol to evaluate and measure patient use, experience and satisfaction of our NLMOC. The team included 2 gynaecologists, a nurse and 2 academic researchers. The preliminary protocol was reviewed by 2 consumers with lived experience of endometriosis, and following collection of feedback and integration of suggested changes (based on the feedback), the protocol was finalised and approved by a local Human Research Ethics Committee.

Results
All new patients, with a scheduled appointment, who are ≥18 years old, have access to internet and understand English will be eligible. A prospective one group, pre-test and post-test analysis will employ five previously validated questionnaires (PGIC(3-5), EHP-30(6), PCS(7), PSQI(8-10), IEXPAC(11)) and 3 study-specific questionnaires. Questionnaires will be completed prior to the first nurse appointment (pre-test) and at 3- and 12- months after the appointment (post-test). Our recruitment target is n=130. The primary outcome is the number of patients responding "very much improved" or "much improved" on the PGIC (3 months post-test). Anecdotally, our centre receives positive feedback about the NLMOC. It is hypothesised that patients who access the NLMOC will report a high satisfaction of care.

Conclusion
By prospectively evaluating patient experience and satisfaction of the NLMOC, we will measure the effectiveness and limitations of this model. This will allow quality improvement efforts to be evaluated, which is a key step towards ensuring accountability, action and quality of care improvements for people with endometriosis (12).

Key words
Model of care, evaluation, nurse-led care

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IS ENDOMETRIOSIS A PROGRESSIVE DISEASE? EXAMINING AGE-RELATED TRENDS IN DISEASE SEVERITY AND SURGICAL COMPLEXITY

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Country where research was undertaken:
United States of America

Introduction/Background
To assess the relationship between age and the phenotypic expression of endometriosis using the American Association of Gynecologic Laparoscopists (AAGL) classification, focusing on disease severity, surgical complexity, and lesion distribution.

Materials and Methods
This retrospective cohort study analyzed patients who underwent surgery for endometriosis. The primary outcome was phenotypic differences in endometriosis across age groups, including disease severity and complexity based on the AAGL classification and the presence of endometriomas or bowel endometriosis. Secondary outcomes included correlations between endometriosis phenotype, clinical presentation, imaging findings, and surgical complications. Patients were stratified into four age groups (≤25, 25–35, 35–45, >45). Multivariable regression models controlled for potential confounders.

Results
A total of 1,293 patients met inclusion criteria. In multivariable regression analysis compared to patients <25 years, those aged 25-35, 35-45, and >45 years had higher odds of AAGL Stage III-IV endometriosis (adjusted odds ratios [aOR] 3.46 95% CI 2.04-5.88, 3.98 95% CI 2.35-6.73, and 3.14 95% CI 1.71-5.78, respectively; all p<.001) and increased surgical complexity (Level C-D) (aOR 2.31 95% CI 1.39-3.86, p=.001; 3.26 95% CI 1.97-5.30, p<.001; and 5.57 95% CI 3.06-10.12,

p<.001, respectively). The presence of endometriomas was significantly higher in the 25-35 and 35-45 age groups (aOR 2.92 95% CI 1.59-5.34, p=.001; and 2.50 95% CI 1.36-4.58, p=.003) but not in those >45 years. Bowel endometriosis was significantly associated only with the 35-45 age group (aOR 1.91 95% CI 1.12-3.27, p=.018).

Conclusions
While endometriosis severity stabilizes beyond a certain threshold, surgical complexity continues to escalate, likely due to progressive fibrosis, adhesions, and anatomical distortion. Early diagnosis and tailored management strategies should be considered in younger patients to mitigate progression and surgical burden. Future research should focus on age-specific treatment approaches.

Key words
Endometriosis phenotype, age, AAGL classification

A MULTIPROFESSIONAL CURRICULUM FOR THE INTERDISCIPLINARY TREATMENT OF DYSMENORRHEA - TRAINING THE EXPERTS

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Country where research was undertaken:
Germany

Introduction/Background
Dysmenorrhea greatly affects many women's quality of life but often receives limited support. The MemaeF-Period App addresses this gap by offering a three-month program for young women and a six-month multimodal treatment for those with persistent pain. It also provides interdisciplinary training for healthcare providers.

Materials and Methods
In the MeMaeF project, clinical experts developed profession-specific learning modules, finalized through team discussions and stakeholder engagement. Modules for gynecology, psychology, physiotherapy, and dietetics cover medical fundamentals, diagnosis, multimodal therapy and interdisciplinary communication. Each e-learning module defines goals, such as understanding hormonal effects, dysmenorrhea epidemiology, and differentiating pain types. Selected Charité case studies are used to illustrate best practice multimodal therapy. Modules will be freely under a Creative Commons license.

Results
The multimodal dysmenorrhea treatment curriculum, developed in the MeMaeF project, is now complete and has been reviewed by stakeholders. This curriculum provides specialized training for doctors, physiotherapists, nutritionists, and psychologists, emphasizing an interdisciplinary, multiprofessional care approach. The e-learning modules cover medical fundamentals, multimodal therapy, and interdisciplinary communication, using Charité case studies to highlight the effectiveness and challenges of this therapy. Once stakeholder feedback is integrated, the curriculum will be available as e-learning for clinicians, aiming to bridge dysmenorrhea treatment gaps, improve interdisciplinary care, and offer diverse perspectives. The training is available free via the Vita training academy under a Creative Commons license.

Conclusion
The MeMaeF curriculum fills a critical gap in dysmenorrhea care by providing interdisciplinary, evidence-based training for healthcare providers. Available as free e-learning, it enhances understanding, fosters collaborative treatment approaches, and aims to improve patient outcomes. This initiative has the potential to raise care standards and reduce societal healthcare costs.

Key words
Multimodal dysmenorrhea treatment, Interdisciplinary training, e-learning curriculum

IMPLEMENTING THE ENDOMETRIOSIS NURSE ROLE: ENHANCING PATIENT-CENTRED CARE AND QUALITY OF LIFE THROUGH SPECIALIZED NURSING SUPPORT

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Country where research was undertaken:
Germany

Introduction/Background
The journey to a definitive diagnosis of endometriosis often takes between six to ten years due to a variety of specific and nonspecific symptoms.[1] This condition can lead to ongoing inflammation, the formation of scar tissue, and adhesions, which may result in infertility, pain, diminished quality of life, and psychological distress, among other complications.[2,3] In the context of comprehensive clinical care, structured nursing support plays a crucial role in empowering patients to take charge of their self-care and in promoting evidence-based improvements in the quality of healthcare.[4]

Materials and Methods
Both Quantitative and qualitative methods were employed to continuously evaluate the establishment of the Endometriosis Nurse role since January 2024. Until November 2024, approximately 248 patients received specialized nursing support and got the questionnaires to assess their experience, satisfaction and quality of life. Qualitative interviews were conducted to gain deeper insights into patient experiences. Statistical and thematic analyses will be conducted, ensuring that a sufficient number of responses were gathered for a comprehensive evaluation.

Results
Following the establishment of clinical activities and the implementation of necessary structures, evaluation commenced. From January to November 2024, the Endometriosis Nurse conducted 248 consultations, focusing on pain education, complementary treatment options, and guidance on a multimodal care approach. Specialized Endometriosis Nurses provide vital support for those affected by endometriosis. A preliminary analysis shows that 40% of patients at the Endometriosis Referral Centre seek counselling, highlighting the importance of a patient-centred approach that improves quality of life and self-management skills while preventing complications.

Conclusion
The integration of nursing consultations by Endometriosis Nurses is essential for improving patient outcomes. With approximately 1000 patients visiting the Endometriosis Referral Centre annually, the data highlights a significant need for specialized nursing support to enhance patient-centred care and address individual needs effectively.

Key words
Patient-centred care, endometriosis nurse, nursing counselling

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THEME: MOLECULAR PROFILING AND HIGH THROUGHPUT TECHNOLOGIES

HSA-MIR-132-5P IS OVEREXPRESSED IN HUMAN OVARIAN ENDOMETRIOTIC STROMAL CELLS AND PROMOTES ENDOMETRIOTIC PHENOTYPE ACQUISITION

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Country where research was undertaken:
Japan

Introduction/Background
A microarray study by our group revealed aberrant expression of several miRNAs in endometriosis.

We investigated the role of hsa-miR-132-5p, an upregulated miRNA in human endometriotic cyst stromal cells (ECSCs), in

the pathogenesis of endometriosis and assessed its proliferative, anti-apoptotic, and migratory properties.

Materials and Methods
We assayed ECSCs isolated from ovarian endometriotic cysts and normal endometrial stromal cells (NESCs) isolated from normal eutopic endometrium without endometriosis. We also investigated the effects of hsa-miR-132-5p on cell proliferation, motility, and apoptosis in hsa-miR-132-5p-transfected NESCs.

Results
Mature hsa-miR-132-5p expression in NESCs was significantly enhanced by transfection of hsa-miR-132-5p precursor ($p < 0.005$). The MTT assay demonstrated a significantly higher viable cell number after hsa-miR-132-5p transfection ($p < 0.05$). The Cell Death Detection ELISA showed that the hsa-miR-132-5p transfection significantly inhibited apoptosis in NESCs ($p < 0.05$). Moreover, hsa-miR-132-5p transfection significantly downregulated caspase-3 and -7 activity in NESCs ($p < 0.05$). The in vitro wound healing assay demonstrated that wound healing was significantly stimulated following hsa-miR-132-5p transfection ($p < 0.005$). The transwell migration assay showed significantly increased cell migration after the hsa-miR-132-5p transfection ($p < 0.05$).

Conclusion
Our findings suggest that hsa-miR-132-5p expression promotes the acquisition of endometriosis-specific characteristics during the development of endometriosis. Thus, hsa-miR-132-5p may be a promising target for treating endometriosis.

Key words
Hsa-miR-132-5p

SPATIAL TRANSCRIPTOMIC ANALYSIS LINKS IMMUNE-RICH REGIONS IN ENDOMETRIOMAS WITH PAIN GENERATION AND FIBROSIS

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Country where research was undertaken:
Singapore

Introduction/Background
Immune cells, particularly T-cells and macrophages, are prevalent in ectopic lesions and play key roles in driving pain and fibrosis, contributing to the chronic inflammation and tissue remodeling characteristic of endometriosis. Understanding the spatial organization of these immune-rich niches is crucial for elucidating disease pathogenesis and identifying potential therapeutic targets.

Materials and Methods
A total of 12 slides from 9 patients (3 with bilateral cysts), containing matched eutopic and ectopic endometrioma sections, were stained for CD45, CD3, pan-cytokeratin, and DAPI. Majority of patients had Stage III endometriosis and were in the follicular phase of their menstrual cycle. Immune-rich regions of interest (ROI) were identified using the Nanostring GeoMx Digital Spatial Profiler, yielding 144 total ROIs. Analysis of these ROIs was performed using the StandR package in R.

Results
UMAP projection of ROIs revealed clear separation between ectopic and eutopic samples, with some evidence of patient-specific clustering. Differential expression analysis of the top 50 DEGs showed elevated immune-related genes (e.g., IGHG2, HLA genes, CXCL1, CXCL8) and macrophage markers (e.g., CD68, CD163) in ectopic tissues. Genes involved in lipid and cholesterol metabolism (e.g., APOE, APOC1) were upregulated, with GPNMB elevated in ROIs associated with severe dysmenorrhea, correlating with pain severity and disease stage. Additionally, NGF expression correlated with reported dysmenorrhea. Spatial deconvolution using CIBERSORTx revealed higher macrophage activity in ectopic samples,

particularly in those with recurrent cysts and severe dysmenorrhea.

Conclusion
Our spatial transcriptomic analysis reveals immune activation and lipid metabolism in ectopic lesions, with GPNMB and NGF correlating with pain severity and disease stage. These findings suggest macrophages and specific biomarkers like GPNMB may be key therapeutic targets for pain and fibrosis management in endometriosis.

Key words
Immune, pain, GPNMB

THEME: PAIN AND ENDOMETRIOSIS

THE ROLE OF HISTAMINE IN ENDOMETRIOSIS-ASSOCIATED PAIN

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Country where research was undertaken:
Germany

Introduction/Background
Histamine, produced by mast cells, basophils, and histaminergic neurons, is essential for physiological regulation and inflammation. It acts as a neurotransmitter through four receptors (HR1-HR4) and has been studied in the context of neuropathic pain and neurogenic inflammation. Given its importance, we examined the effect of histamine on endometriosis.

Materials and Methods
The study employed RT-qPCR to analyze *HR1-HR4* and *IL-6* expression in peripheral blood mononuclear cells (PBMCs) from endometriosis (n=4) and non-endometriosis (n=4) patients. Additionally, gene expression tissue data from the EndometDB (https://endometdb.utu.fi/) was evaluated. Methylhistamine levels, a histamine byproduct, were measured in urine samples from endometriosis (n=35) and non-endometriosis (n=25) patients. Tissue samples (endometriosis, n=10; non-endometriosis, n=10) are being co-stained with histamine receptors and markers for nerve fibers and immune cells (e.g., CD45, PGP 9.5).

Results
The results demonstrated detectable expression of *HR2*, *HR4*, and *IL*-6 in PBMCs. When compared to the EndometDB, the differences in histamine receptor expression patterns between endometriosis lesions and PBMCs were confirmed. Additionally, variations in the gene expression levels of *HDC, COX2, VEGFA, NGF, NGFR*, and *IL-6* were noted across different endometriosis groups. However, no differences in methylhistamine levels were found between patients with endometriosis and those without. Initial findings from immunohistochemistry indicated an increased expression of HR4 surrounding endometriosis lesions.

Conclusion
Our findings suggest histamine's role in endometriosis-related pain, underscoring the need for further research. While current studies do not confirm histamine's involvement, they suggest it could be important in this complex condition. By exploring H1R-H4R expression in endometriosis lesions and surrounding nerve fibers, we aim to assess if anti-histamines could be effective treatment options.

Key words
Histamine, endometriosis-associated pain, inflammation

AN ADVANCED THERAPY FOR ENDOMETRIOSIS

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Country where research was undertaken:
United Kingdom

Introduction/Background
Endometriosis pain can be debilitating, severely impacting quality of life for patients. Pain is signaled via nociceptive sensory neurons which densely innervate endometriotic lesions. Recent data have shown that nociceptor innervation of lesions can drive lesion growth and disruption of nociceptor activity can reduce lesion size, potentially modifying endometriosis.

Materials and Methods
At Sania Therapeutics we are developing a novel therapy for endometriosis that can alleviate the pain associated with the disease that also has the potential to modify lesion

size. This therapeutic consists of an engineered adeno-associated viral vector (AAV) that targets nociceptive sensory neurons only. This AAV causes the expression of an ion channel selectively in nociceptive neurons which acts to suppress neuronal activity in response to an orally taken small molecule.

Results
When expressed in nociceptive sensory neurons, our ion channel, SRx-C490, does not alter baseline activity of these neurons. However, application of a low dose of small molecule activator significantly reduces electrical signaling in these neurons indicating that this system could alleviate nociceptor excitability and therefore pain. In addition, we have developed an in vitro system that recreates nociceptor to endometrium interactions and have used this system to identify AAV vectors that can selectively target nociceptors. These technologies will be used in preclinical models of endometriosis to assess efficacy.

Conclusion
Sania Therapeutics are innovating a novel, disease modifying therapeutic candidate for the treatment of endometriosis pain. Our therapy would be first-in-class and we are currently completing early-stage R&D with a view to reach the clinic in 2028.

Key words
Nociceptor, pain, advanced therapy

CANNABIDIOL OIL EVALUATION FOR ENDOMETRIOSIS SYMPTOM REGRESSION – A PILOT STUDY PROTOCOL (COVER PILOT STUDY)

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Country where research was undertaken:
Australia

Introduction
Chronic pelvic pain (CPP) may or may not occur concurrently with endometriosis. With limitations to treatments (opiate dependence, variable effectiveness, pain recurrence), there is growing interest in Cannabidiol (CBD). This abstract describes the development of a randomised control crossover trial aiming to investigate the impact of CBD on CPP.

Materials and Methods
A team of clinicians, researchers and consumers designed a protocol to investigate the impact of daily CBD on CPP; a double-blinded randomised placebo-controlled pilot study, with a 12-week 2-arm parallel cross-over of CBD versus placebo. We opted to use a blinded cross-over design because we wish to test feasibility, and also to benefit participants (equal opportunity to try treatment). A pilot design was chosen to generate data to inform a larger trial in the future.

Results
To be eligible, participants must have CPP diagnosed by a gynaecologist, and have failed standard treatment(s). They must be >18yrs, not planning to conceive (agree to use contraception), be cannabis naive, and have no acute/unstable systemic medical disorders. Following a 2 week CBD self-titration phase (maximum 200mg/day), the dose of CBD will be continued for another 10 weeks. CBD results will be compared with controls, using a placebo oil. Participants will complete a series of symptom and quality of life surveys at baseline, and 2, 4 and 12 weeks. After 12 weeks, a two-week washout period will commence, and then the treatments will be switched and the above repeated. A minimum of n=25 participants will be required per arm (n=34 allowing for attrition).

Conclusion
This pilot will determine whether CBD reduces pain and improves quality of life in association with CPP. We anticipate that the pilot will allow us to design subsequent larger studies. If positive results are demonstrated, this could provide clinicians with another tool in treating CPP, a challenging condition to manage.

Key words
Chronic pelvic pain, endometriosis, cannabidiol

OBSERVATIONAL OPEN-LABEL MULTICENTER STUDY TO EVALUATE THE EFFECTS OF HORMONAL THERAPY OF ENDOMETRIOSIS: STAGE 3-4 (THE ORCHIDEA STUDY SUBANALYSIS)

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Country where research was undertaken:
Russia

Introduction/Background
Special attention should be paid to the prevention of complications associated with endometriosis therapy. Dydrogesterone does not have estrogenic, androgenic, thermogenic, anabolic and corticosteroid activity. Therapy without ovulation suppression while maintaining hormonal balance may be a good reason to update data on its preferred use in the treatment of endometriosis.

Materials and Methods
Female, age ≥18 and ≤ 45 years. Complaints of chronic pelvic pain with or without dysmenorrhea measured on the 11-point Numbered Rating Scale (NRS). Endometriosis located in lower abdominal area confirmed by laparoscopy.

This study involved 187 patients with stage 3-4 endometriosis. Patients were divided into two subgroups by treatment. The patients received dydrogesterone in a prolonged cyclical regimen —5th-25th day of the menstrual cycle or in a continuous mode.

Results
The number of days in each cycle when analgesics were taken, stage III endometriosis was 1.1 versus 0.2 after 6 cycles of treatment: stage IV endometriosis was 1.7 versus 0.7 after 6 cycles of treatment. The change in the indicator of sexual well-being, qualitatively measured on a 5-point Likert scale: stage III 2.9 vs. 3.9 at the end of follow-up (visit 3), stage IV endometriosis 2.5 vs. 3.7 at the end of follow-up (visit 3). The assessment of the quality of life in accordance with SF-20 showed a statistically significant improvement ($p<0.0001$) of all assessed parameters at both the 2nd and 3rd visits compared with the baseline level. There were no differences in quality-of-life changes between the two treatment regimens.

Conclusion
Based on the results of the study, it can be concluded that dydrogesterone is highly effective in the treatment of stage III-IV endometriosis. Prolonged cyclic and continuous treatment regimens have similar effectiveness in reducing chronic pelvic pain, improving quality of life and sexual well-being.

Key words
Endometriosis, dydrogesterone, pelvic pain

PERCEIVED IMPACT OF MEDICINAL CANNABIS ON PELVIC PAIN AND ENDOMETRIOSIS RELATED SYMPTOMS IN AOTEAROA NEW ZEALAND

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Countries where research was undertaken:
New Zealand and Australia

Introduction/Background
Side effects and discontinuation rates are high and people report low levels of satisfaction with medical management of endometriosis. Novel, non-addictive pain management options are considered a research priority in endometriosis. One pathway which holds potential for targeted treatment is the endocannabinoid system (ECS).

Materials and Methods
This study aimed to investigate medicinal cannabis for the management of endometriosis pain and related symptoms in Aotearoa New Zealand. We recruited people (n=28) aged 18-50, with surgically diagnosed or suspected endometriosis, who were prescribed medicinal cannabis for 3-months (Cannabidiol oil alone or in combination with dried cannabis flower). Weekly pain scores, symptom impacts, and health-related quality of life were measured using surveys and standardised questionnaires (EHP-30). Qualitative interviews were conducted at the end of the study and thematic analysis was used to draw themes from experiences.

Results
Participants reported to experience a decrease in overall and worst pelvic pain and an improvement in endometriosis-related quality of life over the 12-week period. Most participants found CBD to be a helpful tool, and in some cases participants were able to reduce other opioid medications. 3 participants

were able to start trying to conceive because their symptoms were so greatly reduced. Issues around societal pressures, driving and work were raised for those who also used flower, but not for CBD.

Conclusion
This study suggests that medicinal cannabis has the potential to alleviate pelvic pain, improve health-related quality of life, and reduce symptom impact in individuals with endometriosis in Aotearoa New Zealand. Large scale clinical trials are urgently needed to progress medicinal cannabis as a legitimate form of pain management.

Key words
Pain, cannabis, quality of life

DEVELOPMENT OF THE COMPASS MODEL OF ENDOMETRIOSIS: A COMPREHENSIVE MODEL OF PAIN ENCOMPASSING AGENCY, SYSTEMIC FACTORS AND SENSE MAKING

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Country where research was undertaken:
Australia

Introduction/Background
Endometriosis pain is the most common and debilitating symptom for which recommended medical treatments are no panacea (Singh et al., 2020). Psychological interventions are effective in chronic pain but are currently limited for endometriosis (Samami et al., 2023). We aimed to develop a biopsychosocial model of endometriosis pain to improve understanding and guide the development of more efficacious and specific interventions.

Materials and Methods
In this mixed-methods study, 873 participants answered an online survey including pain outcomes. Sixteen participants were then purposively sampled for interview until theoretical saturation was reached, in line with grounded theory. The themes arising from the analysis of interview data formed a novel model of endometriosis pain. The model was then cross-validated and refined using content analysis of 841 open-ended online survey responses regarding system priorities for endometriosis care.

Results
The model proposes that despite the gendered nature of pain and invalidation being almost universally experienced, validation can be experienced, particularly through healthcare professionals who believe and listen to their patients. Validation fosters trust and is the platform from which agency and sense making can develop. Agency and sense making can be mutually reinforcing such that participating in value-based rewarding activities and building an identity beyond endometriosis pain can facilitate acceptance. Together, these processes can culminate in reduced pain distress, impact, and burden, even in the face of high pain severity. These experiences can be further enhanced by broader systemic factors including more accessible care, improved treatment options, and more financial support.

Conclusion
Our findings present a novel model of endometriosis pain informed by mixed methods results from a large sample. These findings shed light on the complex nature of endometriosis pain experiences and the model provides several psychosocial treatment targets that could inform future psychological and multidisciplinary interventions for endometriosis pain.

Key words
Pain, biopsychosocial, mixed methods

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PAINFUL SEXUAL POSITIONS IN ENDOMETRIOSIS PATIENTS: THE PSST! STUDY

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Country where research was undertaken:
Austria

Introduction/Background
Approximately 30-70% of women with endometriosis experience deep dyspareunia, often described as position-dependent. The aim of this study was to investigate the relationship between endometriosis and deep dyspareunia, focusing on the epidemiology of different painful sexual positions and attempting to correlate the location of endometriotic lesions with specific painful positions.

Materials and Methods
This is a prospective monocentric study including women with dyspareunia who chose laparoscopic surgical treatment for suspected endometriosis. After enrollment, patients completed a questionnaire containing questions about dyspareunia and positional dependence. The intraoperative extent of endometriosis was coded according to the Enzian classification. The entire data set was analyzed using descriptive statistics. The study was approved by the institutional ethics committee and registered in the German Clinical Trials Register (ID: DRKS00023833).

Results
531 patients were screened for inclusion in the study. Inclusion/exclusion criteria and dropouts (e.g., no intraoperative endometriosis) reduced the final number of participants to 71 patients. 83.1% complained of deep dyspareunia, 7% of superficial dyspareunia, and 9.9% of both. A dependence of dyspareunia on the sexual positions used was reported in 68.3%. Among patients with positional dyspareunia, the doggy style position was most frequently reported as the most painful sexual position. In 56.7% of cases, sexual intercourse was at least partially avoided due to the presence of dyspareunia.

Conclusion
Positional dependence is common in endometriosis patients with dyspareunia. Further evaluation will show whether there is a dependence on the localization of the endometriotic lesions.

Key words
Dyspareunia, sex position, positional dependency

EVALUATING THE IMPACT OF ORAL CANNABINOID EXTRACTS ON CHRONIC PAIN AND QUALITY OF LIFE IN ENDOMETRIOSIS PATIENTS – A PILOT STUDY

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Country where research was undertaken:
Germany

Introduction/Background
Cannabinoids have proven effective for chronic pain, cramps, spasticity, offering anxiolytic, antidepressant, neuroprotective, and mood-stabilizing effects. In a medical context, cannabinoids have a favorable safety profile, with mild and temporary side effects. This study evaluates the impact of oral cannabis extracts as an adjunct therapy on chronic pain in individuals with endometriosis.

Materials and Methods
Patients with a confirmed diagnosis of endometriosis were treated with oral cannabis extracts (12 mg THC and 14 mg CBD/mL) for 3 months. Before treatment and after 1, 2, and 3 months, patients completed questionnaires assessing symptoms, pain perception, disability, central sensitization, anxiety, and quality of life. To date, 10 patients have completed the 3-month treatment. We aim to enroll at least 20 patients by May 2025.

Results
The average age of patients was 30.93± 4.17 years. No side effects were reported, or they did not differ throughout the treatment period. Patients experienced significant reductions in pain scores ($p= 0.0007$), with lower pain levels observed after 1, 2, and 3 months compared to baseline ($p= 0.0032$ and $p= 0.0194$, respectively). The number of pain days decreased ($p= 0.0009$), but there was no reduction in the use of pain medication ($p= 0.4615$). While no improvement was seen in pre-existing issues, a trend toward improvement was observed in rest needs. Notable improvements were reported in muscle stiffness, anxiety, fatigue, generalized pain, and pelvic pain. Patients also showed reduced frustration, less perception of symptoms dominating their lives, and improvements in recreational, social, and occupational activities.

Conclusion
Oral cannabis extracts significantly reduced pain intensity and pain days in endometriosis patients over 3 months. While pain medication use remained unchanged, improvements were reported in quality of life, including recreation, social, and occupational activities. These results suggest cannabis extracts may be a promising adjunct for pain management, warranting further research.

Key words
Cannabis extracts, chronic pain, quality of life

QUALITY OF LIFE, PAIN, AND FERTILITY IN PATIENTS WITH ENDOMETRIOSIS AND/OR ADENOMYOSIS DIAGNOSED USING ADVANCED ULTRASOUND

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Country where research was undertaken:
Canada

Introduction/Background
Advanced ultrasound is increasingly used to diagnose endometriosis and adenomyosis, offering an alternative to surgical diagnosis[1,2]. However, the role of these ultrasound-diagnosed lesions on symptomatology needs to be updated. This study aims to compare quality of life, pain and infertility among patients with endometriosis, adenomyosis, or both on advanced ultrasound.

Materials and Methods
This population-based cohort study was conducted from March 2021 to October 2024. All participants underwent advanced ultrasound, and those diagnosed with endometriosis and/or adenomyosis were included. Participants completed validated questionnaires to document symptoms and health profiles. Quality of life was assessed using the Endometriosis Health Profile (EHP score)[3], and pain symptoms were reported on a 10-point scale. Groups were compared using ANOVA and linear regression analyses.

Results
Of the 165 eligible participants, 44.8% (74/165) had endometriosis alone (E), 18.8% (31/165) had adenomyosis alone (A) and 36.4% (60/165) had both (A+E). Patients with combined endometriosis and adenomyosis were significantly more likely to present with infertility compared to those with either pathology alone (A=7.14%, E=35.72%, A+E=57.14%, p=0.029). Severe dyspareunia was less likely in participants with adenomyosis alone compared to the other groups (A=4.4/10, E=5.9/10, A+E=5.6/10, p=0.025). There were no significant differences between groups for dysmenorrhea, dyschezia, dysuria, and chronic pelvic pain. Quality of life scores were low in all groups, with no significant differences observed between groups.

Conclusion
Adenomyosis is frequently diagnosed with endometriosis, and the combination of these conditions is associated with a higher risk of infertility than either condition alone. Deep dyspareunia is less common in patients with adenomyosis alone. Both pathologies are associated with poor quality of life.

Key words
Endometriosis, adenomyosis, ultrasound

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ASSOCIATION BETWEEN DEEP ENDOMETRIOSIS IN THE BOWEL WITH DYSPAREUNIA AND DYSCHEZIA

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Country where research was undertaken:
Sweden

Introduction/Background
Women with endometriosis findings may have different pain symptoms, however, none of symptoms is pathognomic for the disease. The aim of this study was to describe prevalence of dyspareunia and dyschezia in women with deep endometriosis (DE) in the bowel detected at transvaginal ultrasound examination.

Materials and Methods
Women with DE in the bowel detected at transvaginal ultrasound examination were eligible for the study. All women were systematically examined with transvaginal ultrasound by an experienced examiner at the Ultrasound Unit at the Department of Obstetrics and Gynaecology, Skane University Hospital, Malmö, Sweden using GE E8 or E10 ultrasound equipment (Milwaukee, WI, USA) with vaginal transducer of 5-9 MHz. Ultrasound findings of endometriosis lesions at different locations and size of the lesions was described according to the IDEA consensus. Before the ultrasound examination women filled in questionnaire regarding presence and intensity of dyspareunia and dyschezia measured using visual analogue scale with arbitrary units 0-100.

Results
Out of 151 women with bowel DE at ultrasound 143 women were included. Of these, 29 had isolated bowel DE. Other ultrasound findings included endometriomas n = 77 (53%), adenomyosis n = 47 (33%) and deep endometriosis in the uterosacral ligaments n = 33 (23%). Dyspareunia was reported by 103 (72%) women and dyschezia by 102 (71%) women. The length of the bowel lesion was larger in women with dyspareunia than those without (p=0.033). No difference has been observed between dyschezia and the length of the bowel lesion. Women reported lower intensity of dyspareunia and dyschezia when they were on hormonal treatment compared to those without hormonal treatment (p= 0.001).

Conclusions
Dyspareunia and dyschezia were reported by two thirds of women with DE in the bowel. Length of DE lesion in the bowel may be associated with dyspareunia.

Key words
Endometriosis, bowel, ultrasonography, dyspareunia, dyschezia

REGULATING THE ENDOCANNABINOID PATHWAY IN ENDOMETRIOSIS

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Country where research was undertaken:
Australia

Introduction/Background
Endometriosis is an estrogen dependent gynaecological disease marked by chronic pelvic pain. Palmitoylethanolamide (PEA) is an endocannabinoid that modulates nociceptive pain perception via TRVP1 and degraded by the enzyme FAAH. This study was designed to investigate the PEA pathway, receptors and enzymes in an invitro model of endometriosis

Materials and Methods
PEA pathway gene expression was determined by qPCR under vehicle, estradiol and PEA treatment conditions. Proliferation assays were used to assess PEA effects on cell growth and immunohistochemistry (IHC) was used to identify protein expression of PEA pathway regulators in endometrial tissue and endometriotic lesions.

Results
Under estrogenic conditions, stromal cell expression of *TRVP1* was unchanged, while PEA synthesis enzymes (*DAGL, NAPE/PLD*) and PEA receptors (*PPARA, CNR1, CNR2*) were downregulated, while the degradation enzyme FAAH was significantly upregulated. This demonstrated a direct interaction between estrogen and the nociceptive functionality and synthesis of the PEA pathway. Treatment of stromal cells with exogenous PEA significantly reduced *FAAH* expression and slowed cell growth in a dose dependent manner. However, in the presence of estradiol, these effects were reversed indicating other factors were able to override the influence of excess PEA. This led to the evaluation of *FAAH* protein expression in

endometrium where FAAH was diffusely localised to basalis stromal cells and strongly expressed in severe forms of endometriotic lesions.

Conclusion
The PEA pathway may be disrupted in severe forms of endometriosis due to the highly estrogenic environment and upregulation of the endocannabinoid degradation enzyme *FAAH*. High expression of FAAH in endometriotic lesions indicates FAAH inhibition may be required to make PEA effective in pain relief in a highly estrogenic environment

Key words
Pain, endometriosis, endocannabinoids

DEEP DYSPAREUNIA AND CENTRAL SENSITIZATION IN ENDOMETRIOSIS: A LONGITUDINAL STUDY WITH ONLINE DAILY PAIN DIARY

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Country where research was undertaken:
Canada

Introduction/Background
A role for central nervous system sensitization has been suggested for endometriosis-associated pain, including deep dyspareunia. We aimed to explore the relationship between prospective deep dyspareunia scores with pain-pressure threshold (PPT) at extra-pelvic sites and bladder/pelvic floor tenderness (BPFT).

Materials and Methods
Observational prospective study from January 2017-April 2019 at a tertiary center for endometriosis. Inclusion criteria: 18-49 years; endometriosis; new or re-refereed to the center and consented to the center's data registry [cases]. People without endometriosis were also recruited [controls]. Extra-pelvic PPT was measured at bilateral deltoids and first-dorsal interosseous muscles. After PPT testing, cases prospectively completed a daily pain diary over six weeks, with the deep dyspareunia (0-10) severity at each episode of sexual intercourse.

Results
36 people with endometriosis and 19 controls were included in this study. No significant differences in extra-pelvic PPT were found between controls and cases. Among people with endometriosis, PPT at the deltoids and first-dorsal interosseous muscles trended lower in people with higher deep dyspareunia on the prospective daily diaries, although not significantly different. In contrast, BPFT (present/absent) was significantly associated with higher deep dyspareunia on the prospective daily diaries (5.90±2.77 vs 3.65±2.39, p=.029).

Conclusion
In people with endometriosis, prospective daily diaries of deep dyspareunia were not associated with extra-pelvic PPT but were associated with BPFT. The role and nature of central nervous system sensitization in endometriosis-associated deep dyspareunia remains unclear.

Key words
Deep dyspareunia; central sensitization; pain-pressure threshold

ENDOMETRIOSIS AND THE AUTONOMIC NERVOUS SYSTEM: UNVEILING SYSTEMIC DYSREGULATION

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Country where research was undertaken:
Canada

Introduction/Background
Endometriosis is a pervasive and often a debilitating disease, yet its impact on the autonomic nervous system (ANS) remains unexplored. This study pioneers an understanding of ANS in endometriosis, aiming to uncover mechanisms that may drive chronic pain, symptom variability, and significantly impair quality of life (QOL) in affected individuals.

Materials and Methods
This observational study assessed autonomic function in endometriosis patients using age-

adjusted HRV metrics—Low Frequency (LF) power, High Frequency (HF) power, LF/HF ratio, and Respiratory Sinus Arrhythmia (RSA)—across baseline, deep breathing, and active standing. Dysfunction was categorized by overexcitation, lack of response, cross-pathway imbalance, and delayed recovery, with severity scored as mild (+1), moderate (+2), or severe (+3). Composite scores ranged from None (0), Mild (1–3), Moderate (4–6), High (7–9), to Severe (10–12). Non-parametric tests evaluated associations with disease subtype, symptom severity, and QOL.

Results
Among 42 participants, autonomic dysfunction was prevalent, with most patients exhibiting moderate to severe dysfunction. High dysfunction affected 35.7% (15/42) of patients, while extreme dysfunction was observed in 19.0% (7/42), with 9.5% (4/42) showing no dysfunction and 35.7% (15/42) showing mild/moderate dysfunction. Sympathetic “fight-or-flight” overexcitation occurred in 76.2% (32/42) of patients, particularly during active standing, while 52.4% showed delayed parasympathetic recovery, and 38.1% (16/42) demonstrated reduced parasympathetic tone during deep breathing. Cross-pathway imbalances, such as inappropriate sympathetic activation during parasympathetic phases, occurred in 16.7%, and persistent sympathetic tone post-stress affected 47.6% (20/42). Dysfunction presence and severity were not significantly associated with endometriosis disease subtype, symptom severity, or QOL scores.

Conclusion
This study highlighted the prevalence of ANS dysfunction in endometriosis, suggesting that its impact may extend beyond pelvic organs. Recognizing this broader effect could inform more targeted interventions to alleviate symptoms and improve QOL for individuals affected by endometriosis.

Key words
Endometriosis, autonomic nervous system, persistent pelvic pain

THEME: PATHOGENESIS AND AETIOLOGY OF DISEASE

IMPACT OF PROGESTERONE ON MITOCHONDRIA IN EPITHELIAL ORAL MUCOSA CELLS FROM PATIENTS WITH ENDOMETRIOSIS AND HEALTHY VOLUNTEERS.

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Country where research was undertaken:
United Kingdom

Introduction/Background
Many of the hormones used to treat endometriosis only manage symptoms, leading to symptom recurrence upon cessation. Increases in the enzymes involved in glycolysis have been detected in endometriotic tissue, suggesting a preferential utilisation of oxidative glycolysis, which occurs in the cytoplasm rather than oxidative phosphorylation, which occurs in mitochondria.

Materials and Methods
Epithelial oral mucosa cells were collected from healthy volunteers (HV) and patients with deep and superficial endometriosis and symptomatic controls following informed controls. We fluorescently stained and analysed the mitochondria using the confocal microscopy, ImageJ, and Mitochondria Analyzer. Statistical analysis, including R^2 values for correlation and T-tests for significance were performed using Microsoft Excel.

Results
There were no significant differences in mitochondrial quantity between cheek cells from HV (n=46) and patients (n=19). Further analysis of mitochondrial features such as count, area, perimeter, aspect ratio, form factor and branches with age or BMI showed no significant differences. However, mitochondrial numbers varied in patients and HV depending on their contraceptive hormone use. Notably, there was an increase in the number of mitochondria in patients taking the progesterone only pill (POP) and a decrease in HV taking POP, when compared to patients and healthy volunteers taking other contraceptives (IUD, HRT, COCP, injection or implant) or none.

Conclusion
To further understand the impact of endometriosis on epithelial mucosa cells, we will investigate further healthy volunteers and patient samples. Our aim is to determine the impact of hormone use and disease on mitochondria morphology and function.

EIF2AK3 SPLICE VARIANT-DRIVEN SURVIVAL REPROGRAMMING VIA THE ER STRESS-MITOPHAGY AXIS IN ENDOMETRIAL ECTOPIC IMPLANTATION

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Country where research was undertaken:
China

Introduction/Background
Endometriosis (EMs) impacts over 10% of women of reproductive age; nonetheless, the fundamental mechanisms that contribute to its development are inadequately comprehended. Although retrograde menstruation occurs in over 90% of women, only a minority develop endometriosis, indicating a potential innate survival advantage of endometrial cells. Recent evidence underscores the involvement of EIF2AK3 gene mutations in facilitating aberrant endometrial cell survival through dysregulated endoplasmic reticulum (ER) stress and mitochondrial autophagy. This work seeks to clarify the molecular mechanisms behind endometrial survival and ectopic colonisation in endometriosis.

Materials and Methods
This study included endometriosis patients undergoing surgery and a control group with uterine diverticulum. Whole blood and endometrial tissue samples were collected. EIF2AK3 (rs7571971) mutation sequencing, mitochondrial function assays, oxidative phosphorylation analysis, and metabolic profiling were conducted. PERK-GRP78 interaction, mitochondrial autophagy, and stress pathway activation were analyzed using Western blot, qPCR, and transmission electron microscopy. An in vitro hormone withdrawal model was established to assess endometrial cell survival and ectopic colonization potential.

Results
Our data indicate that the rs7571971 mutation produces a new PERK isoform with reduced GRP78 binding, leading to sustained ER stress activation. This imbalance initiates mitochondrial autophagy, allowing endometrial cells to circumvent apoptosis. Functional experiments indicate that detached endometrial cells in patients with endometriosis display increased survival and adhesion properties, validating their potential for ectopic colonisation. Structural modelling of mutant PERK indicates a molecular connection between EIF2AK3 mutations and prolonged endometrial cell survival, offering a genetic explanation for the paradox of "high retrograde, low morbidity" in endometriosis.

Conclusion
This study identifies EIF2AK3 mutation-driven ER stress dysregulation as a critical factor in EMs pathogenesis. By elucidating the interplay between ER stress, mitochondrial autophagy, and endometrial survival, our findings offer novel insights into EMs pathophysiology and potential therapeutic targets.

Key words
Endometriosis, EIF2AK3, ER stress

CASED REPORT ENDOMETRIOSIS IN ADOLESCENT: RUPTURED ENDOMETRIOMA IN HYMEN IMPERFORATE PATIENT

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Country where research was undertaken:
Indonesia

Introduction/Background
Endometriosis defined as the presence of endometrial glands and stroma outside the uterus. TheMost researchers have been proposed the ectopic implantation of endometrial tissue following retrograde menstruration as the cause of this condition. There is several risk factor associated with endometriosis in adolescent like early menarche, low BMI, positive family history, mullerian anomalies with obstruction might cause increased retrograde menstruration.

Case
A 12- years old girl was consulted durante operation by surgery departement. She is virgin and never had her period. Surgery departement consult with ruptured cyst and acute abdominal pain. I found ruptured bilateral cyst with endometriosis lesion in cyst wall, bilateral hydrosalphinx, free fluid in the abdomen that contain chocolate cyst fluid. Patient had been cyclical pain since three months ago. We do serial examinations after operation and find hymen imperforate.

Conclusion
There is an strong association between endometriosis in adolescent and mullerian anomalies. We should do several examinations to detect mullerian anomalies

Key words
Adolescent endometriosis, mullerian anomalies, retrograde menstruration

N-ACETYLCYSTEINE INHIBITION OF LESION GROWTH IN ENDOMETRIOSIS VIA TARGETING THE ROS-CHK1-SGK1 PATHWAY

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Country where research was undertaken:
China

Introduction/Background
Endometriosis is a common estrogen-dependent disorder that significantly impacts the quality of life for reproductive-aged women. While antioxidant therapies like NAC, curcumin, and others show promise, the specific molecular mechanisms behind their effects are not well understood.

Materials and Methods
We investigated the effects of NAC on lesion size using both cell and animal models. We assessed the role of reactive oxygen species (ROS) in endometrial stromal cells (ESCs) and identified CHK1 as a key ROS sensor. Additionally, we tested inhibitors of CHK1 and SGK1 in a murine model of endometriosis.

Results
NAC significantly reduced lesion size by inhibiting the enhancement of ESC vitality and their resistance to senescence that is caused by low levels of reactive oxygen species (ROS). CHK1 was found to translocate from the nucleus to the cytoplasm upon ROS activation, stabilizing SGK1 via TRIM32 modulation. Inhibitors targeting CHK1 or SGK1 effectively suppressed lesion growth in the murine model.

Conclusion
This indicates that antioxidant therapy primarily acts to alleviate oxidative stress in the microenvironment by targeting the CHK1/TRIM32/SGK1 signaling pathway, highlighting potential therapeutic targets for endometriosis.

Key words
Endometriosis, antioxidants, CHK1

HORMONAL AND EPIGENETIC RESPONSES OF NORMAL AND ENDOMETRIOTIC STROMAL CELLS

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Country where research was undertaken:
New Zealand

Introduction/Background
This study explores how steroid hormone signaling and hydroxymethylation (5hmC) modulation, regulated by Ten-Eleven Translocase Enzymes (TETs), affect endometrial stromal cells (ESCs) and endometriotic stromal cells (eESCs). It aims to understand the relationship between steroid hormone receptors and epigenetic modifications of DNA, in eutopic endometrium and its dysregulation in endometriosis.

Materials and Methods
ESCs and eESCs were treated for 21 days with vehicle, estrogen, or combined estrogen and progesterone with or without estrogen priming. Cells were also treated for 3 days with TET inhibitor Bobcat339, with or without estrogen. Samples were collected at multiple time points for proliferation and gene and protein expression analysis for estrogen receptors alpha (ERα) and beta (ERβ), total progesterone receptor (PR isoforms A and B)

and androgen receptor (AR).

Results
Hormonal treatment did not influence proliferation of either cell line, though eESCs displayed a slower and flatter growth curve distinct from ESCs. No hormonal treatment effects were observed in ERα nor ERβ mRNA expression in either cell line, though protein expression data indicates potential cell-line and treatment effects. PR and AR mRNA expressions were higher in ESCs than eESCs at days 14 and 21. At day 14 in ESCs, PR and AR mRNA levels were elevated with estrogen treatment alone, but not with added progesterone. These hormonal treatment effects were not observed in eESCs. Proliferation of ESCs and eESCs was reduced in a dose-dependent manner in response to 5hmC inhibition, with a trend toward a synergistic anti-proliferative effect in response to added estrogen in ESCs.

Conclusion
This study highlights differential hormonal and proliferative responses of endometrial and endometriotic stromal cells and has identified potential roles for 5hmC in the regulation of endometrial stromal cells and the development of endometriosis.

Key words
Stroma, epigenetics, hormones

THEME: PERSONALISED MEDICINE AND ENDOMETRIOSIS

THE POTENTIAL OF ROR1 AS A NOVEL THERAPEUTIC TARGET FOR ENDOMETRIOSIS

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Country where research was undertaken:
Australia

Introduction/Background
Personalised medicine represents a promising therapeutic avenue in endometriosis, addressing the diversity of clinical manifestations, enhancing treatment efficacy and minimising side effects. Embryonic cell surface receptor ROR1 is a key target in oncology owing to its role in regulating cell growth, differentiation, and survival, but remains unexplored in endometriosis.

Materials and Methods
ROR1 mRNA expression was analysed in a cohort of superficial (SUP n=76), deep infiltrating (DIE n=88), and endometrioma (OMA n=28) lesions, and control peritoneal (n=37) and endometrial (n=102) tissues. ROR1 protein expression was validated in an endometriosis tissue microarray (n=53). An *in silico* ligand-based virtual screening approach was undertaken to identify drugs with potential ROR1-binding activity, favourable pharmacokinetics and minimal side effects. A shortlist of 3 agents were tested in endometriosis cell lines and organoids.

Results
ROR1 is transcriptionally upregulated in peritoneal endometriosis tissues, but not endometrioma, irrespective of patient stage, age, or menstrual phase. Protein translation was confirmed in majority of patients within endometriosis microarrays (49/53, 92.5%), including SUP (9/12, 75/0%), DIE (33/33, 100.0%) OMA (6/9, 66.7%) and adenomyosis lesions (8/9, 88.9%). Ligand-based screening identified 263 agents with potential ROR1 inhibitory activity. Of these, cabergoline (a dopaminergic agonist), pirenzepine (an antimuscarinic and PARP inhibitor), and rimegepant (CGRP antagonist for migraine nociception) were prioritised and tested in a ROR1-expressing adherent cell line and patient-derived organoids. While no difference in cell proliferation or viability was observed after 72h of cabergoline or pirenzepine treatment, rimegepant demonstrated cytotoxic potential *in vitro*.

Conclusion
ROR1 is a promising target for precision endometriosis treatment due to its upregulation in endometriosis lesions and low expression in adult tissues. Investigating ROR1-targeting therapies is warranted, including the repurposing of migraine drug rimegepant, which may exert nociception effects while also preventing endometriosis lesion growth through ROR1 inhibition.

Key words
Drug repurposing, personalised medicine, organoids

THEME: PUBLIC HEALTH POLICY AND GLOBAL CHALLENGES

ENDOMETRIOSIS AWARENESS AND MENSTRUAL HEALTH INITIATIVE FOR TEENAGERS (ENDO-HIT)

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Country where research was undertaken:
Spain

Introduction/Background
Although affecting 45-95% of adolescents, dysmenorrhea is often overlooked due to menstruation stigma, contributing to endometriosis historic and well-known diagnostic delay and negatively impacting their quality of life. Menstrual health education initiatives de-normalizing menstrual pain and informing about endometriosis are a potential approach to improve endometriosis awareness and early diagnosis.

Materials and Methods
A pre-post survey study was conducted with high school students aged 12-16 from six centers in Barcelona, Spain (N=384 pre; N=186 post). A workshop on menstrual health and endometriosis was conducted between both surveys to assess its impact on students' knowledge and opinion on the topic. Menstruating individuals (N=185) provided clinical data regarding their periods and associated pain. Students' participation in ENDO-HIT concluded with the creation of informative materials about their learnings.

Results
The results of the ENDO-HIT study highlight the importance of such initiatives, as more than 75% of the surveyed students were unfamiliar with the term endometriosis. The provided workshop had a positive impact in the students' knowledge of menstrual health and endometriosis, independently of their gender. Initial acceptance was moderate (40%), but the workshop received positive feedback; in the post-intervention survey, 74% of the students found it useful and only 7% would have preferred to not attend. In our menstruating cohort, 60.5% of adolescents reported experiencing monthly menstrual pain. Despite the frequent use of painkillers for pain relief, only 10.3% have ever sought medical advice about their menstrual symptoms.

Conclusion
The ENDO-HIT project is a pioneering study in Spain that, in line with findings from other countries, demonstrates the need for and benefits of educational interventions and comprehensive menstrual health programs. Although the use of painkillers and period pain experiences are common, dysmenorrhea remains undervalued and normalized in Spanish classrooms.

Key words
Adolescents, endometriosis awareness, menstrual pain

STATISTICAL SIGNIFICANCE REPORTING AND PUBLICATION REPORTING BIAS IN ABSTRACTS OF ENDOMETRIOSIS LITERATURE

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Country where research was undertaken:
Australia

Introduction/Background
Selective publishing of statistically significant findings can result in biased estimations of disease management methods, with serious implications for clinical guidelines, patient care and future research. Further, use of effect measures and decreased reliance on p-values as determinants of result importance is encouraged to increase clinical relevance of result reporting.

Materials and Methods
We created a database of abstracts of endometriosis studies between 1990-2024 from Dimensions.AI. Studies were categorized into 'Basic Research', Randomised Controlled Trials (RCTs), 'Non-Randomised Clinical Studies' and Meta-Analyses/Systematic Reviews using text-mining. We excluded studies for which quantitative analysis was not relevant (e.g. literature reviews). 'R' programming was used to text mine abstracts for p-values, effect measures and

accompanying confidence intervals and Bayesian statistics.

Results
We identified 17,087 abstracts. The percentage of abstracts reporting p-values increased from 18.9% in 1990-1999 to 35.7% for abstracts in the recent period of 2020-2024. Comparatively, only 14.2% of abstracts reported effect measures between 2020-2024. This relative emphasis placed on reporting p-values is particularly pertinent within RCTs, where 53.6% of abstracts reported a p-value compared to only 7.45% reporting an effect measure across the 1990-2024 period.

Of the 17,344 p-values extracted from abstracts, 14,706 (84.8%) were less than or equal to 0.05. This high proportion of statistically significant results, reported as either a p-value or effect measure with accompanying confidence interval, remained above 90% consistently between 1990-2024 with no clear trend of decline.

Conclusion
In the report of endometriosis research, p-values were the main reporting method compared to effect measures within abstracts. There was a high number of significant p-values not reducing overtime, suggesting selective publication.

Key words
Endometriosis, research evaluation, metaresearch

ENDOMETRIOSIS CLINICAL AND SURGICAL CARE DURING THE COVID-19 PANDEMIC

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Country where research was undertaken:
Canada

Introduction/Background
Endometriosis, a chronic, inflammatory condition, affects approximately 10% of people assigned female at birth. During the COVID-19 pandemic, endometriosis care shifted towards virtual appointments. Our aim was to evaluate diagnostic and treatment outcomes before and after the introduction of pandemic restrictions, and in those who received only virtual care.

Materials and Methods
Registry data analysis was conducted at a tertiary referral center for endometriosis and pelvic pain. Pre-Pandemic (n=776; 2018-March 16, 2019) and Pandemic patients (n=265; March 17, 2020-2021) were compared. During the Pandemic (2020-2022), we compared patients with an initial virtual assessment followed by virtual care alone (Virtual Only, n=203) or an in-person physical exam (Physical Exam, n=186). Outcomes included surgery, pain scores, mental health, and quality of life scores at baseline and one-year follow-up.

Results
Preliminary results show the Pandemic group had higher pelvic pain scores ($p<0.05$), were less likely to take combined hormonal contraceptives ($p<0.05$), and more likely to have surgery following their initial visit ($p<0.001$) compared to the Pre-Pandemic group. At one-year follow-up the groups were similar in pain, mental health, and quality of life scores.

The Virtual Only group was more likely to have a histological diagnosis of endometriosis ($p<0.01$) based on previous surgery. The Physical Exam group was more likely to have surgery at the centre after the initial assessment compared to the Virtual Only group ($p<0.001$). The two groups had similar pain, mental health and quality of life scores at baseline and one-year following care at the centre.

Conclusion
These results suggest care during the pandemic and virtual only care was utilized effectively in this setting, including in patients undergoing surgery. Future research could incorporate population-based administrative data or qualitative approaches to understanding patient experiences and physician perspectives on virtual care for endometriosis.

Key words
Endometriosis, virtual care, pelvic pain

THEME: SURGICAL MANAGEMENT

ABANDONING THE SHAVE: IS RECTAL SHAVING OBSOLETE?

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Country where research was undertaken:
Australia

Introduction/Background
Deep infiltrating endometriosis (DIE) involving the bowel often necessitates surgical intervention, with shaving and discoid resection being the primary techniques. Shaving, a minimally invasive approach, is faster but risks leaving residual disease, leading to recurrence (Roman et al., 2016). Discoid resection provides complete lesion removal, resulting in better outcomes and fewer recurrences (Farella et al., 2021).

Materials and Methods
This retrospective analysis included 420 patients who underwent discoid resections for bowel DIE between 2012 and 2024. Patient outcomes, including symptom-free intervals and postoperative complications, were compared to data from the literature on shaving. Key studies by Ip et al. (2020) and Ng et al., (2016) were also reviewed to evaluate the role of nodule volume reduction via shaving before discoid resection.

Results
Discoid resection achieved significant symptom relief, with disease-free intervals exceeding those reported for shaving. Among our cohort, no cases of fistula formation or anastomotic leakage occurred, confirming the safety of the procedure. Emerging evidence (Ng et al., 2016; Li et al., 2014) indicates discoid resection improves bowel and bladder function, while shaving may assist as a pre-resection technique to reduce nodule volume, particularly in complex cases. This dual approach facilitates safer, more effective discoid resections.

Conclusion
Discoid resection offers superior outcomes in bowel DIE management, with extended symptom-free intervals and low complication rates. While not advocating for eliminating shaving, its role as a preparatory step for volume reduction may enhance discoid resection outcomes. Further prospective studies are needed to refine this dual-strategy approach.

Key words
Endometriosis, discoid resection, shaving

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INTRAOPERATIVE ULTRASOUND IN ENDOMETRIOSIS SURGERY, A FEASIBILITY STUDY.

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Country where research was undertaken:
Denmark

Introduction/Background
Intraoperative ultrasound has recently been introduced in surgery on patients with endometriosis, however, feasibility in both laparoscopic and robot-assisted surgery is still unclear. We evaluated the use of intraoperative ultrasound in our department during a three-week period. The purpose was to assess feasibility during surgical removal of endometriotic lesions.

Materials and Methods
All patients had a trans vaginal ultrasound scan (TVUS) done in the outpatient clinic and six patients had a pre-operative MRI scan. Furthermore, a TVUS was done prior to surgery on the patient when sedated and then the patient was scanned during surgery using intraoperative ultrasound. We used both the laparoscopic ultrasound probe (I13C3f, BK-Medical, Copenhagen, Denmark) as well as the drop-in probe designed and for robot-assisted surgery (Rob12C4, BK-Medical, Copenhagen, Denmark).

Results
In a three-week period, we included eleven patients with endometriosis in bowel, bladder and vagina. The included patients had deep infiltrating endometriosis. The drop-in probe was used both in conventional laparoscopic surgery and robot-assisted surgery. Scans were done prior, during and after surgical removal of endometriotic lesions. Images of lesions from pre-operative, per-operative and intraoperative scans as well as MRI were compared. Pre-operative TVUS and MRI provided similar findings to per-operative and intraoperative scans. Most surgeons found that scans done during removal facilitated surgical removal of lesions. Furthermore, scans on lesions in the bowel helped determine borders of the lesions prior to surgical removal.

Conclusion
It is feasible to use intraoperative ultrasound during surgery, in both laparoscopic and robot-assisted surgery. Intraoperative ultrasound may help guide surgical removal of endometriotic lesions. Furthermore, intraoperative ultrasound may also help determine the borders of lesions in the bowel and guide decision making when choosing between disc-resection and complete resection.

Key words
Intraoperative ultrasound, robot-assisted laparoscopy,

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INTRA-OPERATIVE INTRAVENOUS TRANEXAMIC ACID DURING LAPAROSCOPIC SURGERY FOR SEVERE ENDOMETRIOSIS – A DOUBLE-BLINDED RANDOMIZED PLACEBO CONTROLLED TRIAL.

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Country where research was undertaken:
Australia

Introduction/Background
Tranexamic acid (TXA) has been shown to significantly reduce surgical blood loss across a range of different specialties and procedures. We investigated its utility in laparoscopic treatment of severe endometriosis.

Materials and Methods
Patients undergoing laparoscopic surgery for

suspected severe endometriosis were randomized to receive 1g of intravenous tranexamic acid or placebo at start of surgery, in a single centre tertiary women's hospital. Primary outcome was weighed blood loss (suction output minus irrigation and cyst fluid). Secondary outcomes were estimated blood loss by surgeon as continuous (mls) and categorical (minimal/small/moderate/large) variables and surgeon reported impact of bleeding on surgical conditions (minimal/small/moderate/large).

Results
Results following are from blinded analysis of the near-complete cohort (reported as groups A and B). At the time of the conference complete, unblinded data will be presented.

139/196 participants had a mean weighed blood loss in the negative range, due to irrigation fluid unable to be completely suctioned. Mean weighed blood loss in group A was -31ml vs group B -85ml, p=0.102. Estimated blood loss by surgeon was less in group A (134ml) vs group B (186ml) p=0.041. Estimated blood loss by category was also lower in group A with frequency of reporting minimal/small/moderate/large blood loss of 23%/39%/37%/2% vs group B of 20%/25%/50%/7% p=0.046. Impact of bleeding on surgery was reported as minimal/small/moderate/large at a frequency of 31%/41%/26%/3% in group A compared to 27%/26%/38%/5% in group B, p=0.415.

Conclusion
Tranexamic acid use in severe endometriosis surgeries appears to result in changed blood loss. Group A had lower blood loss in all domains measured, reaching statistical significance in estimated blood loss by surgeon (mls) and categorical amount of bleeding reported by surgeon. The overall differences are small and unlikely to be of clinical significance.

Key words
Tranexamic acid, endometriosis surgery

SURGICAL THERAPY FOR SUSPECTED ENDOMETRIOSIS OF UTEROSACRAL LIGAMENT [USL] – EVALUATION OF PAIN CONTROL AND IMPACT ON QUALITY OF LIFE

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Country where research was undertaken:
Austria

Introduction/Background
The USL is a common location for deep endometriosis causing pelvic pain, dysmenorrhea or dyspareunia. The aim of this study was to evaluate the surgical treatment approach and its effects on typical symptoms of deep endometriosis and the patients' quality of life (1–3).

Materials and Methods
This explorative, retrospective questionnaire-based study refers to patients who underwent resection of the USL between 2015 and 2020 at Kepler University Hospital due to symptoms suggestive of endometriosis. The questionnaire contains information on pre- and postoperative complaints, surgery-related complications, additional therapies carried out, quality of life and obstetric aspects. Further relevant information was retrieved by medical records of the enrolled patients.

Results
A total of 73 patients aged between 19 and 48 could be included in the study. A comparison of preoperative Visual Analog Scale (VAS) scores with those recorded 12 months postoperatively reveal a reduction of 75.3% in pelvic pain, 76.7% in dysmenorrhea, 69.9% in dyspareunia, and 45.2% in both dyschezia and dysuria. Additionally, the quality of life (QoL) increased, with the median preoperative score of 4 out of 7 rising to 6 out of 7 at the 12-month follow-up. Preoperatively, 36 patients were regularly using analgesics, comprising 34 on non-opioids and 2 on opioids. Postoperatively, this number decreased to 20 patients relying on non-opioid analgesics. Four patients reported complications following surgery and four patients indicated experiencing difficulties with urination postoperatively.

Conclusion
The resection of the uterosacral ligament due to deep endometriosis represents a viable treatment strategy, as it is associated with a reduction in pain and an improvement in the patients' quality of life with a low complication rate.

Key words
Endometriosis, Uterosacral ligament

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MULTIDISCIPLINARY SURGICAL MANAGEMENT OF CATAMENIAL PNEUMOTHORAX DUE TO THORACIC ENDOMETRIOSIS

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Country where research was undertaken:
India

Introduction/Background
Catamenial pneumothorax, a rare complication of thoracic endometriosis, manifests as recurrent pneumothorax related to menstrual cycles. This surgical case emphasizes the importance of recognizing thoracic endometriosis in patients with known endometriosis presenting with pneumothorax and other respiratory symptoms.

Materials and Methods
A 31-year-old female with a history of endometriosis and prior robotic endometriosis excision presented with dyspnea and chest discomfort. Initial assessment included clinical evaluation, imaging studies (HRCT), and a multidisciplinary approach involving pulmonology and gynecology. Video-assisted thoracoscopic surgery (VATS) was performed to confirm and excise thoracic and diaphragmatic endometriosis.

Results
HRCT revealed right-sided moderate pneumothorax with partial lung collapse and minimal pleural effusion. VATS findings included extensive thoracic endometriosis involving both hemidiaphragms, fenestrations in the right hemidiaphragm, and endometriotic nodules in the apical pleura, chest wall, and superior vena cava. Surgical management involved diaphragmatic endometriosis-excision and repair, and apical pleurectomy. Histopathology confirmed endometrial tissue implants, supporting the diagnosis of thoracic endometriosis.

Conclusion
Early diagnosis and surgical intervention are critical in managing catamenial pneumothorax secondary to thoracic endometriosis. Multidisciplinary coordination and hormonal therapy are essential to prevent recurrence and improve quality of life.

Key words
Catamenial pneumothorax, thoracic endometriosis, VATS

THEME: SURGICAL VIDEOS

MULTI-DISCIPLINARY SURGICAL EVALUATION AND MANAGEMENT OF A RARE CASE OF CONCOMITANT LATERAL AND POSTERIOR COMPARTMENT DEEP-INFILTRATING ENDOMETRIOSIS

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Country where research was undertaken:
Australia

Introduction/Background
This video is a presentation of the pre-operative evaluation, surgical and post-operative management of a 48-year-old female patient with extensive deep-infiltrating endometriosis of both lateral and posterior compartments requiring multi-disciplinary team management

Materials and Methods
This video represents a rare case report highlighting multi-disciplinary pre-operative, intra-operative and post-operative

management of extensive deep-infiltrating endometriosis.

Results
A 48-year-old female patient initially presented with symptoms of severe dysmenorrhea and heavy menstrual bleeding for several years, chronic pelvic pain, right flank pain, severe dyschezia and inter menstrual bleeding. Initial computed tomography (CT) of abdomen and pelvis revealed a large 10 cm pelvic mass with extensive right hydroureteronephrosis attributed to compression by the pelvic mass. Further imaging via specialized ultrasound and Magnetic resonance imaging (MRI) pelvis suggested extensive adenomyosis and the pelvic mass to be a posterior compartment endometrioma extensively involving the posterior uterus and anterior rectal wall with no plane of separation and compressing the right ureter causing hydroureteronephrosis prompting right ureteric stenting. The patient was adequately counselled by all three specialties Gynaecology, Colorectal and Urology and went on to have a robotic hysterectomy, bilateral salpingectomy, left oophorectomy, extensive adhesiolysis, anterior resection and right ureteric reimplantation (video inclusive of surgical steps)

Conclusion
Concomitant extensive deep endometriosis of both posterior and lateral compartments requiring hysterectomy, anterior rectal resection and ureteric reimplantation is very rare. This surgical video highlights the significance of multi-disciplinary team management for diagnosis, intra-operative and post-operative management of rare and significantly morbid cases of endometriosis ultimately aiming to achieve the best possible patient outcome through coordinated care.

Key words
Deep-infiltrating endometriosis, ureteric reimplantation, adenomyosis

RELEVANCE OF UNDERSTANDING RELATION BETWEEN UTEROSACRAL LIGAMENT, URETER AND INFERIOR HYPOGASTRIC NERVE IN UTEROSACRAL NODULES EXCISION

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Country where research was undertaken:
India

Introduction:
Endometriosis is an enigmatic disease affecting around 20% of women in her reproductive age group. It's mainly of three types : Common locations for DIE are: Uterosacral Ligament, Rectovaginal Septum, Parametrium, Bowel lesions, Urinary lesions involving bladder and or ureter & Nerves. According to a study thickening of unilateral or bilateral uterosacral is found in approximately 36.4% of ovarian endometriosis cases. Excision of uterosacral nodules is important part of excision surgery and in distorted anatomy it has close proximity to two important structures like ureter and hypogastric nerve. Preservation of IHN is important to reduce postoperative morbidity like bladder, rectal and sexual dysfunction.

We are presenting a case with
- Step by step approach to deal with uterosacral nodule excision.
- To safeguard ureter and preservation of IHN to prevent postop dysfunction of bladder, rectum.

Case History:
A 32 Year female P1L1, with previous history of laparoscopic bilateral Endometrioma cystectomy for severe dysmenorrhoea, dyspareunia one year back, but her symptoms were not relieved much and on MRI there was mild to moderate hydroureter and nodular lesion in left parametrium.

Steps of safely excising uterosacral nodules:
- Ureterolysis on left side starting from pelvic brim
- Creation of left medial para rectal space
- Rectum and ureter protected
- Visualization of inferior hypogastric nerve 2cm inferior to ureter.
- Excision of left nodule with preservation of IHN.
- Same steps repeated on right side.

Conclusion
Most of the ovarian endometriomas are associated with Deep infiltrating lesions in posterior compartment involvement of uterosacral ligaments being commonest.Excision of uterosacral nodules should be done after ureterolysis and safeguarding hypogastric nerve which is located in Okabayashi space medial and

inferior to ureter. Preservation of this nerve at least on one side in case of bilateral involvement is important for preventing postop dysfunction of bladder rectum and sexual functions.

Key words
Uterosacral nodules, hypogastric nerve, ureter, okabayashi space.

THEME: TRANSLATIONAL SCIENCE/MEDICINE

ANTAGONIZING THE CORTICOTROPIN-RELEASING HORMONE RECEPTOR 1 WITH AN ORALLY BIOAVAILABLE DRUG REDUCES ENDOMETRIOSIS PAIN AND ASSOCIATED ADHESIONS.

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Countries where research was undertaken:
United States of America and Puerto Rico

Introduction/Background
Estrogen facilitates the expression of corticotropin-releasing hormone (CRH) in endometrial tissue[1]. CRH, in turn, mediates inflammatory mechanisms and pain perception, making CRH a suitable downstream target of estrogen. Endometriosis lesions from a rat model have increased CRH receptor-1 (CRHR1) expression compared to normal uteri[2].

Materials and Methods
Starting 25 days after endometriosis induction by auto-transplantation, rats received orally 10 mg/kg of Drug P, a selective CRHR1 antagonist or vehicle in oyster crackers, or elagolix (14 mg/kg positive control). Drugs were given for 7 days followed by 7 days drug-free, repeated three times until day 60. Measures included mechanical, thermal, and inflammatory pain, lesion size, cytokines, serum FSH and LH, and colonic macroscopic score.

Results
Drug P decreased immunohistochemical staining of nerve growth factor (NGF), vascular endothelial growth factor (VEGF), and Ki67, and the mRNA for IL-6 and TNF-alpha within endometriotic lesions compared to the vehicle group. A significant decrease in mechanical and inflammatory pain parallelled these effects: 34% and 38% lower than the vehicle group, respectively. While elagolix altered the peritoneal leptin-to-weight ratio and serum FSH-to-LH ratio, this was not observed for Drug P. There was a significant decrease in the macroscopic score, primarily driven by a two-fold decreased adhesions score for Drug P, which was not observed in the vehicle or elagolix groups. None of the drug treatments changed the gross area or weight of the endometriosis lesions.

Conclusion
Targeting the CRHR1 receptor decreases proliferative activity within endometriosis vesicles, with minimal disruptions in gonadal signaling, compared to a gonadotropin-releasing hormone antagonist. Furthermore, the compound effectively minimizes endometriosis-associated adhesions for which no pharmacological treatment options exist. A decrease in mechanical and inflammatory pain represents a clinically relevant finding.

Key words
Corticotropin, treatment, non-endocrine

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DEVELOPMENT OF ENDOMETRIUM-ON-CHIP TO UNDERSTAND ENDOMETRIOSIS

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Country where research was undertaken:
France

Introduction/Background
Endometriosis affects the quality of life of approximately 10% of women of childbearing age. Oral contraception is the first line of treatment but 30% of endometriosis women do not respond. The development of a tool to understand endometriosis and predict the response to current treatments is therefore an innovative strategy.

Materials and Methods
The PDMS on-ChiP endometrium is a system that reproduces the physiology of the endometrium by recreating the different cellular layers composing this organ. Epithelial, stromal, and immune cells are isolated from menstrual blood from women with and without endometriosis, a strategically relevant, easily accessible, and non-invasive biological fluid. These cells are injected into different channels to build the endometrium-on-ChiP, then their morphology and secreted proteins are studied.

Results
We have strongly focused on defining the optimal culture conditions for obtaining easily comparable relevant endometrium-on-chip: type of hydrogel, number of cells and microscopy imaging. Our Endometrium-on-ChiP model enables comparison of the growth, morphology of the cells and their secreted proteins from women with and without endometriosis, in the presence or not of hormones. Comparing these outcomes in women with endometriosis for which the hormonal treatment was efficient versus inefficient is of particular interest.

Conclusion
The Endometrium-on-ChiP we developed will enable a better understanding of the disease impact on the eutopic endometrium and may help to establish a non-invasive personalized predictive test for hormonal treatment for each woman. Such a model could also be used to test new (non-contraceptive) therapies for endometriosis and associated infertility.

Key words
Endometrium-on-ChiP, hormones, menstruation

POSTER SESSION 2

THEME: ADENOMYOSIS

BUILDING A DIGITAL ECOSYSTEM FOR ADENOMYOSIS MANAGEMENT: MAPPING AND IMPLEMENTATION

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Country where research was undertaken:
Australia

Introduction/Background
Adenomyosis management can be offered via a multidisciplinary set up, often challenging within traditional care frameworks. This study explores the development of a digital ecosystem to streamline adenomyosis management through hybrid care, integrating telehealth, in-person visits, hybrid reception, use of a digital patient portal and advanced connectivity using FHIR (Fast Healthcare Interoperability Resources) standards. Ultrasound imaging is an important diagnostic tool, offered on and off site in this care model, and is incorporated into the digital workflow/

Materials and Methods
A comprehensive mapping of the adenomyosis care pathway was conducted, identifying barriers and enablers for a digitally integrated, hybrid model. Key components included piloting a digital patient portal for engagement, AI-driven applications for clinical documentation, scheduling, and patient follow-up, as well as FHIR-compliant data exchange for seamless interoperability. Ultrasound imaging results were incorporated into the ecosystem, enabling remote access to diagnostic data for multidisciplinary teams. (The ethics application for the use of ultrasound part in this context is submitted at present.)

Results
Results will review patient engagement and assess documentation time for clinicians. FHIR connectivity facilitated real-time data

sharing, improving inter-specialty communication and continuity of care, while ultrasound integration will assess diagnostic workflows based on clinician interviews.

The hybrid model offering flexibility and accessibility, especially beneficial for rural or time-constrained patients. Barriers primarily included initial data privacy concerns and training requirements for effective tool use. Overall the digital ecosystem enabled a streamlined care, model for adenomyosis.

Conclusion
The digital ecosystem for adenomyosis management demonstrates a promising model for hybrid care, connecting patients and providers more effectively through FHIR interoperability and ultrasound integration. Addressing privacy and training needs is essential for sustaining these benefits, which mark a significant advancement in patient-centered, multidisciplinary care.

Key words
Digital ecosystem, hybrid care, adenomyosis

DIFFERENCES IN CLINICAL CHARACTERISTICS AND RELATED FACTORS IN INTRINSIC AND EXTRINSIC ADENOMYOSIS

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Country where research was undertaken:
China

Introduction/Background
Adenomyosis (AM) can be categorized into four subtypes based on magnetic resonance imaging (MRI) [1], with the intrinsic (31.5%) and extrinsic (43.9%) forms being the most prevalent[2]. However, the clinical characteristics, associated risk factors, and distinguishing features of these two subtypes remain largely uncertain, warranting further investigation.

Materials and Methods
This retrospective observational study was conducted between June 2019 and August 2022. Women who underwent hysterectomy with a confirmed diagnosis of intrinsic or extrinsic AM on the basis of MRI and pathological examination were included in the study. The presence of demographic characteristics, clinical features, treatment effect and related factors were evaluated. Multiple logistic regression analyses were also performed to screen for potential intrinsic and extrinsic AM-related factors.

Results
The study included 131 patients, with 77 in the intrinsic group and 54 in the extrinsic group. Gravidity, parity, abortion, and endometrial curettage were significantly higher in the intrinsic group, while education levels were lower. The extrinsic group exhibited earlier menarche, more ovarian endometrioma (OMA), deep infiltrating endometriosis (DIE), and severe dysmenorrhea. In contrast, women in the intrinsic group experienced heavier menstrual blood loss, longer surgery times, greater operative blood loss, and higher hospitalization costs. Multivariate analysis indicated that education level (OR 0.62, 95% CI 0.44-0.87), gravidity (OR 1.80, 95% CI 1.17-2.76), and endometrial curettage (OR 2.23, 95% CI 1.07-4.68) were associated with intrinsic AM, while OMA (OR 22.32, 95% CI 2.94-124.42) and DIE (OR 24.22, 95% CI 10.35-149.33) were strongly linked to extrinsic AM.

Conclusion
The intrinsic and extrinsic AM have specific clinic profiles and related factors, respectively.

Key words
Intrinsic adenomyosis, Extrinsic adenomyosis, Clinical characteristics

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THYROID AUTOIMMUNITY MARKERS IN WOMEN WITH ADENOMYOSIS AND CONTROLS

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Country where research was undertaken:
South Korea

Introduction/Background
Adenomyosis is characterized as the presence of ectopic endometrial tissue within the myometrium, and the only difference between adenomyosis and endometriosis is the site of endometriotic tissue. Endometriosis is well known to be frequently associated with various autoimmune phenomena.

Materials and Methods
This study was performed to compare the prevalence of autoimmune thyroid disease (AITD) assessed by thyroid peroxidase antibody (anti-TPO Ab) and thyroid ultrasonography (USG) in women with adenomyosis (n= 364) and age-matched controls (n=451). Adenomyosis was diagnosed if a woman had presence of features typical of adenomyosis on 2-dimensional transvaginal USG. All age-matched controls also received transvaginal USG, and they did not have adenomyosis, myoma or ovarian endometrioma.

Results
There was no difference in the frequency of anti-TPO Ab positivity between the women with adenomyosis and the controls (5.0% (10/201) in patients and 7.4% (25/338) in controls). The frequency of heterogeneous or hypoechoic parenchyma on USG also did not differ between the patients and controls (9.3% (23/246) in patients and 12.2% (54/441) in controls). Within the adenomyosis group, the subjects with AITD (who had either Ab positivity or sonographic findings compatible with thyroiditis) showed significantly higher body mass indexes, waist circumferences and homeostasis model assessment for insulin resistance levels than the patients without AITD.

Conclusion
In conclusion, AITD was not more prevalent in women with adenomyosis than in controls. However, among women with adenomyosis, subjects with AITD showed significantly higher adiposity and insulin resistance index than those without AITD.

Key words
Adenomyosis, autoimmune, thyroiditis

THEME: ALLIED HEALTH, COMPLEMENTARY AND ALTERNATIVE MANAGEMENT

WOMEN'S EXPERIENCES WITH ENDOMETRIOSIS-ASSOCIATED PELVIC PAIN FOLLOWING PARTICIPATION IN A PELVIC FLOOR MUSCLE EXERCISE AND MINDFULNESS INTERVENTION: A QUALITATIVE STUDY

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Country where research was undertaken:
Australia

Introduction/Background
Pelvic floor muscle (PFM) exercise is commonly prescribed to women with endometriosis-associated pelvic pain (EAPP).[1] However, women's experiences with this intervention are unknown. The purpose of this study was to explore the experiences and perceptions of women with EAPP who participated in a PFM exercise program that included mindfulness.

Materials and Methods
This was a qualitative study nested within a pilot randomised controlled trial. Semi-structured interviews were performed with participants with EAPP who participated in an 8-week intervention program that included either PFM contraction-plus-relaxation (PFMC+R) or PFM relaxation-only (PFMR). Both groups also received mindfulness training. Interview data were recorded and transcribed verbatim. Direct content analysis[2] was conducted using a combination of deductive and inductive processes guided by the Theoretical Framework of Acceptability.[3]

Results
A total of 16 participants (PFMC+R=9; PFMR=7) with a mean age of 30 (SD=4.23) were interviewed. Participants in both groups reported positive experiences in terms of the intervention components, delivery mode, exercise progression and perceived beneficial

effects on their EAPP symptoms. Factors that facilitated engagement with the intervention in both groups included a well-explained program and tailoring of PFM exercises, while severe pelvic pain and fatigue were the main barriers identified. Some differences in participants' experiences were observed. For example, more participants in the PFMC+R group reported that the intervention helped them to better cope with pain, reduced their dyspareunia, and perceived changes in PFM strength. There were also more participants from this group that would recommend the intervention for women with EAPP.

Conclusion
Although participants from both groups reported positive experiences and perceptions about the intervention, the PFMC+R protocol might be more acceptable than the PFMR protocol. Clinicians and researchers need to consider the facilitators and barriers identified by participants to implement these interventions into clinical practice.

Key words
Endometriosis, pelvic pain, pelvic floor muscle.

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DIETARY AND LIFESTYLE MANAGEMENT IN WOMEN WITH ENDOMETRIOSIS WANTING TO CONCEIVE: INCREASING OUR UNDERSTANDING IN AN AUSTRALIAN CONTEXT

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Country where research was undertaken:
Australia

Introduction/Background
Nutrition therapy is recommended for holistic endometriosis care [1]. During preconception nutrition may be an easy, low-cost, non-invasive therapy to optimise fertility and pregnancy outcomes [2, 3]. We aimed to understand dietary patterns in people with and without endometriosis wanting to conceive in Australia.

Materials and Methods
This cross-sectional survey recruited participants who had been trying to conceive within the last 6 months and not currently pregnant from October 2023 – August 2024 through social media platforms and was administered through RedCap. Questions queried demographics, lifestyle changes to optimise fertility, the impact of pelvic pain on quality (Impact of Female Chronic Pelvic Pain) and diet quality (Mini-Eating Assessment Tool) in those with and without endometriosis.

Results
The 123 participants included were aged 34±4.3 years, assigned female at birth (99%), of Australian/New Zealand/ Melanesian, Papuan or Polynesian ethnicity (63%), were bachelor (44%) or postgraduate degree (31%) qualified, married (71%) and working fulltime (68%). Unsurprisingly, people with endometriosis were more likely to report experiencing pelvic pain ($p<0.001$) and had a greater impact of pelvic pain on their quality of life ($p=0.04$). Having endometriosis increased the likelihood of following a particular diet to help increase fertility ($p=0.02$), with gluten-free or Mediterranean diet being the most followed. Supplement use was reported in both groups ($p=0.71$) however people with endometriosis supplemented with a greater number of tablets daily, with prenatal multivitamins, vitamin D, fish oil, folic acid and co-enzyme Q10 being the most popular.

Conclusion
To optimise fertility, people with endometriosis were more likely to follow a diet and consume more supplements daily but had the same diet quality as people without endometriosis trying to conceive. Evidence-based nutrition and supplement use should be provided for holistic healthcare to people with endometriosis

wanting to fall pregnant.

Key words
Preconception, diet, supplements

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CHRONIC PELVIC PAIN AND DYSPAREUNIA IN ENDOMETRIOSIS PAIN THERAPY USING A NERVE AND MUSCLE STIMULATION DEVICE WITH BIOFEEDBACK FUNCTION

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Country where research was undertaken:
Germany

Introduction/Background
Endometriosis causes chronic lower abdominal pain (cLAP) and dyspareunia, with severe cLAP often leading to hypertonic pelvic muscles that worsen pain and quality of life[1]. Current treatments, including hormones and surgery, are often ineffective[2]. This study aims to reduce cLAP and improve quality of life using an electromyography biofeedback device.

Materials and Methods
In this prospective observational study, 201 women were given an intravaginal electromyography device for home use over three months with a recommended usage of up to eight times per week. Standardized questionnaires capturing typical endometriosis-associated pain using numerical rating scales, among others, were used. Pain scores were compared pre- and post-device application. In addition to the descriptive statistics, Wilcoxon signed-rank test for paired samples and linear regression analysis were performed.

Results
Of the 201 patients initially enrolled in the study, 108 completed it, while 93 withdrew. Patients' ages ranged from 16 to 51 years. Data analysis revealed that using electromyography devices significantly reduced pelvic floor pain ($n = 58$; $p < 0.001$) and pain during sexual intercourse ($n = 63$; $p < 0.001$) in patients with endometriosis. Additionally, those who used the electromyography biofeedback device more than three times per week experienced a greater reduction in pain during sexual intercourse ($B = 1.3$; 95% CI [0.06, 2.6]) compared to those who used it less than three times per week. However, no significant difference was observed for pelvic floor pain between the groups ($B = -0.99$; 95% CI [-2.51, 0.54]).

Conclusion
This evaluation suggests that electromyography devices used in endometriosis patients can be a promising addition to conventional therapy. The significant reduction in pelvic floor pain and dyspareunia indicates a notable improvement in myofascial functionality and may be associated with a decreased need for pain medication.

Key words
Pelvic floor dysfunction, endometriosis pain management, electromyography biofeedback device

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AIDEN-STUDY(I): THE EFFECT OF AN ANTI-INFLAMMATORY DIET INTERVENTION ON HEALTH-RELATED QUALITY OF LIFE AND PAIN SYMPTOMS IN PATIENTS WITH ENDOMETRIOSIS

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Country where research was undertaken:
The Netherlands

Introduction/Background
Inflammation is a key factor in the development, proliferation and symptoms of endometriosis. Nutritional factors are involved in modulating immune function. Therefore, an anti-inflammatory diet intervention (AIDEN-intervention) may improve immune function and reduce inflammation, leading to better health-related quality of life (HRQoL) and less pain symptoms in endometriosis.

Materials and Methods
In this prospective feasibility study, a 12-week predominantly plant-based diet, promoting the intake of anti-inflammatory foods while restricting pro-inflammatory foods was examined. Before and after the AIDEN-intervention, pain levels (Numeric Rating Scale (NRS)), HRQoL (Endometriosis Health Profile-30 (EHP-30), 36-Item Short-Form Survey (SF-36)) and diet adherence (Food Frequency Questionnaire (FFQ) Eetscore) were assessed. In addition, patients completed an evaluation form after the AIDEN-intervention. Evaluation of the immunologic changes after the AIDEN-intervention are described in abstract II.

Results
Eighteen patients completed the AIDEN-intervention, with sixteen filling out all questionnaires. Total FFQ Eetscore improved ($p = < 0.001$), rising from 106.3 to 141 on a 160-point scale. After the AIDEN-intervention an improvement was observed in pain levels (NRS): average pain level decreased from 5.7 to 4.0 ($p = 0.018$). For maximum pain level there was a decrease from 8.6 to 6.7 ($p = 0.012$). In addition, patients showed an improvement in HRQoL on the total ($p = 0.003$), as well as on all core subdomains ($p = 0.036 – p < 0.001$) of the EHP-30. For the SF-36, the Mental Component Summary (MCS) scale improved ($p = 0.019$) after the AIDEN-intervention. Overall, patients valued the AIDEN-intervention with a score of 8.3 out of 10.

Conclusion
Endometriosis patients who modify their diet by increasing the intake of vegetables, fruits, whole grains, legumes, nuts, dairy, fish, and healthy fats, and decreasing processed meats, sugary drinks, and unhealthy choices experience a decrease in pain levels and improvement in HRQoL. They evaluate the AIDEN-intervention as tasty, affordable, and feasible.

Key words
Anti-inflammatory diet, health related quality of life, pain

THE UNEXPLORED LIVED EXPERIENCE OF ENDOMETRIOSIS AND THE POTENTIAL FOR OCCUPATIONAL THERAPY: A SCOPING REVIEW

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Country where research was undertaken:
United Kingdom

Introduction/Background
Occupational therapists are allied health professionals, who aim to empower individuals to engage in daily activities which bring meaning and purpose to a person's life known as "occupations". This scoping review highlights the potential for occupational therapy to address the disruptions to daily life and activities experienced by those living with endometriosis.

Materials and Methods
To address the critical gap in research on the role of occupational therapy in managing endometriosis, a comprehensive scoping review based on the Arksey and O'Malley (2005) framework was conducted as part of a larger doctoral study. A systematic search of

Key words and terms was conducted through a database search of PUBMED, CINHAL, and PSYCHINFO (Ovid); grey literature, and hand searching occupational therapy/science journals.

Results
The search returned 5,445 results, which were screened for relevance based on the research question and inclusion/exclusion criteria. After removing duplicates, 332 articles were selected for full-text review, ultimately including 130 articles in the scoping review. Each article was charted and mapped to occupational therapy concepts and domains. Content analysis revealed three key themes: (1) endometriosis impacts a wide range of daily meaningful activities, or “occupations”; (2) endometriosis not only affects participation in occupation but also influences the meaning and choices individuals make regarding which occupations to engage in or avoid; and (3) existing research predominantly focuses on occupations like sex, work, and health management, while occupations such as social activities, leisure, parenting, and daily living tasks remain underrepresented in the literature.

Conclusion
This scoping review highlights how endometriosis impacts daily occupations, with limited research covering the full spectrum of daily life. It emphasizes the potential role of occupational therapy and the development of interventions to support endometriosis management, focusing on enhancing quality of life through engagement in meaningful daily activities.

Key words
Occupational therapy, daily life, allied health

Reference
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THEME: BEHAVIOURAL HEALTH, MEDICINE AND PSYCHOSOCIAL CONDITIONS

YOUNG PEOPLE’S MENSTRUAL KNOWLEDGE: PERCEIVED VERSE ACTUAL

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Country where research was undertaken:
Australia

Introduction/Background
The LongSTEPPP study examines young people's (YP) experiences with period and pelvic pain. Armour et al. (2021) found Australian YP can't identify abnormal menstrual symptoms and may avoid seeking medical advice. We compared perceived versus actual knowledge and explored how age and menarche may influence understanding.

Materials and Methods
We asked YP enrolled in the LongSTEPPP to rate their perceived knowledge on three topics periods, pelvic pain and endometriosis using a four-point scale via online questionnaires. We then asked 15 true false questions to ascertain their actual knowledge across the same three topics. Participants are surveyed on the same topics with some repeating and some new questions at yearly intervals.

Results
Questionnaires on menstrual health were answered by 217 participants aged 12-18 years, with a mean age of 15 years. Mean age of menarche was 11.5 years (range: 12-16). Sources of education included healthcare professionals (89%), mothers/primary female carers (84%), and social media (58%). Knowledge ranged from 40% to 93%, with an average of 73%. The largest knowledge gap was found in 13-14 year-olds, with an average period knowledge score of 55%. Those aged 15-18 years scored higher (68%) on average. YP with ≥2 years of menstruation experience reported greater perceived knowledge across all areas, while those with <2 years of experience had higher knowledge of pelvic pain (81%) and endometriosis (89%).

Conclusion
This study reveals young people overestimate their knowledge of periods while underestimating their understanding of pelvic pain and endometriosis. Primary sources of information were medical professionals and family members. Notably, general period knowledge showed the largest gap between perceived and actual knowledge, regardless of age or years of menstruation experience.

Key words
Knowledge, period, endometriosis

Reference
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THEME: BIOLOGICAL MECHANISMS

PARACRINE COMMUNICATION FROM OMENTAL ADIPOSE TISSUE TO ECTOPIC ENDOMETRIAL CELLS

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Country where research was undertaken:
United Kingdom

Introduction/Background
Epidemiological studies highlight an inverse correlation between Body Mass Index and endometriosis occurrence (1-3) and endometriosis rarely spreads through the omentum (4). A mechanistic link between adiposity and endometriosis has not been adequately assessed. This study aimed to uncover whether paracrine signaling from omental adipose tissue influences ectopic lesion development.

Materials and Methods
Human omental and endometriosis tissues were donated from consenting women undergoing surgical treatments for suspected endometriosis. Omental adipose tissue was incubated in pheno-red free media for 24-hours at 37°C, before conditioned media (OACM) was collected. Ectopic endometrial cells from endometriomas were isolated and cells were exposed to OACM from women with or without endometriosis. This was followed by colorimetric MTT assays, scratch assays and seahorse XF analysis to determine the metabolic impact of paracrine factors.

Results
MTTs tended to increase metabolism of cells exposed to omental adipose conditioned media from women with endometriosis. Despite this, further scratch assays showed a significant decrease in cell migration when cells were exposed to OACM, irrespective of disease status, compared to a vehicle control. The addition of mitomycin C increased time to close further, but only for cells exposed to OACM from women without endometriosis. Seahorse XF glycolysis stress tests are currently underway to determine whether a metabolic shift could be responsible for these outcomes. Reverse transcription qPCR shows a trend of lower PPARy expression in endometriosis patients' omental adipose tissue, compared to women without the disease. Further work will focus on determining levels of inflammatory cytokines in OACM.

Conclusion
Omental adipose conditioned media inhibits migration of ectopic endometrial cells, irrespective of disease status of the donor conditioned media. This may highlight a protective effect against endometriosis spread in the peritoneal cavity. Further studies are underway to identify the mechanism of action and may highlight treatment targets for endometriosis.

Key words
Paracrine, adipose, metabolism

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CAN WE MODEL ENDOMETRIAL BREAKDOWN AND REPAIR USING A MINIMALLY INVASIVE MODEL OF EARLY PREGNANCY LOSS IN MICE?

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Country where research was undertaken:
New Zealand

Introduction/Background
Current mouse models of menstruation are invasive, often requiring multiple injections and ovariectomy. The result of these models is a rapid and extensive break down of endometrial tissue. Our aim is to develop a minimally invasive mouse model of menstruation utilising the endometrial changes that occur in early murine pregnancy and subsequent miscarriage to use in studies of menstrual disorders including endometriosis.

Materials and Methods
Female mice (C57/B6) were mated and housed until gestational day (GD) 4.5 (day of embryo implantation) or 5.5. Miscarriage was then induced using the progesterone antagonist mifepristone (2 mg/kg). Mice were monitored for signs of vaginal bleeding and then culled between 6 and 48 hours after the mifepristone injection. Breakdown, bleeding and repair of the endometrium were assessed.

Results
Administration of mifepristone at GD 4.5 resulted in structural changes within the uterus; however, no vaginal bleeding was observed. At 12 hours, decidualised tissue was still present. By 6 hours, red blood cells (RBCs) were noted within decidual tissues, these persisted to 24 hours. Vaginal bleeding was noted in mice treated with mifepristone at GD5.5. All lavages after 24 hours were viscous, and cells clumped together. Onset of endometrial breakdown was noted from 36 hours as decidual cells began to lack definition and nuclear staining reduced. RBCs began to group around the embryo at this time also. Embryos were still present by 48 hours indicating the breakdown process occurs across several more days. We are currently extending tissue sampling to 120 hours post mifepristone.

Conclusion
We propose that menstrual-like endometrial breakdown and bleeding can be induced in mice by inducing early miscarriage. We postulate that this model will provide an invaluable method of investigating factors impacting endometrial breakdown and repair in a minimally invasive manner.

Key words
Menstruation, endometrium, mouse

THE ACTIVATED PERITONEAL IMMUNE ENVIRONMENT IN ENDOMETRIOSIS IS CHARACTERISED BY A LACK OF PD-1 INHIBITION

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Country where research was undertaken:
Australia

Introduction/Background
Endometriosis is characterised by chronic inflammation in the peritoneal cavity, largely explained by dysregulation within peritoneal fluid. The activation of peritoneal immune cells is unclear. A comparison with the status of the systemic immune system is desirable to

explore avenues of diagnosis and treatment of endometriosis-related inflammation and pain.

Materials and Methods
This was an observational study in patients undergoing laparoscopy for diagnosis or treatment of peritoneal endometriosis or for unrelated conditions; PF was collected from n=7 endometriosis patients and n=8 controls, blood from n=6 endometriosis patients and n=7 controls. Data were analysed for statistical significance using ANOVA, the Kruskal-Wallis or Mann-Whitney U test, with a p-value below 0.05 considered significant.

Results
We observed a prevailing of myeloid immune cells in the peritoneal fluid as opposed to lymphoid cells in the blood. The main differences between endometriosis and control samples, however, were found in the smaller compartments, i.e., in lymphoid populations in peritoneal fluid and myeloid populations in blood. PD-1 levels in peritoneal fluid endometriosis samples were significantly lower than in controls ($p<0.05$), suggesting an impaired regulatory mechanism within the local immune environment.

Conclusion
These findings highlight distinct immune signatures in endometriosis patients' peritoneal and systemic compartments. The immune checkpoint PD-1 could be a new angle of treating endometriosis-related inflammation and pain in women suffering from this chronic and intractable condition.

Key words
Immune checkpoint, activation, inflammation

LINC01638 PROMOTES EPITHELIAL-TO-MESENCHYMAL TRANSITION IN ENDOMETRIOSIS EPITHELIAL CELLS BY UPREGULATING RHOB VIA HDAC1 SUPPRESSION.

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Country where research was undertaken:
Austria

Introduction/Background
LINC01638 is a long non-coding RNA (lncRNA) that in several cancers has been implicated in the regulation of proliferation and epithelial-to-mesenchymal transition (EMT). Given that these processes are also important in endometriosis, we investigated the role of *LINC01638* in this disease.

Materials and Methods
We combined expression and localization studies in patient eutopic and ectopic endometrium with functional experiments in the 12Z endometriosis epithelial cell line to investigate the role of *LINC01638* in endometriosis. We assessed the phenotype following *LINC01638* knockdown, performing proliferation, adhesion, migration and invasion assays, as well as assessing apoptosis and cell cycle changes with flow cytometry assays. To assess the relationship between *LINC01638* and HDAC1 we combined *LINC01638* knockdown with HDAC inhibition with romidepsin.

Results
We found that *LINC01638* is upregulated in the epithelial layer of endometriosis lesions, and that *LINC01638* knockdown in 12Z cells led to reduced proliferation, adhesion, migration and invasion. The reduction in proliferation was associated with increased p21 and p27 expression and G1 phase arrest. Further analysis of *LINC01638* control and knockdown cells revealed that a number of transcription factors associated with EMT are downregulated in the knockdown along with the cytoskeleton regulatory gene RHOB, while HDAC1 was upregulated. Chromatin immunoprecipitation analysis and HDAC1 inhibitory treatment combined with *LINC01638* knockdown indicated that *LINC01638* regulates *RHOB* expression via HDAC1 mediated promoter deacetylation. RHOB is upregulated in the epithelial layer of endometriosis lesions compared to the eutopic endometrium supporting a role in the disease.

Conclusion
These results indicate that *LINC01638* is an epigenetic regulator of pathogenesis of endometriosis promoting proliferation and EMT of endometriosis lesions.

Key words
EMT, RHOB, HDAC1

THEME: CLINICAL MANAGEMENT

BARRIERS TO CARE FOR TRANSGENDER AND GENDER DIVERSE PEOPLE WITH ENDOMETRIOSIS; GAPS IN AUSTRALIAN AND AOTEAROA HEALTH CARE PROVIDER CURRICULUM

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Country where research was undertaken:
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Introduction/Background
Trans people are disproportionately impacted by chronic pelvic pain and endometriosis [1], yet lack access to gender affirming gynaecological care [2, 3]. Little attention has been paid to the inclusion of trans health in Australian medical curriculum, despite those living in Australia reporting poor access to gender affirming healthcare.

Materials and Methods
This commentary was constructed using the conceptual frameworks of queer theory and intersectionality theory and reviews the research literature on the state of gender inclusive education in Australia. We explore the barriers and enablers to the inclusion of trans health in curriculum, provide examples of successful curricular interventions and strategies for change globally, and outline a series of recommendations for increasing gender affirming content moving forward.

Results
Research broadly assessing the inclusion of LGBTQIA+ content finds no teaching of LGBTQIA+ health amongst 55% of preclinical and 89% of clinical students [4]. Of this content, trans health was amongst the least covered sub-topics [4, 5]. Barriers to teaching gender affirming care included a lack of national guidelines, institutional barriers, time constraints in curriculum and a lack of gender inclusive educational materials [6-9]. Our finding emphasised the importance of a curriculum that addresses the intersecting needs of trans First Nations people [10], educates faculty on gender affirming care [11, 12], integrates trans health content throughout mandatory curriculum [11], includes the basics of gender affirming care and gender affirming gynaecological care in graduate learning outcomes and reduces student biases by centering lived experience and avoiding the pathologising of trans medical care [13, 14].

Conclusion
Poor inclusion of gender affirming care in Australian medical curriculum contributes to trans and gender diverse people's poor access to gynaecological care, potentially resulting in longer delays and delayed treatment for endometriosis. A thorough curriculum assessment and curriculum reform is urgently required to ensure equitable healthcare for those with endometriosis.

Key words
Transgender, gynaecology, curriculum

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USE OF UNOPPOSED OESTROGEN MENOPAUSE HORMONE THERAPY (MHT) IN MENOPAUSAL WOMEN POST HYSTERECTOMY WITH A HISTORY OF ENDOMETRIOSIS: LITERATURE REVIEW

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Country where research was undertaken: Australia

Introduction/Background
There is growing evidence of the malignant potential of endometriosis, with endometriotic lesions having a 1% risk of malignant transformation (1,2). The effect of MHT on the malignant transformation of postmenopausal endometriosis, in particular in women who have had a hysterectomy is important to understanding how to treat these women.

Materials and Methods
Objective: To investigate the risk of developing ovarian cancer in hysterectomised endometriosis patients who have been treated with MHT. A literature review will be performed of the current evidence in Pubmed, Cochrane and relevant guidelines.

Results
Recent evidence suggests increased risk of clear cell and endometrioid cancer in women who have used estrogen alone MHT in hysterectomized women. Lee et al[3] performed a nationwide cohort study of post-menopausal women with de novo endometriosis or a history of endometriosis. They determined that use of estrogen only MHT was a significant risk factor of ovarian cancer. Khoja et al[4] evaluated the association between hysterectomy and ovarian cancer, and the role of MHT use and endometriosis. In women with endometriosis, slight inverse association between hysterectomy and ovarian cancer risk, especially after adjusting for duration of MHT use. The ESHRE endometriosis guidelines[5] from 2022 recommended combined MHT for the treatment of postmenopausal symptoms due to the higher risk of malignant transformation.

Conclusion
MHT but not estrogen alone, can be used to improve post-menopausal symptoms in women with endometriosis. Current literature highlights the importance of clinician education as to whether to recommend hysterectomy when considering the risk of ovarian cancer in patients with endometriosis.

Key words
Ovarian cancer, endometriosis, hysterectomy

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CLINICAL EFFECTS OF PULSED ELECTROMAGNETIC FIELD (PEMF) STIMULATION IN PATIENTS WITH ENDOMETRIOSIS: A RANDOMIZED CONTROLLED DOUBLE-BLIND PILOT STUDY

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Country where research was undertaken:
Germany

Introduction/Background
Endometriosis causes chronic pain and inflammation, often limiting the quality of life. Traditional treatments like hormones and surgery can be inadequate. This pilot study examines pulsed electromagnetic field (PEMF) therapy with the Oska Pulse device as a complementary treatment to relieve symptoms and improve life quality for endometriosis patients.

Materials and Methods
This randomized, double-blind, controlled study examines the effects of daily PEMF therapy over 84 days. Patients with proven endometriosis and ongoing chronic acyclical pelvic pain were invited to participate, and randomly assigned to either an intervention group (PEMF stimulation) or a control group (sham stimulation) in a 3:1 ratio. PEMF device is applied near the affected area for two sessions of three hours daily. Participants track symptom's severity, analgesic use, and any adverse events using questionnaires.

Results
Out of the 20 participants enrolled in the study, 10 dropped out due to scheduling conflicts and participation in other studies, and 2 did not complete the final questionnaire yet. Our preliminary results showed a significant main effect of the VAS scores (pain levels before and after treatment) on the outcome, with an F-value of 8.100 (df = 1, 6) and p = 0.029, resulting in a large effect size ($\eta^2 = 0.574$). However, the interaction between VAS scores and treatment type (PEMF stimulation versus control) was not significant, with an F-value of 0.225 (df = 1, 6) and p = 0.652 ($\eta^2 = 0.036$). This indicates that the impact of VAS scores did not differ between the treatment groups.

Conclusion
Preliminary results indicate a significant reduction in pain, measured by VAS scores, over time with PEMF therapy. However, this reduction did not differ between the PEMF stimulation and control group. More analysis is needed to determine if PEMF provides specific pain management benefits for endometriosis.

Key words
PEMF, endometriosis, pain relief

INFECTED ENDOMETRIOMAS – ACUTE AND LONG-TERM MANAGEMENT

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Country where research was undertaken:
Singapore

Introduction/Background
Infected endometrioma is a special subgroup of pelvic infections, having a different epidemiology and pathophysiology[1,2,3], and yet may be difficult to distinguish from routine pelvic inflammatory disease (PID)[4]. Optimal management remains unknown[3]. We present a series of 10 cases of infected endometrioma including clinical progress and eventual

outcomes.

Materials and Methods
10 cases of infected endometriomas were prospectively recruited at a tertiary university hospital over 10 months (January to October 2023). Blood cultures and vaginal swabs - for cultures and sexually transmitted infection (STI) testing – were collected prior to intravenous antibiotics. Cases that failed antibiotic therapy underwent drainage and the endometriotic fluid sent for cultures. All cases were offered hormonal suppression immediately after acute episode paired with definitive surgery at >2 months interval.

Results
All cases presented via emergency department with fever, pelvi-abdominal pain. Ultrasound imaging demonstrated endometriomas. Following a trial of intravenous broad spectrum antibiotics; 2 failed to respond and underwent drainage (1 transvaginal, 1 transabdominal). Blood and vaginal cultures were negative in all cases while STI testing yielded only 1 positive for Trichomonas vaginalis. Drainage cultures returned positive for Hemophilus influenzae and Peptoniphilus. The median age was 40 years. Half were nulliparous. None had prior STIs, recent pelvic instrumentation, obesity or immunocompromise. Only 6/10 cases had preceding diagnoses of endometriosis, Subsequently, 9/10 agreed for hormonal suppression and 8/10 cases underwent definitive surgery with visual and histopathological confirmation of endometriosis; 2 declined surgery. No recurrence of infection or endometriosis was present at 1 year post-operatively.

Conclusion
Infected endometriomas may affect older, nulliparous women lacking traditional risk factors for PID e.g. STIs or prior instrumentation[1,2]. Careful history, examination and targeted ultrasound[5] is required. Antibiotics should cover gut flora and anaerobes, with early drainage considered for culture-directed therapy. Hormonal suppression and definitive surgery are essential in preventing relapse.

Key words
Tubo-ovarian abscess, endometrioma, pelvic inflammatory disease

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MALIGNANT TRANSFORMATION OF URINARY BLADDER ENDOMETRIOSIS

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Country where research was undertaken:
Sweden

Introduction/Background
Deep endometriosis of the urinary bladder is rare, affecting approximately 0.5% of women with symptoms suggestive of endometriosis. Malignant transformation of bladder endometriosis is an uncommon and manifests as endometroid or clear-cell carcinoma.

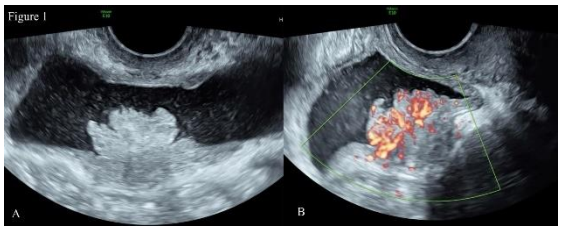
Materials and Methods
This is a case report of a 47-year-old woman with history of laparoscopy because of endometrioma, hematuria during menstruation, and bladder endometriosis found at transvaginal ultrasound examination

in 2010. In 2023, due to persistent hematuria for three months and heavy menstrual bleeding, she consulted urologists and underwent computer tomographic urography. Exophytic tumor in the urinary bladder of 42x20x26mm was detected, suspected connection to the uterus. Cystoscopy showed a 3 cm tumor, non-typical for urothelial tumor.

Results
Gynecological ultrasound examination showed heterogenous richly vascularized tumor in the urinary bladder of 30x29x23 mm with connection but not overgrowth to the uterus (Figure 1a,b). Additional findings were left endometrioma (30x20x23mm), deep endometriosis in the bowel (rectosigmoideum 18x8x14 mm and sigmoideum 18x4x9 mm), and adhesions. Magnetic resonance imaging showed a tumor deep in the urinary bladder wall, with clear border between the uterus and urinary bladder. Multidisciplinary conference proposed the possibility of a tumor arising in an endometriosis lesion in the bladder. The woman underwent hysterectomy, bilateral salpingoophorectomy, partial cystectomy including the tumor, omentectomy and appendectomy. Histological examination confirmed endometroid carcinoma (FIGO grade 1) in the bladder with underlying endometriosis as well as findings of endometriosis in the left ovary, omentum and appendix.

Conclusion
In this case malignant transformation occurred in a lesion of deep endometriosis in the bladder known for 14 years, being investigated because of hematuria. Malignant transformation of deep endometriosis is rare and patient history can be helpful in the diagnosis. Multidisciplinary approach in patient managing is recommended.

Key words
Malignant transformation; deep endometriosis; urinary bladder endometriosis.



CARDIOVASCULAR RISK ASSESSMENT, CAROTID AND FEMORAL ARTERY INTIMA-MEDIA THICKNESS IN WOMEN WITH ENDOMETRIOSIS BEFORE SURGERY AND 6 MONTHS AFTER SURGERY

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Country where research was undertaken:
Turkey

Introduction/Background
Studies revealed subclinical atherosclerosis in endometriosis patients due to endothelial dysfunction related to chronic inflammation (1). However, the effect of surgical removal of endometriosis on cardiovascular disease (CVD) risk remains unclear. We investigated CVD markers, carotid, and femoral artery Doppler ultrasounds in endometriosis patients before and 6 months after surgery.

Materials and Methods
This prospective longitudinal study included women with endometriosis (n=52) and women without endometriosis (n=52). All subjects underwent surgery for suspected benign gynecological disorder. Fasting blood samples were taken for biochemical CVD risk markers. Baseline and exercise ECG tests were performed. Before surgery, all subjects were assessed for measurement of common carotid artery intima-media thickness (IMT) and femoral artery (IMT). Moreover, endometriosis patients were measured for carotid and femoral artery IMT 6 months after surgery.

Results
The mean age of the patients was 37.96±7.675 years in the endometriosis group and 39.69±7.048 years in the control group (p=0.237). Baseline and exercise ECG tests were normal for all participants. Before surgery, the mean carotid artery (IMT) (mm) was not significantly different between the endometriosis (0.619±0.4424) and control groups (0.606±0.1178) (p=0.833). In contrast, the mean femoral artery IMT (mm) was significantly higher in endometriosis patients (0.871±1.7625) than those in the control group (0.802±0.9138) (p=0.03). No significant difference was observed in the mean carotid and femoral artery IMT between the baseline and 6-months after surgery in the endometriosis group (p=0.480 and p=0.381, respectively). The mean femoral artery IMT was positively correlated with triglyceride (r=0.269; p=0.006) and negatively correlated with HDL-cholesterol (r=-0.240; p=0.014)

Conclusion
The present study documented increased femoral artery intima-media thickening in women with endometriosis compared to the normal controls,indicating subclinical atherosclerosis without overt cardiovascular disease. However, the surgical removal of endometriosis had no effect on the mean carotid and femoral artery IMT 6 months after the surgery, compared to the baseline.

Key words
Endometriosis, cardiovascular disease, intima media thickness

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ANTIBIOTICS REDUCE ENDOMETRIOSIS PROGRESSION, POSSIBLY BY GUT MICROBIOME AND INFLAMMATORY REACTIONS: A SYSTEMATIC REVIEW OF IN-VITRO, IN-VIVO AND CLINICAL STUDIES.

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Country where research was undertaken:
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Introduction
Endometriosis is a gynaecological condition with no definitive treatment options. Recent studies have highlighted changes in the gut microbiome and inflammatory reactions contribute to its pathogenesis. However, the effect of antibiotic treatment on altering gut microbiome and inflammatory responses and their impact on the sequel of endometriosis remain largely unknown.

Materials and Methods
PubMed, Embase, Scopus, and Web of Science databases were thoroughly searched. This systematic review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Data were extracted using customized Microsoft Excel sheets. We included in vitro, in vivo and clinical studies published in English until October 30, 2024. SYRCLE's RoB, QUIN and ROBINS-I tools were used to evaluate the risk of bias for in-vivo, in-vitro and clinical studies respectively.

Results
This systematic review demonstrated that using antibiotics to treat endometriosis significantly reduces *Gardnerella, Prevotella, Acidibactor, Atopobium in clinical study and Fusobacterium nucleatum in vivo study.* Additionally, in vivo, in vitro, and clinical studies showed that antibiotic treatment exhibited significantly smaller endometriotic lesions with fewer proliferating cells. These antibiotics, including chloramphenicol, vancomycin, doxycycline, macrolides, metronidazole, levofloxacin, ampicillin and ornidazole, were shown to decrease the abundance of bacteria, reduce the size and microvessel density of endometriotic lesions, and suppress inflammatory markers such as interleukins (IL-6, IL-1β), vascular endothelial growth factor (VEGF), matrix metalloproteinases (MMP2 and MMP9), M2 macrophage infiltration, tumor necrosis factor (TNF-α), and transforming growth factor-beta (TGF-β1), indicating their crucial role in mitigating the progression of endometriosis by targeting inflammation and angiogenesis pathways.

Conclusion
Treatment with antibiotics restricts the development of endometriosis, possibly by targeting gut bacteria via immune cell adaptations, suppressing inflammatory and

angiogenesis effects. Given the difference between human and animal microbiomes, clinical studies are urgently needed to examine the efficacy and safety of antibiotics as a potential treatment strategy for endometriosis.

Key words
Endometriosis, microbiome, antibiotics

KIDNEY LOSS DUE TO DEEP ENDOMETRIOSIS - STILL A SERIOUS HEALTH PROBLEM

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Country where research was undertaken:
Czech Republic

Introduction/Background
Deep endometriosis is a severe form of endometriosis that can lead to significant complications, including ureteral stenosis and subsequent kidney loss. It is estimated that deep endometriosis affects the urinary system in approximately 1-2% of all endometriosis cases, with the ureters being involved in about 0.1-0.4% of cases. This involvement can lead to ureteral obstruction, hydronephrosis, and ultimately, loss of kidney function if not diagnosed and treated promptly. This study aims to highlight the ongoing health issue of kidney loss due to late diagnosis and treatment of deep endometriosis.

Materials and Methods
We conducted a retrospective analysis of prospective follow-up data from 71 patients who underwent surgery for ureteral stenosis caused by deep endometriosis. The patient cohort primarily consisted of women of fertile age, although 6 patients were older than 45 years. The age range of the patients was from 21 to 52 years. The primary outcome measured was the incidence of nephrectomy due to complete renal function loss.

Results
Out of the 71 patients, 10 (14.1%) required nephrectomy due to irreversible kidney damage. The high rate of nephrectomy underscores the critical need for early diagnosis and intervention in patients with deep endometriosis to prevent severe renal complications.

Conclusion
Kidney loss due to deep endometriosis remains a significant health problem, primarily driven by delayed diagnosis. Despite our efforts to raise awareness and inform not only the medical community, this issue persists. This study emphasizes the importance of early detection and timely surgical intervention to preserve renal function and improve patient outcomes.

Key words
Deep endmetriosis, ureter, nephrectomy

ACUTE PRESENTATION OF PERSISTENT PELVIC PAIN: A CLINICAL GUIDELINE

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Country where research was undertaken:
Australia

Introduction/Background
The management of acute episodes of persistent pelvic pain (PPP) presents a significant challenge in emergency departments (EDs). Queensland Clinical Guidelines have developed what is believed to be the first Australian clinical guideline aimed to provide evidence-based and trauma-informed approaches for the assessment and management of women presenting with acute pelvic pain exacerbations in the context of known PPP.

Materials and Methods
A comprehensive literature review focusing on the assessment and management of acute pelvic pain in women with known PPP was conducted along with a review of clinical guidelines developed by other reputable groups relevant to the clinical specialty. Stakeholder consultations ensured the guideline's applicability across Queensland public and private health facilities.

Results
The guideline emphasises a trauma-informed and culturally safe approach using a

biopsychosocial framework for assessing acute pelvic pain exacerbations. Key goals include validating the patient's pain experience and responding empathetically while avoiding unnecessary admissions and invasive procedures. Clinicians should confirm symptoms are consistent with a flare of PPP and identify potential pain contributors and triggers. Appropriate analgesia should be provided while minimising opioid use. Red flag symptoms indicating acute pathology, such as appendicitis or ectopic pregnancy, must be assessed to exclude serious conditions. For patients with repeated presentations, communication with primary care providers is essential, considering visit frequency and encouraging attendance at routine scheduled outpatient appointments. Early introduction of pain mechanisms is advised, alongside recommendations for ongoing support services to enhance care continuity.

Conclusion
These guidelines aim to enhance the quality of care for women presenting with acute episodes of PPP in ED's thereby improving patient outcomes and streamlining care processes within Queensland's healthcare facilities.

Key words
Pelvic pain, guideline, emergency care

CLINICAL SIGNIFICANCE OF BONE TURNOVER BIOMARKERS IN LONG-TERM PHARMACOTHERAPY FOR ENDOMETRIOSIS

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Country where research was undertaken:
China

Introduction/Background
Prolonged gonadotropin-releasing hormone agonist (GnRH-a) therapy (>6 months) in endometriosis patients may induce bone density alterations, thereby increasing the risk of osteoporosis. However, there is limited knowledge on metabolic abnormalities that could serve as early warning indicators prior to changes in bone density.

Materials and Methods
Fifty patients with stage III-IV endometriomas were enrolled and received three cycles of GnRH-a postoperatively, followed by DNG maintenance. Estradiol (E2), follicle-stimulating hormone (FSH), β-C-terminal telopeptide (β-CTX), N-terminal propeptide of type I procollagen (P1NP), and osteocalcin (OC) were measured at baseline, 4, 8, and 12 weeks after GnRH-a, and 3 months after DNG. Menopausal symptoms and dysmenorrhea were assessed. 30 healthy women served as control group whose parameters were evaluated on cycle days 1-3.

Results
After 4, 8, and 12 weeks of GnRH-a treatment, the modified Kupperman score increased, E2 levels decreased, and β-CTX, P1NP, and OC levels rose. At 12 weeks, E2 was (12.80±6.92) pg/ml, while β-CTX, P1NP, and OC were (516.64±234.88) pg/ml, (39.77±10.51) ng/ml, and (16.31±4.10) ng/ml, respectively ($P<0.01$). Following 3 months of DNG, the modified Kupperman score decreased, and E2 rose to (41.29±28.69) pg/ml. β-CTX, P1NP, and OC decreased to (332.22±157.65) pg/ml, (32.26±5.75) ng/ml, and (12.69±2.26) ng/ml, respectively ($P<0.01$). Bone turnover marker differences were not statistically significant ($P>0.05$), despite E2 levels being lower than baseline. E2 correlated negatively with bone markers ($P<0.05$) and the Kupperman score ($R=-0.608$, $P<0.001$), and positively with VAS ($R=0.804$, $P<0.001$).

Conclusion
Reducing E2 levels below a specific threshold in endometriosis patients can worsen perimenopausal symptoms and increase bone turnover biomarkers. Therefore, monitoring E2 and bone turnover markers during long-term pharmacotherapy for endometriosis is beneficial for disease management and may allow for early prediction of osteoporosis development.

Keywords
Endometriosis, gonadotropin-releasing hormone agonist (GnRH-a), bone turnover biomarkers

THEME: DIAGNOSIS OF ENDOMETRIOSIS

EFFECT OF TWO DIFFERENT TYPES OF ENDOMETRIOSIS (OMA AND DIE) AND THEIR SURGERY ON OVARIAN RESERVE: A LARGE SINGLE-CENTER, CROSS-SECTIONAL STUDY

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Country where research was undertaken:
Iran

Purpose
Hence, there is scarce and no reliable data or evidence-based protocol for the management of DIE (deep infiltrating endometriosis) lesions in reproductive age women, in this study we examined ovarian reserve in endometriosis surgeries to aid in decision-making for surgery and fertility preservation.

Material and methods
This prospective single-center case-control study included 508 women who underwent laparoscopic endometriosis surgery in three groups (OMA (n=156), OMA+ DIE (n=235), and DIE (n=117)), from June 2018 to December 2022. Their AMH levels were compared to 50 healthy controls before surgery and at 3, 6 months post-surgery.

Results
The DIE group had lower baseline AMH levels compared to other groups. ($P < 0.0001$) Following surgery, AMH levels decreased notably across all groups. ($P < 0.0001$) Reductions in AMH levels after surgery were as follows: OMA group 49.84%, DIE+OMA group 62.20%, DIE group 43.46%, with the most substantial decline observed in the DIE+OMA group. There was no significant difference in AMH levels between 3 and 6 months post-surgery.

Conclusion
According to this study, the presence of DIE lesions alone, which are often overlooked in clinical and ultrasound examinations, such as the presence of OMAs, significantly impacts the reduction of ovarian reserve in affected women.

Key words
Endometriosis, Infertility, anti-mullerian hormone

INVESTIGATING UNILATERAL OVARIAN ENDOMETRIOMA'S EFFECT ON OVA AND EMBRYO QUALITY IN 409 INFERTILE ENDOMETRIOTIC PATIENTS

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Country where research was undertaken:
Iran

Introduction/Background
This document investigates the impact of unilateral ovarian endometrioma on the quality and quantity of oocytes and embryos in a study involving 409 infertile patients diagnosed with endometriosis. The findings are significant for understanding the implications of endometriosis in reproductive health.

Materials and Methods
This prospective study, conducted from March 2022 to March 2024 at Shiraz University of Medical Sciences, examined infertility outcomes in patients with unilateral endometriomas, focusing on reproductive parameters (Total follicles, Total oocyte, GV, MI, MII, Total embryo, Grade A embryos, Grade B embryos, Grade C embryos). Following strict inclusion and exclusion criteria, the research analyzed oocyte and embryo quality and quantity from affected ovaries, considering factors like endometrioma size and AMH levels, and compared these parameters to the contralateral healthy ovary.

Results
This study analyzed ovum pickups and ART outcomes in 409 women with unilateral ovarian endometriosis, revealing critical insights into reproductive performance. Participants had an average age of 33.55 years and a basal AMH level of 2.26 ng/dl, categorized into poor (25.2%), normal (57.2%), and high (17.6%) responders based on their AMH levels. Comparison of outcomes showed that healthy ovaries yielded significantly more MII oocytes, total embryos, and grade C embryos than affected ovaries, although no significant differences were found across various endometrioma sizes regarding follicular development and egg/embryo quality ($P>0.05$). Notably, the good responder group outperformed others in terms of GV oocytes, MII oocytes, and total embryos retrieved. Ultimately, among 40 embryo transfers conducted, 21 resulted in successful pregnancies (52.5%).

Conclusion
Endometriomas lead to fewer M2, total number of embryos. However, embryo quality remain unchanged. Future studies should compare ART outcomes in operated and non-operated ovaries and assess deep infiltrating

THE ASSOCIATION BETWEEN ULTRASOUND-DETECTED ENDOMETRIOMA AND OTHER ULTRASOUND FINDINGS

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Country where research was undertaken:
Israel

Introduction:
While few previous studies explored the correlation between endometrioma and surgical findings, the association between ultrasound-detected endometrioma (UDE) and additional imaging findings remains understudied. Hence, we aimed to assess the association between various UDE characteristics and concurrent ultrasound findings, providing insights that may enhance diagnostic precision and treatment planning.

Methods:
A retrospective study at an endometriosis unit including women with an UDE between 2019-2023. We first explored frequencies of other ultrasound findings (adhesions, Pouch of Douglas (POD) obliteration and bowel lesions, uterosacral ligaments (USL) lesions, bladder lesions and adenomyosis) in the presence of an UDE. We then compared the presence of these findings according to UDE size (<4cm vs ≥4cm) and laterality (unilateral vs bilateral). Various demographic and clinical factors were compared between groups.

Results
A total of 102 women were included in the study. Mean age was 33±**6.9** years. Of the entire cohort, 35.3% (n=36) had bowel involvement or POD obliteration, 39.2% (n=40) had deep USL lesions, 53.9% (n=55) had pelvic adhesions and 23.5% (n=24) had adenomyosis. Women with bilateral endometriomas were more likely to have endometriomas≥ 4cm, as compared to unilateral endometriomas (44% vs 16%, P<0.003). Deep USL lesions were more common in women with endometriomas >4cm, as compared to smaller endometriomas (62.5% vs 32.5%, respectively, p=0.03). Other ultrasound findings did not differ between groups. Women with bilateral endometriomas were more likely to have ultrasound-detected POD obliteration or bowel lesions (52.2% vs 47.8%, p=0.05), deep USL lesions (68.2% vs 27.3%, p=0.008) and pelvic adhesions (73.9.9% vs 26.1%, (p=0.03).

Conclusions:
Women with endometriomas larger than 4 cm and women with bilateral endometriomas are more likely to have additional imaging findings, suggesting more severe disease. Our findings may warrant referral of women with ultrasound detected endometriomas to expert imaging (endometriosis-dedicated ultrasound or MRI) to aid treatment decision and planning.

Key words
Endometrioma, ultrasound

ASSESSING THE UTILITY OF PERIOD IMPACT AND PAIN ASSESSMENT (PIPPA) SCREENING TOOL IN YOUNG MENSTRUATING WOMEN IN BENIN CITY, NIGERIA

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Country where research was undertaken:
Nigeria

Introduction and background
Endometriosis is a menstrual cycle dependent chronic inflammatory condition characterized by significant delays in diagnosis. Prompt assessment of menstrual morbidities could

improve diagnostic delays. Our study seeks to assess the utility of the Period ImPact and Pain Assessment (PIPPA) tool in triaging at risk young menstruating Nigerian women to an endometriosis ultrasound.

Materials and Methods
A survey was conducted among 330 female undergraduates at the University of Benin, Nigeria using a questionnaire adapted from the Menstrual disorder of teenagers (MDOT) questionnaire[1]. The degree of menstrual morbidities was generated using the Period Impact and Pain Assessment (PIPPA) screening tool for menstrual morbidity[1]. Respondents with PIPPA score 3 - 5 had significant menstrual morbidity, PIPPA Score 1-2 had minimal and PIPPA score 0 had no menstrual morbidity. Data were analyzed with univariate and multinomial logistic regression.

Results
Among the 330 participants, the most frequent symptoms associated with menstruation were feeling generally unwell, menorrhagia, pelvic pain, and lifestyle disorders. Using the PIPPA screening tool for menstrual morbidity, 53 (16.1%) reported no menstrual morbidity, 246 (74.6%) reported minimal menstrual morbidity and 31 (9.4%) showed significant menstrual morbidity. Results of multinomial logistic regression showed that women who report bloating, lower back pain, aching outside the vagina, family member with period problems and fatigue during menstruation were at greater odds of significant menstrual morbidity. By contrast, those experiencing diarrhea/constipation, and stabbing pelvic pain at least once experienced minimal menstrual morbidity.

Conclusion
The PIPPA screening tool may be effective in identifying young Nigerian women with menstrual morbidities and facilitating their early referral for an endometriosis assessment using ultrasound. However, further studies are needed to assess how sonologic features of endometriosis in respondents with significant menstrual morbidity compare to those with minimal morbidity.

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GLOBAL TRENDS IN UPTAKE OF SPECIALIST DIAGNOSTIC ULTRASOUND AND MRI SCANS FOR ENDOMETRIOSIS

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Countries where research was undertaken:
Australia/International

Introduction/Background
New methods of identifying endometriosis using transvaginal ultrasound and MRI are recognised by ESHRE, NICE and RANZCOG as a non-invasive way of identifying lesions, although they are not able to exclude endometriosis. It is unclear how these different imaging modalities are being used across different jurisdictions around the world.

Materials and Methods
Hosted by FIGO, an online survey was advertised via social media channels by key opinion leaders in endometriosis imaging. We aimed to determine where specialised endometriosis scans are used, find out the professional groups that are performing the scans and any barriers to their use. This will provide an accurate picture of any change in clinical practice specialist endometriosis scanning has made, and areas where further skill acquisition or resources may be needed.

Results
Clinicians from 77 countries elicited a total of 446 responses, with 361 (80.6%) of participants completing the survey in full. When asked how widespread imaging was in the diagnosis of endometriosis, 37.2% said it was “broadly used”, 54.7% of respondents stated they were “confident” in distinguishing between routine and specialist endometriosis ultrasounds and MRIs, 67.7% of respondents said that in their country they had gynaecologists that could undertake specialist endometriosis ultrasounds, but only 10% of respondents said that 100% of clinicians did use imaging in the diagnosis of endometriosis. The main method of diagnosis was “ultrasound” at 71.3% followed by “MRI” at 37.4%. Other information regarding qualifications, specialization, main clinician group for endometriosis diagnosis, main method place of practice and barriers to

imaging.

Conclusion
Diagnostic imaging for endometriosis is clearly a topic of interest across many different countries. Different models of practice have evolved from preferences of clinicians in each jurisdiction. As imaging skills and evidence increases, with established guidelines, we may continue to see an uptake of imaging as the preferred diagnostic.

Key words
Diagnosis, ultrasound, magnetic resonance imaging

DECREASING THE NEGATIVE LAPAROSCOPY RATE FOR PELVIC PAIN: SPECIALIST VERSUS GENERALIST TRAINED ENDOSCOPISTS. THE AUSTRALIAN PUBLIC AND PRIVATE HEALTHCARE SECTORS.

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Country where research was undertaken:
Australia

Introduction/Background
Systematic reduction of negative laparoscopy is crucial to reducing surgical morbidity and minimising healthcare costs, balanced with diagnostic accuracy. The aim of this study is to determine the rate of negative laparoscopy in women presenting with symptoms of pelvic pain and qualitatively assess variations in practice across healthcare providers.

Materials and Methods
A 5-year, multicentre, retrospective cohort study was undertaken for women undergoing laparoscopy for pelvic pain. Recruitment was from one public hospital and one private clinic with demographic data, symptoms and histology collected from the medical records. A 'negative' laparoscopy was defined by visual inspection only, or vision and a negative biopsy on histology. The endometriosis detection rate in the public and private sector was compared using the two sample two tailed Z test of proportions.

Results
Of 1309 eligible women, 174 (13%) had a negative laparoscopy. Dysmenorrhoea was the presenting symptom in 85/174 (49%) and 91/174 (52%) women were not using hormonal treatment prior to surgery. Negative laparoscopy in the private sector 26/442 (6%) was significantly lower than the public sector 148/867 (17%) $p<0.05$.

Visually negative laparoscopy was made in 48/174 (28%) of cases, all from the public sector, with 41/48 (85%) of laparoscopies without biopsy performed by general gynaecologists. This was significantly higher than the 7/48 (14%) women who did not have biopsies taken by fellowship trained laparoscopists ($p<0.05$). Endo-gynaecologists in the combined public and private sectors had a significantly lower negative laparoscopy rate of 87/897 (9.7%), compared with 87/412 (21%) for general gynaecologists ($p<0.05$).

Conclusion
Overall, negative laparoscopy rates are low. Negative laparoscopy discrepancy rates in the public/private sectors are likely related to patient factors (e.g., sociodemographic), clinician bias and training. Superficial endometriosis may be missed by not taking biopsies at time of laparoscopy. Peritoneal biopsy for all symptomatic patients undergoing laparoscopy should be considered.

Key words
Endometriosis, laparoscopy, detection

COMPARISON OF ENDOMETRIOSIS SEVERITY BETWEEN PATIENTS DIAGNOSED INCIDENTALLY AND THOSE DIAGNOSED AFTER SYMPTOM AWARENESS

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Country where research was undertaken:
Japan

Introduction/Background
Endometriosis is sometimes detected incidentally during medical examinations or health checks, which may lead to comparatively early diagnosis. However, it is not yet clear whether there is a difference in endometriosis severity between these patients and patients diagnosed after becoming aware

of symptoms.

Materials and Methods
The study included 24 patients in an incidental group, in whom endometriosis was detected incidentally via transvaginal ultrasound performed during gynecological examinations co-conducted with annual cervical cancer screening, examination of other diseases, or elevated tumor markers. It also included 42 patients in a symptomatic group, in whom endometriosis was detected via gynecological examination performed due to pain or infertility. Menstrual pain, CA125, maximum cyst diameter, and r-ASRM score were compared in the two groups.

Results
There were no significant differences in age, height, weight, or age at menarche between the two groups. Eighteen patients (75%) in the incidental group and 41 (97.6%) in the symptomatic group reported pain symptoms during an initial interview. Median visual analog scale scores for menstrual pain were significantly lower in the incidental group (5.0 vs. 6.9; $p = 0.014$). There were no significant differences in median CA125, maximum cyst diameter, or r-ASRM score in surgical cases in the incidental and symptomatic groups.

Conclusion
It was unclear whether incidental detection contributed to early diagnosis and treatment of endometriosis, but it could lead to the diagnosis of endometriosis in patients with mild pain.

Key words
Endometriosis, identical diagnosis, VAS score

DOES THE SIZE OF USL AND TU ENDOMETRIOSIS LESIONS AND THE STATUS OF POD ON ULTRASOUND AFFECT PREDICTION OF DISEASE?

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Country where research was undertaken:
Australia

Introduction/Background
The aim of this study was to evaluate the effect of the increasing size of uterosacral ligament (USL) and torus uterinus (TU) deep endometriosis (DE) lesions and the status of the pouch of Douglas (POD) on transvaginal ultrasound (TVS) to predict disease these locations.

Materials and Methods
This was a retrospective multi-center study. Patients with possible endometriosis in the USLs or TU who had complete ultrasound, surgical and histological data were included in final analysis. All TU and USL lesions (right and left) with maximal diameter in longest plane ≥ 5 mm, ≥ 10 mm, ≥ 15 mm, ≥ 20 mm, ≥ 25 mm, ≥ 30 mm on TVS were included. The presence of a positive or negative 'sliding' sign (marker for POD obliteration) was also recorded. We then examined the data to assess the performance of TVS to predict USL and TU DE when the POD was predicted to be either non-obliterated or obliterated. Reference standard was histological confirmation of endometriosis. The overall performance of ultrasound to predict DE in the USLs and TU were determined using the area under the receiver operating curve (AUC). Data were analyzed using SAS version 9.4.

Results
288 lesions for USLs (right 119 and left 104) and TU (65) were identified. The AUCs for prediction of left USL DE without and with POD obliteration were 0.56 and 0.62, respectively. The AUCs for prediction of right USL DE without and with POD obliteration were 0.51 and 0.65, respectively. The AUCs for prediction of TU DE without and with POD obliteration were 0.64 and 0.54, respectively. As DE lesion size on ultrasound increases for right USL, left USL and TU specificity and PPV increase but sensitivity decreases.

Conclusion
POD obliteration is associated with improved diagnostic performance of ultrasound in predicting USL DE but not TU DE.

Key words
Deep endometriosis, ultrasound, lesion size

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ANOGENITAL DISTANCE IN ADULT WOMEN - EXAMINING A NEW BIOMARKER IN GYNAECOLOGY: A COHORT STUDY.

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Country where research was undertaken: Australia

Introduction/Background
Anogenital distance (AGD) has gained attention as a potential physiologic biomarker in gynaecology. Recent studies have shown variances in AGD may be associated with diagnosis of endometriosis. We aimed to define normal anogenital distance in adult women and examine AGD's suitability as a biomarker by testing potential confounders, and the reproducibility of measurement.

Materials and Methods
This was a cross-sectional study involving 324 participants undergoing gynaecological surgery. Demographics and past medical history were collected pre-operatively using an online questionnaire. AGD was then measured before and after surgery, under general anaesthetic.

Two measurements were taken: AGD-AC (anus to clitoris) and AGD-AF (anus to posterior fourchette) by two clinicians before and after surgery. Inter and intra-observer variability was calculated. Univariate and multivariate analysis was used to examine associations with patient characteristics.

Results
Both measurements were normally distributed. AGD-AC was positively associated with body mass index (BMI), age, parity and previous perineal tear, but AGD-AF was not. AGD-AF was shorter in participants with a history of smoking. There were no clear associations or patterns with participants' ethnicity for either measure.

AGD-AC had acceptable levels of error for intra and inter-observer variability, (relative error of 3.9% and 7.3% respectively). The absolute error rate was lower for AGD-AF than AGD-AC. However, due to the shorter overall distance, the relative error was higher, at 9.8% for intra-observer and 17.3% for inter-observer.

Conclusion
AGD-AC and AGD-AF are normally distributed measurements. AGD-AC had significant

associations with confounding factors, likely limiting its utility as a biomarker in gynaecology. AGD-AF had less association with potential confounders, indicating more promise as a potential biomarker.

Key words
Endometriosis, biomarker, anogenital distance

POSTMENOPAUSAL ENDOMETRIOSIS CASE SERIES

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Country where research was undertaken:
United States of America

Introduction/Background
Postmenopausal endometriosis reportedly affects 2-5% of women with endometriosis. It can present as deep infiltrating endometriosis (DIE), and women may experience severe symptoms like those seen in premenopausal women. This case series of 21 patients with histologically proven postmenopausal endometriosis aims to supplement the literature regarding this difficult diagnosis.

Materials and Methods
Known menopausal patients with chronic pelvic pain undergoing excisional surgery for suspected endometriosis were evaluated. Those with histologically proven endometriosis on final pathology were included in the analysis. Demographics, medical history, preoperative imaging, intraoperative findings, and pathology results were collected. Descriptive statistics were performed.

Results
Patients were 37-74 years old (mean 50.1), primarily white, and averaged 7.7 years from menopause. The mean age of menopause was 42.6, with 81% being surgically menopausal and 19% naturally menopausal. Patients had an average of 2 previous discrete gynecologic surgeries secondary to pain. 81.0% were on hormone replacement prior to surgery.

All patients had visual findings of superficial scarring; 47.6% displayed nodularity, 28.6% powder burn lesions, 19.0% clear vesicles, and 23.8% adhesions. On pathology, every patient had superficial disease and 47.6% had DIE. Preoperative imaging identified 100% of DIE lesions. Bowel involvement affected 42.9%. Of these, 5 underwent bowel shaving, 1 underwent discoid resection, and 2 required segmental resections. Those with bowel involvement were on average 3.89 years from menopause (range 0-10).

Conclusion
Postmenopausal patients can be affected by advanced stage endometriosis many years after menopause. Despite a high rate of surgical menopause at younger ages, this cohort had persistent symptoms requiring surgery. Postmenopausal women with symptoms concerning for endometriosis should receive thorough evaluation and be offered appropriate surgical intervention if indicated.

Key words
Postmenopausal, excision, surgery

PROSPECTIVE VALIDATION OF PRE-OPERATIVE AND SURGICAL ENDOMETRIOSIS STAGING SYSTEMS USING MOBILE DEVICE INTERFACE

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Country where research was undertaken:
Australia

Introduction/Background
This study aims to prospectively validate pre-operative staging systems by contemporaneously using a mobile app database. The revised American society for reproductive medicine (rASRM), American association of gynaecologic laparoscopists (AAGL), ultrasound based endometriosis scoring system (UBESS) and endometriosis fertility index (EFI) staging systems, among others, have been used pre-operatively to predict surgical stage.

Materials and Methods
This prospective multi-centre observational study, recruited patients attending

gynaecology outpatient clinics undergoing assessment for endometriosis. Data was collected contemporaneously utilising a cloud-based database with mobile app interface. Collection commenced December 2023 and is ongoing. Participants included had undergone advanced imaging and progressed to surgical intervention. Imaging findings of deep endometriosis recorded as per IDEA consensus description and corresponding imaging staging methodology. Surgical findings were recorded to produce a score for each endometriosis surgical staging system.

Results
53 participants, mean age 33.5 years, underwent imaging and surgical management. Mean age 33.5 years 10 excluded from analysis due to pending surgical procedures. AAGL ultrasound (AAGL-U) prediction of AAGL laparoscopic (AAGL-LPS) stage produced weighted kappa (WK) 0.62. Association between AAGL-U and AAGL-LPS scores gave linear coefficient 1.0, R squared 57.2, correlation coefficient 0.76, $p<0.001$. rASRM ultrasound (rASRM-U) association with rASRM surgical (rASRM-S) produced WK 0.59. rASRM-U score predicting rASRM-S score gave linear coefficient 0.75, R squared 42.4, correlation coefficient 0.65, $p<0.001$. UBESS prediction of surgical based endometriosis staging system (SBESS) gave WK 0.32. As a threshold-based staging, there is no score for UBESS/SBESS. EFI ultrasound score regression with EFI surgical score produced linear coefficient 0.79, R squared 29.7, correlation coefficient 0.55, $p<0.001$.

Conclusion
Across the endometriosis pre-operative staging systems there was not high performance for stage nor score correlation. The AAGL staging system performed best in predicting both staging and scores. EFI performance was limited in this cohort due to incomplete scoring with pre-operative tubal patency often absent

Key words
Endometriosis, ultrasound surgery

DETECTION OF ENDOMETRIOSIS BY TRANSVAGINAL ULTRASOUND IN A GENERAL RADIOLOGY SETTING IN REGIONAL QUEENSLAND: A FIVE-YEAR RETROSPECTIVE AUDIT

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Country where research was undertaken:
Australia

Background
Transvaginal ultrasound (TVUS) is used to diagnose endometriosis during routine pelvic scans (rTVUS) in a general radiology setting. This contrasts with the current consensus recommending diagnosis via targeted endometriosis ultrasound (eTVUS) performed by a gynaecologist in a centralised specialist setting (1). Regional areas often lack specialised endometriosis imaging centres creating inequitable access for people with suspected endometriosis. An audit was performed to explore sonographer's capacity to detect endometriosis in a general radiology setting.

Methods
A retrospective clinical audit was performed over a five-year period from 01/05/2019 to 01/05/2024 in a regional radiology unit. Patients were referred for rTVUS for any clinical reason. Ultrasound images and radiologist reports were reviewed to confirm the diagnosis of endometriosis. rTVUS was performed by accredited general sonographers with varied levels of training and experience.

Results
In this audit 150 cases of undiagnosed endometriosis were identified in a cohort of 12,746 patients (1.1%). Most patients were referred by a general practitioner 87/150 (56%) or by a gynaecologist 59/150 (39%). The most common clinical indication was 'pain' including dysmenorrhoea, dyspareunia, dyschezia or dysuria (79/150 (52%). The mean age at presentation was 31.4 years (range 16-60 years). Endometriosis was most frequently observed in the ovary and uterosacral ligament (USL), 102/150 (68%) and 70/150 (46%) respectively. Endometriosis was identified in two or more observable anatomical locations in 78/150 (52%) of patients and a single observable location in 67/150 (44.6%). Pouch of Douglas (POD) obliteration was identified in 60/150 (40%) of patients.

Conclusion
This audit demonstrates endometriosis is being identified on rTVUS by accredited general sonographers in a regional outpatient setting. It highlights the importance of training front-line sonographers to identify

endometriosis to improve detection rates and reduce diagnostic delay for patients (2).

Key words
Endometriosis, audit, sonographer

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DEVELOPMENT OF A URINE TEST FOR DEEP INFILTRATING ENDOMETRIOSIS

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Country where research was undertaken:
United Kingdom

Introduction/Background
Endometriosis impacts 1 in 10 women of reproductive age worldwide and is associated with an average 9-year diagnostic delay resulting in patient distress and disease progression. Currently there is no accurate non-invasive diagnostic test that would promptly triage patients into the best practice treatment pathway.

Materials and Methods
RNA-sequence analyses were used to identify commonly dysregulated genes in endometriosis. To determine whether any of these genes encoded proteins that could act as biomarkers of endometriosis we collected urine samples from patients with endometriosis symptoms undergoing elective laparoscopy. Patients were allocated into deep, superficial or symptomatic control groups by two BSGE-accredited surgeons and a pathologist. Healthy volunteers were carefully screened and recruited. Additional urine samples from comparable endometriosis patients (Liverpool) were also analysed.

Results
Urine samples were collected from 209 women with endometriosis (111 deep, 98 superficial), 49 symptomatic controls and 33 healthy volunteers. The mean age of participants was 33 (range 19-47) and BMI 27 (range 16-43) with no significant difference between age and BMI between groups. PGAM1 was detectable in all samples with a mean level of 16ng/ml (range 0.4 - 267.2). Urinary PGAM1 levels were significantly lower in endometriosis patients compared to healthy volunteers (MW p=0.0003) and correlated with disease severity in a stepwise effect with the lowest values seen in patients with deep infiltrating endometriosis. PGAM1 levels were not impacted by stage of the menstrual cycle.

Conclusion
PGAM1 is detectable in the urine of women of reproductive-age and is an excellent biomarker for deep endometriosis. Recruitment is ongoing to determine the impact of comorbidities on PGAM1 levels.

Key words
PGAM1, liquid biopsy

TRANSVAGINAL ULTRASOUND FOR THE DETECTION OF RECURRENT ENDOMETRIOSIS: A DIAGNOSTIC ACCURACY STUDY

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Country where research was undertaken:
Australia

Introduction/Background
Transvaginal ultrasound (TVUS) is known to

be highly accurate in diagnosing endometriosis (1). However, women with previous surgical diagnosis and treatment are typically excluded from diagnostic studies to reduce bias. It is unknown if the accuracy of TVUS for recurrent disease is equivalent to those undergoing first laparoscopy.

Materials and Methods
Data from the National Endometriosis Clinical and Scientific Trials Registry were retrospectively analysed. Women aged 18-50 years who underwent TVUS prior to gynaecological laparoscopy were included. Diagnostic accuracy of TVUS was compared between women having their first laparoscopy for endometriosis with those undergoing a subsequent laparoscopy. The reference standard was visual identification of lesions, with or without histological confirmation. Subgroup analysis was performed based on location, phenotype and severity of disease.

Results
437 women with 468 paired ultrasound and operation reports were available for analysis, with 247 first and 221 subsequent laparoscopies. The incidence of endometriosis was 95.3%. The diagnostic accuracy of TVUS for first laparoscopy was 40.5% compared to 47.5% for subsequent laparoscopy, sensitivity 39.9% vs 45.3%, specificity 75.0% vs 72.2%, positive predictive value 98.9% vs 94.8%, negative predictive value 2.0% vs 10.5%, positive likelihood ratio 1.60 vs 1.63 and negative likelihood ratio 0.80 vs 0.76. The area under the curve of the receiver operating characteristic curve was 0.58 for the first laparoscopy group and 0.59 for subsequent laparoscopies.

Conclusion
When not performed in research specified conditions, TVUS performed poorly compared to the published literature. These data reinforce that a negative ultrasound does not exclude endometriosis. There was no substantial difference in diagnostic accuracy of TVUS for women with recurrent disease compared to those undergoing first laparoscopy for endometriosis.

Key words
Endometriosis, diagnosis, transvaginal ultrasound

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CORRELATION OF MAGNETIC RESONANCE IMAGING OF PELVIC ENDOMETRIOSIS WITH SURGICAL FINDINGS: PICTORIAL DEPICTION

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Country where research was undertaken:
India

Introduction/Background
Endometriosis is an enigmatic disease which commonly affects women of reproductive age group. It most commonly involves pelvic structures like ovaries, uterosacral ligaments, fallopian tubes, rectosigmoid, uterus and urinary bladder. Though USG is a sensitive imaging modality for detecting ovarian endometrioma but MRI is considered more sensitive and specific for evaluating Deep Infiltrating Endometriosis. We are showcasing pictorial correlation of Preop MRI images with intra-op surgical pictures in some of our patients of endometriosis.

Materials and Methods
MRI was done on patients with symptoms/suspicion of endometriosis like dysmenorrhea, dyschesia, dysuria and infertility. Images were taken on a 1.5 T Image .Axial T1-weighted sequence ;axial ,coronal and sagittal T2W;Axial T1 fat suppressed ;sequences are taken. In some cases we also give Gadolinium chelate dye for getting contrast images in axial, coronal and sagittal planes.

Results
MRI findings: #ENZIAN Staging and correlating with per op scoring.

Ovarian Endometriomas

Deep infiltrating endometriosis:
- Involvement of uterosacral ligaments
- Retro cervical involvement

Bowel lesion:
- Most common is rectosigmoid
- Mushroom cap sign with mucosal involvement
- Peritoneal implants not easily picked up on MRI
- Bladder involvement
- Ureteric involvement

- Uterine adenomyosis
- Poster will have all preop MRI and Intraop Images of same patients for correlation.

Conclusion
MRI can be a better imaging modality than ultrasound especially for deep infiltrating lesions because of large field of view, superior contrast resolution and multiplanar images.

Therefore, for understanding and better planning the surgical management MRI is a better modality for evaluating and mapping deep infiltrating Endometriosis.

Key words
Deep infiltrating endometriosis, #enzian classification, magnetic resonance imaging

TRANSVAGINAL ULTRASOUND FOR DIAGNOSING ENDOMETRIOSIS: PRACTICES, BARRIERS AND FACILITATORS AMONG AUSTRALIAN SONOGRAPHERS

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Country where research was undertaken:
Australia

Introduction/Background
Transvaginal Ultrasound (TVUS) is a valuable tool in the assessment of suspected endometriosis (eTVUS). However, eTVUS remains a non-routine examination, for reasons not fully understood. This study aimed to explore the current performance of eTVUS among Australian sonographers, and the barriers and facilitators encountered implementing eTVUS into practice.

Materials and Methods
An online cross-sectional survey was disseminated to Australian sonographers. Quantitative and qualitative questions were asked regarding demographics information, eTVUS performance, and experiences encountered when learning and implementing eTVUS. Statistical and thematic analyses were performed.

Results
Of the 127 responses included in the final analysis, 47.8% reported routinely performing full or partial eTVUS (18.4% full vs 29.8% partial). When a partial eTVUS was performed, this predominantly included an assessment of the sliding sign and ovarian mobility, rather than a search for endometriotic nodules at key sites like the uterosacral ligaments or rectosigmoid colon (94.6% and 97.3% vs 37.8%). Only 41.5% of participants reported confidence in performing eTVUS.
The main barriers that limited the uptake of eTVUS were limited supervision/mentors (42.3%), limited reporting of eTVUS findings from reporting radiologists/sonologists (39.6%), and its steep learning curve (38.7%). The main facilitators included sonographer's desire to answer the clinical question (84.0%), external education (38.7%), local department protocols (30.7%) and colleagues who perform eTVUS (30.7%).

Conclusion
Less than half of Australian Sonographers routinely perform eTVUS, with less than one quarter performing full eTVUS assessments. Inconsistency exists for the anatomical structures assessed during an eTVUS examination. Although barriers exist, more education surrounding eTVUS for sonographers, reporting doctors, and referrers could help increase uptake into routine practice.

Key words
Transvaginal ultrasound, endometriosis, barriers

FIBROBLAST ACTIVATED PROTEIN IN ENDOMETRIOTIC LESIONS: A POTENTIAL TARGET FOR PET BASED IMAGING

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Country where research was undertaken:
Australia

Introduction/Background
Fibroblast Activated Protein Inhibitor (FAPI) which targets activated fibroblasts has been used in Positron Emission Tomography scanning to revolutionize the diagnosis and treatment of cancers. The presence of activated fibroblast in the endometrial stromal

cells and in endometriotic lesions raises the possibility to apply this technology to endometriosis diagnosis.

Materials and Methods
The presence of the target for FAPI, Fibroblast activated protein (FAP) within endometriotic lesions was determined via 10X Visium gene expression arrays of SUP, DIE and OMA lesions. The extent of lesions within the excised tissue was determined via the presence of EPCAM and PDGRFB, as markers for endometrial epithelial and stromal cells respectfully. Finally, protein expression was confirmed via immunofluorescence with specific anti FAP antibodies.

Results
Analysis of bulk RNA sequencing revealed strong expression of FAP in all samples. However, no significant differences were observed between women with and without endometriosis. Comparison of single cell data however that was able to split the endometrial stromal cells into different cell states found an increase in mature fibroblast compared to mesenchymal stem cells with a significant increase in the fibroblast cells of endometriosis cases, compared to controls. Subsequent spatially resolved gene expression revealed FAP was present most commonly within endometriotic lesions, compared to surrounding tissue. It was expressed in all three subtypes, although strongest expression was observed in SUP. Finally, immunofluorescences confirmed FAP protein expression in endometriotic lesions.

Conclusion
PET imaging represents a truly transformative approach to endometriosis diagnosis and treatment. This data confirms strong expression of FAP in the stromal cells of endometriotic lesions, reveals a stronger expression can be detected in mature fibroblasts and thus represents an excellent choice for PET-based diagnosis and targeted treatment of endometriosis.

Key words
Diagnosis, imaging, PET

THEME: DIGITAL HEALTH AND ARTIFICIAL INTELLIGENCE

REVOLUTIONISING PRE- AND POST-SURGICAL ENDOMETRIOSIS MANAGEMENT THROUGH DIGITAL HOLISTIC CARE

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Country where research was undertaken:
Australia

Introduction/Background
Endometriosis surgery is a crucial yet often distressing aspect of care, with factors like pre-operative anxiety and poor physical health linked to poorer outcomes[1]. Digital holistic prehabilitation and rehabilitation programs aiming to optimise physical and psychological health show promise as an accessible solution, though research on their feasibility remains limited.

Materials and Methods
A mixed-methods study explores the feasibility of a co-designed digital endometriosis surgery optimisation program with 10 high-volume gynecologists in Australia. Utilising the Bowen Framework[2], we investigate adherence, satisfaction, adverse events, and preliminary impacts on pre-operative anxiety and self-efficacy, as well as post-operative pain, length of stay, and quality of life. Implementation outcome measures evaluate the success of implementation efforts[3] while semi-structured interviews analysed via a framework analytical approach capture participant and clinician experiences[4].

Results
The presentation shares early findings on the feasibility and implementation of a digitally delivered holistic endometriosis surgery optimisation program. Reported outcomes include participant demographics, adherence, satisfaction, program-related adverse events, changes in preoperative anxiety and self-efficacy, and exploration of the impact on post operative pain, length of stay, and quality of life. The eight-week prehabilitation and rehabilitation program incorporates multidisciplinary education modules, guided

exercise classes, lifestyle tracking, peer support, and weekly clinician-led group calls.

Qualitative findings reveal the most valued aspects identified by participants and clinicians, along with areas for improvement. The insights help explore the program's feasibility and inform future development while providing a strong foundation to inform future research trials and scale the program for broader application.

Conclusion
Digital programs offer a promising opportunity to enhance outcomes and experiences for people undergoing endometriosis surgery. This presentation highlights the feasibility of Australia's first holistic digital endometriosis surgery optimisation program, sharing early findings that will help guide future trials on clinical and cost-effectiveness compared to standard care.

Key words
Surgery, optimisation, digital

DEMOGRAPHIC AND CLINICAL PROFILES OF PATIENTS WITH ENDOMETRIOSIS

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Demographic and Clinical Profiles of Patients with Endometriosis

Country where research was undertaken:
United States of America

Introduction/Background
Endometriosis affects 176 million women, with an average diagnostic delay of up to twelve years. We sought to evaluate differences between patients diagnosed with and without endometriosis, using electronic health record (EHR) data. Our goal was to use feature selection to determine the elements most predictive of endometriosis.

Materials and Methods
Adult patients (18 and older) with a visit to the OB/GYN clinic from 2011 to 2020 were included. Endometriosis diagnosis was defined by ICD9 or ICD10 codes (N80). Demographics, visit data, diagnoses, comorbidities, and medications were extracted. Multiple methods of feature selection (SelectKBest, VarianceThreshold, and SelectFromModel RandomForestRegressor) were used to determine the elements most relevant in prediction of endometriosis. The two groups were compared using Chi-squared and Welch's T-tests.

Results
There were 13,231 patients with visits from 2011 to 2020 at the UCMC clinic; 1,332 unique patients were included in the analysis. Patients with an endometriosis diagnosis had an average age of 39.8 years (57% White, 32% Black), compared to average age of 42.6 years (76% White, 18% Black, p=0.985 for race) without endometriosis ($p<0.05$ for age). Those with endometriosis had 5 times more medication orders for tramadol, ibuprofen, medroxy progesterone, metronidazole, and fluconazole. There was no statistical difference between the proportion of visit types between the groups. The most common comorbidities for the patients with endometriosis were abdominal and pelvic pain, other abnormal uterine bleeding, and non-inflammatory disorders of the ovary.

Conclusion
We used feature analysis to identify key clinically-relevant differences in patients diagnosed with endometriosis, to begin developing predictive algorithms to aid in diagnosis. Race and ethnicity features were not included, as algorithmic reliance on these features risks perpetuating inequities already ingrained in healthcare systems.

Key words
Machine learning, medical informatics, diagnosis

AI SCRIBES IN THE GYNECOLOGY HUB: A TRANSFORMATIVE TOOL FOR MULTIDISCIPLINARY CARE

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Country where research was undertaken:
Australia

Introduction/Background
The integration of AI scribe technology in gynecology hubs has shown potential in revolutionizing patient care, particularly for managing conditions like heavy menstrual bleeding (HMB), endometriosis and adenomyosis. This study evaluates the 1-year long application of AI scribes in a multidisciplinary gynecology setting, focusing on enhancing care delivery, improving clinical documentation, and supporting patient-centered pathways.

Materials and Methods
We mapped the above mentioned gynecology care pathways, identifying barriers and enablers the use of AI scribe implementation in consultation settings, recording clinician and administration team feedback, and analysing documentation time, accuracy, and clinician satisfaction. Key measures included the AI scribe's impact on consultation flow, data entry precision, and overall clinician satisfaction.

Results
Our findings indicate that AI scribe usage significantly reduced documentation time and improved clinician satisfaction.

Key enablers included ease of AI scribe integration and user-friendly interfaces, while identified barriers related to establishing a process for informed consent and initial clinician training. Furthermore, the multidisciplinary approach facilitated by the scribe allowed for better collaboration across specialties interviewed.

Conclusion
AI scribes offer transformative potential for patient-centered care in gynecology, fostering efficiency and inter-specialty collaboration in HMB, endometriosis and adenomyosis management. Adoption requires addressing privacy and training needs but holds promise for enhanced clinician satisfaction.

Key words
AI scribes, gyaecology, digital health

PREDICTING ENDOMETRIOSIS DIAGNOSIS USING MACHINE LEARNING: A RANDOM FOREST APPROACH

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Country where research was undertaken:
Australia

Introduction/Background
Endometriosis often presents as a diagnostic challenge requiring histological confirmation. Machine learning algorithms offer the potential to enhance presurgical diagnosis and reduce negative laparoscopy rates by identifying patterns beyond the scope of human analysis. This study explores the application of machine learning to predict endometriosis diagnosis using various clinical features.

Materials and Methods
A Random Forest algorithm was trained on a single operator dataset containing clinical features such as dysmenorrhoea, dyspareunia, dysuria, dyschezia, infertility, family history and ultrasound features. The model's performance was evaluated using cross-validation accuracy, F1 score, recall, and area under the receiver operating characteristic curve (AUC-ROC). Feature importance and pairwise interactions were also analysed using Partial Dependence Plots (PDPs).

Results
The trained algorithm achieved a mean accuracy of 76.3%, an F1 score of 96.0%, and perfect recall (100%). The AUC-ROC was 0.67, indicating some limitations in distinguishing between outcomes. Feature importance analysis revealed that dyspareunia and family history were the most influential predictors, contributing 27.1% and 19.0%, respectively. Dysmenorrhea, however, had the lowest feature importance, contributing only 3.34%. PDPs revealed that family history, when combined with other features such as dysmenorrhea, dysuria, and dyschezia, increased the predicted probability of endometriosis, with the combination of dysmenorrhea and family history showing the highest predicted probability of 0.957.

Conclusion
Machine learning tools hold promise in developing predictive algorithms that assist in the presurgical diagnosis of endometriosis by identifying key clinical markers. Although the model shows potential, further refinement and training on a larger dataset are necessary to improve diagnostic accuracy and mitigate potential biases.

Key words
Presurgical diagnosis, machine learning, predictive algorithms

A MULTIDICIPLINARY APPROACH TO SEVERE DYSMENORRHEA IN YOUNG PATIENTS (16-24Y.O.A.) AFTER APP-BASED STRATIFICATION

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Country where research was undertaken:
Germany

Introduction/Background
Dysmenorrhea occurs in up to 90% of the menstruating population. MeMäF is a hybrid model with clinical and digital components offering evidence-based content on the menstrual cycle, causes of pain, treatment options and self-help techniques through a free app. The project aims to enhance women's health and advance research.

Materials and Methods
The period app, part of a scientific project funded by the Innovation Fund (G-BA), aims to improve care for young women with menstrual pain. It offers 3,000 participants free resources on hormones, menstruation, pelvic floor health, a pain diary, exercises and self-care. After three months of use, 220 participants are selected for interdisciplinary treatment at the Charité Endometriosis Centre, covering gynecology, psychology, physiotherapy, and nutrition, provided on-site or via video consultation over six months.

Results
MeMäF is a large-scale, ongoing collaboration between Charité and leading institutions across Germany, running until November 2026. Our mission is to improve care of girls and young women with dysmenorrhea. Two innovative care solutions are offered: the app “period.” and on top a specialized multimodal treatment at Charité. With this study, we aim to determine whether our service can effectively alleviate menstrual pain and improve symptom management. More than 1,800 young women are already participating, engaging with both the digital and clinical components.

Conclusion
The app “period.” is a comprehensive medical tool offering approved resources and exercises to help users understand and manage menstrual pain. Prioritizing data security it is exclusively used for scientific research. It offers free flexible access to health resources anytime and anywhere with an internet connection.

Key words
Multimodal-womens-health, hybrid care model, dysmenorrhea

EVALUATION OF A RULE-BASED PHENOTYPING ALGORITHM FOR ENDOMETRIOSIS

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Country where research was undertaken:
United States of America

Introduction/Background
Endometriosis is a complex and heterogeneous condition, posing challenges for accurate case identification. Electronic health record (EHR)-based phenotyping algorithms can facilitate large-scale studies but require rigorous validation. Here, we report the performance of a rule-based algorithm in generating diverse endometriosis phenotypes.

Materials and Methods
As an initial step, we evaluated a previously developed, expert-validated phenotyping algorithm that incorporates ICD and CPT codes related to endometriosis diagnosis to identify three distinct phenotypes: 1) wide excluding adenomyosis (Wex), 2) procedure-confirmed (PCN), and 3) surgically-confirmed (SCN). The algorithm was tested in a cohort chart reviewed cases and controls as the gold standard. For larger-scale application, we utilize symptom and unstructured patient notes data from the EHR to generate a rule-based classification system that provides more accurate diagnoses.

Results
For the Wex phenotype, the algorithm demonstrated a negative predictive value (NPV) of 99.0% (778/786) and a positive predictive value (PPV) of 77.6% (201/259). For the PCN phenotype, the NPV was 98.3%

(282/287) and the PPV was 82.0% (50/61). For the SCN phenotype, the NPV was 96.2% (25/26) and the PPV was 91.3% (21/23).

Conclusion
Rule-based EHR phenotyping algorithm successfully identified diverse endometriosis phenotypes with high accuracy, as demonstrated by the strong NPV and PPV values. The wide exclusion phenotype can facilitate large-scale genetic and epidemiological studies, while the procedure-confirmed and surgically-confirmed phenotypes offer greater specificity for in-depth biological investigations. This robust EHR-based approach enables efficient and scalable endometriosis research across diverse clinical settings.

Key words
EHR-based phenotyping, chart reviews, rule based

THEME: EPIDEMIOLOGY, CO-MORBIDITIES AND RISK FACTOR(S)

SUGAR SWEETENED BEVERAGES, ARTIFICIALLY SWEETENED BEVERAGES, FRUIT JUICE CONSUMPTION AND RISK OF LAPAROSCOPICALLY CONFIRMED ENDOMETRIOSIS

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Country where research was undertaken:
United States of America

Introduction/Background
Dietary factors may play a role in endometriosis risk. Sugar with its proinflammatory actions might influence risk of endometriosis, but literature is sparse on this topic. We examined the associations of sugar-sweetened beverages (SSB), artificially-sweetened beverages (ASB), and fruit juice consumption with risk of laparoscopically-confirmed endometriosis.

Materials and Methods
This is a prospective cohort study utilizing data from 72,354 premenopausal participants in the Nurses' Health Study II first reporting diet via food frequency questionnaire (FFQ) in 1991 (age range=27-44y) and reporting endometriosis diagnoses through 2017 Cumulative averaged intakes of beverages from FFQs (assessed every 4 years) were tested for association with incidence of laparoscopically-confirmed endometriosis using Cox regression models. We also evaluated associations stratified by infertility status, physical activity, and body mass index (BMI).

Results
We documented 3383 incident cases of laparoscopically-confirmed endometriosis. Compared to infrequent intake (<1/month), neither high intake (>2/day) of SSB (hazard ratio(HR)=1.01; 95% confidence interval(CI)=0.85-1.20; p-trend=0.45), ASB (HR=1.01; CI=0.91-1.13; p-trend=0.54) or fruit juice (HR=1.02; CI=0.84-1.24; p-trend=0.80) was associated with endometriosis diagnosis in multivariable models. Stratification revealed that more frequent SSB consumption was associated with greater risk of endometriosis diagnosis (p-trend=0.03) among women with a greater than median level of physical activity (≥21 metabolic equivalent task hours/week) (p-heterogeneity=0.0003). No informative differences for ASB or fruit juice by physical activity and no clear patterns of heterogeneity for SSB, ASB, or fruit by infertility status or BMI were found.

Conclusion
Overall we observed no informative associations of SSB, ASB or fruit juice intake with risk of endometriosis diagnosis. These first ever exploration of sweetened beverage and endometriosis risk findings need confirmation, however, this large cohort study of medical professionals found no evidence of association.

Key words
Sugar-sweetened beverages, laparoscopically-confirmed endometriosis**,** inflammation

NAVIGATING DEEP ENDOMETRIOSIS: PREDICTING CONSERVATIVE TREATMENT OUTCOMES

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Country where research was undertaken:
United States of America

Introduction/Background
We aim to assess characteristics of patients desiring conservative management for deep endometriosis (DE) compared to surgical intervention.

Materials and Methods
A retrospective chart review at a tertiary care institution was conducted from 2015-2024 to identify patients undergoing conservative management for DE. Patients ages 16-55 with >5mm DE lesions on imaging were included, patients with obstructing lesions or with appearance concerning for malignancy were excluded. Endometriomas alone were not considered DE. Patients desiring conservative (expectant or medical) management were compared to those desiring surgical management. Failure of conservative management was defined by progression to surgery. Chi-squared and ANOVA tests were performed for categorical and continuous variables.

Results
Fifty-eight patients with DE were included, 34 undergoing conservative management. Seven (20.6%) failed conservative management after a median of 5.3 months following consultation at a specialty clinic. Patients undergoing conservative management were of a similar age, parity, and had similar history of hormonal treatments, initial pain scores, and number/type of presenting symptoms to those desiring surgery. Those desiring conservative management had a greater number of disease locations (2.7 and 2.6 vs 1.4, $p<0.001$ for those that failed conservative management, ongoing conservative management, and surgical management respectively), more bladder disease (42.9% and 11.1% vs 0%, $p=0.005$), and more frequent history of pelvic floor physical therapy (28.6% and 11.1% vs 0%, $p=0.049$). Patients that failed conservative management more frequently experienced chronic pelvic pain (57.1% and 48.1% vs. 16.7%, $p=0.031$) and chronic overlapping pain conditions (1.6 and 1.1, vs. 0.6, $p=0.041$). The most common reason for failing conservative management was incomplete symptom relief.

Conclusion
Conservative management is a viable treatment option for patients with DE. Further research is needed to identify patients ultimately requiring surgery.

Key words
Deep endometriosis, non-surgical, pelvic pain

FACTORS ASSOCIATED WITH MULTIPLE COMORBIDITIES AMONG WOMEN WITH ENDOMETRIOSIS IN THE COMPARE-ENDOMETRIOSIS COHORT

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Country where research was undertaken:
France

Introduction/Background
Endometriosis has been associated with a higher risk of several other chronic diseases, and patients often live with several comorbidities. The presence and number of comorbidities could be associated with different clinical characteristics and outcomes among patients with endometriosis and potentially contribute to disease heterogeneity.

Materials and Methods
ComPaRe-Endometriosis is a prospective e-cohort initiated in 2018, following 10,000 endometriosis patients among whom various disease characteristics and patient-reported outcome and experience measures were collected. We considered 87 diseases that were reported by >=0.1% participants. We classified comorbidity counts in addition to endometriosis into four groups (0, 1, 2, and 3+) and used ordinal polytomous logistic regression to describe disease and patient characteristics associated with the number of comorbidities at cohort entry.

Results
Among 10,761 participants, 35.8% reported at least one comorbidity (among whom 52.7% reported 1, 22.9% 2, and 24.4% 3+). In multivariable models, number of comorbidities was positively associated with a higher diagnostic delay (15 years or more vs. 5 years or less: OR=1.77; 95%CI=1.54–2.02), family history of adenomyosis (OR=1.31;

95%CI=1.11-1.54) or pelvic pain (OR=1.21; 95%CI=1.10-1.32) especially among first-degree relatives, and diagnosis of adenomyosis, either alone (OR=2.59; 95%CI=2.10–3.20) or combined with endometriosis (OR=2.44; 95%CI=2.13–2.81). However, it was inversely associated with later age at endometriosis symptom onset (age 22 or older vs. age 13 or younger: OR=0.69; 95%CI=0.60–0.79) and earlier age at menarche (13 years or more vs. 11 years or less: OR=0.63; 95%CI=0.52-0.76).

Conclusion
This cross-sectional study highlights several patient characteristics associated with number of comorbidities. Further research is needed to better understand these relationships and determine their temporality. This research could help to identify factors leading to higher comorbidity risk, to highlight the consequences of multiple comorbidities, or to better characterize disease heterogeneity.

Key words
Endometriosis, comorbidity

THE LONG-TERM INTERNATIONAL DUAL-SOURCE ENDOMETRIOSIS AND ADENOMYOSIS (LIDEA) REGISTRY: PROGRESS, CHALLENGES, AND STRATEGIES FROM THE GERMAN COHORT

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Country where research was undertaken:
Germany

Introduction/Background
The challenging diagnoses of endometriosis and adenomyosis delay the initiation of targeted treatment, which may lead to prolonged pain, abnormal bleeding, and infertility. It is essential to develop a better understanding of endometriosis and adenomyosis from both patients´ and doctors´ perspectives to advance treatment selection and discovery of novel treatments.

Materials and Methods
The German cohort of the Registry intend to recruit 2,000 participants with presumed or confirmed endometriosis and/or adenomyosis diagnoses, utilizing a longitudinal dual-source data collection method. Data are collected from patients and healthcare practitioners (HCPs) on research areas: pain, disease burden, diagnostic challenges, and treatment outcomes. In Germany, recruitment is ongoing through a network of HCPs, with data collected via electronic Patient Reported Outcomes (ePRO) and regular clinical assessments.

Results
The purpose of LIDEA Registry is to create a comprehensive view of endometriosis and adenomyosis characteristics. The German cohort follows the international study protocol, with patients enrolled for a minimum of three years and contributing data via ePRO at 6, 12, 24, and 36 months. HCPs provide clinical updates and (surgical) treatments at 12 and 36 months. Challenges encountered include HCP selection and engagement, patient recruitment rate, technical adoption of ePROs, and ensuring consistent data input from HCPs. Early learning highlights the importance of clear communication from study responsibilities towards patients and practitioners, as well as the need for flexible recruitment strategies in different clinical settings. Early results will be available to present at World Congress on Endometriosis 2025.

Conclusion
The German cohort of the LIDEA Registry is progressing toward its goal of recruiting 2,000 participants. The dual-source data collection model, while challenging to implement at scale, provides valuable insights into patient and physician perspectives on endometriosis/ adenomyosis, with early results already informing improvements in data collection and recruitment strategies.

Key words
Registry study, LIDEA

MENSTRUAL HEALTH PROFILE AND EDUCATION SOURCES IN PUERTO RICAN ADOLESCENTS

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Country where research was undertaken:
United States of America

Introduction
Recognizing normal and abnormal features of the menstrual cycle is crucial for early detection and treatment of gynecologic conditions including endometriosis. There are data gaps regarding the menstrual health profile of Hispanic adolescents and sources of information, limiting insights to guide educational and medical interventions for this population.

Materials and Methods
An anonymous online cross-sectional study of 1,195 Puerto Rican adolescents (ages 13-20) was conducted to assess menstrual cycle's features and prevalence of menstrual cycle dysregulations and gynecologic health conditions. We also assessed impact of menstrual disturbances on daily life, sources of education about menstrual topics, trusted figures, and perceived levels of comprehension and comfort. We analyzed differences based on age (<14, 15-17, 18-20 years old), region (Metropolitan, non-Metropolitan), school type (public/private) and setting (Urban/Rural).

Results
Mean age at menarche was 11.9 y/o; early menarche (8-10 y/o) was reported by 18.6%; 9.5% reported late menarche (15-17 y/o). We uncovered alarmingly high prevalence of dysmenorrhea (86%), irritability (69%), severe pelvic pain (37%), profuse bleeding (38%) and irregular cycles (41%) that may indicate gynecological pathologies requiring medical intervention including endometriosis. 1 in 10 reported Emergency Room visits due to pelvic pain. Despite high rates of menstrual symptomatology, there was a low use of over-the-counter pain medications (<30%) and hormones (<1%), and very low rates of diagnosed endometriosis, PCOS and PMS (<1%). The study also revealed differences in likelihood of receiving education, levels of understanding and comfort, and trusted figures regarding menstrual health topics based on age, school type, region, and setting.

Conclusion
These results will contribute to designing tailored menstrual health curricula to improve the understanding of the menstrual cycle, including normal and abnormal features requiring medical intervention. Additionally, the insights gained in the study will guide awareness initiatives to reduce diagnostic delays in menstrual related disorders in the adolescent population.

Key words
Menstrual health, menstrual education, adolescents

A FEASIBILITY STUDY TO EXAMINE THE LINK BETWEEN LONGITUDINAL ENVIRONMENTAL EXPOSURE AND ENDOMETRIOSIS PHENOTYPE

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Country where research was undertaken:
Australia

Introduction/Background
Participants with histologically confirmed endometriosis between 2015-2022 completed an environmental exposure questionnaire. The aim is to evaluate environmental toxin exposures and their impact on phenotype and disease severity in patients with histologically confirmed endometriosis. Correlation of epidemiological and clinical data is required to identify exposure risks for future generations.

Materials and Methods
In this retrospective study, demographic details were collected and an Environmental Study questionnaire containing 473 fields was completed. All participants had undergone surgical evaluation of disease with detailed phenotypic mapping between 2015 and 2022 following the American Society for Reproductive Medicine (rASRM) Classification of Endometriosis. Differences in metropolitan and regional participants and lesion types were assessed via Chi-squared test, Fisher's exact test, logistic regression or ANOVA depending on the nature of the variables.

Results
Analyses included 218 and 78 participants in the metropolitan regional groups respectively (73.6% vs 26.4%) with a mean age of 38 years (37.7 +/- 8.7). There were no differences in age, education level or ancestry between the groups. Participants from regional areas had higher body mass indices (27.16 +/- 5.39 vs 25.22 +/- 4.93, p=0.004), reported greater animal and plant toxin (14.0% v 3.0%, p=0.002) and pesticide (20.0% vs 6.0%, p=0.006) exposure and trended toward higher rates of deep infiltrating endometriosis (DIE) (43.4% vs 28.6%, p=0.05) than the metropolitan group. Increasing age was associated with higher rates of DIE and ovarian endometrioma compared with superficial disease (38.56 +/- 8.42 & 40.27 +/- 7.85 vs. 33.93 +/- 8.42, p=4x10-6).

Conclusion
This study confirms the applicability of this environmental survey that captures detailed longitudinal exposure to potential toxins. It confirms that this data capture and statistical modelling system is scalable, potentiating our understanding of life-course contributions to endometriosis and aiding risk assessment and counselling for people with endometriosis.

Key words
Toxin, disease phenotype, modifiable risks

FACTORS FOR OPTIMAL LONG-TERM CONTROL AND HORMONE-SENSITIVE CANCER RISKS IN PATIENTS WITH ENDOMETRIOSIS: A RETROSPECTIVE COHORT STUDY

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Country where research was undertaken:
Taiwan

Introduction/Background
Medical treatments have become the mainstay for the management of endometriosis, reserving surgery for treatment failures or suspected malignancy[1]. Dienogest, a fourth-generation progestin, effectively controls dysmenorrhea and prevents endometrioma recurrence over the long term with minimal side effects. Nonetheless, concerns regarding cancer and thromboembolism from extended hormone therapy remain[2,3].

Materials and Methods
The study analyzed data from patients with endometriosis (January 1, 2017 - December 31, 2022) using an institutional database. Medication types and dosages, including dienogest, danazol, combined oral contraceptives, levonorgestrel intrauterine device, and leuprolide were assessed. The primary outcome was the uptake of definitive surgery (oophorectomy or hysterectomy); secondary outcomes included the development of hormone-sensitive cancers and thromboembolism. Analysis was conducted via one-to-one propensity score matching and the Cox proportional hazard model.

Results
The study enrolled 12,104 patients, with 38.8% diagnosed with adenomyosis and 9.6% with endometrioma. The average age at diagnosis was 41.21 (± 8.06) years. Over an average follow-up of 1,223 days, older age and higher BMI increased the risk of hysterectomy in adenomyosis patients (HRs 1.08 and 1.07, respectively). Longer use of dienogest effectively reduced this risk (HR 0.997). In endometrioma patients, age was associated with a higher oophorectomy risk (HR 1.10), with no effective preventive treatments. There were 55 (0.45%) cases of breast cancer, 30 (0.25%) cases of endometrial cancer, 22 (0.18%) cases of ovarian cancer, and 87 (0.7%) cardiovascular/cerebrovascular events. Overall, medical treatments had a limited effect on the incidence of these cancers, cardiovascular events, or cerebrovascular diseases.

Conclusion
In the Asian population, dienogest effectively reduced the need for definitive surgeries in

patients with adenomyosis, but not for endometrioma, without increasing the risk of hormone-sensitive cancers and thromboembolic events. More evidence is needed from larger cohorts and long-term follow-up in populations of different ethnicities and cultures.

Key words
Sterilization, neoplasms, thromboembolism

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SPONTANEOUS HEMOPERITONEUM IN A 29-WEEK PREGNANCY WITH A HISTORY OF ENDOMETRIOSIS: A CASE REPORT

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Country where research was undertaken:
Turkey

Introduction
Spontaneous hemoperitoneum in pregnancy (SHIP) is defined as sudden, nontraumatic intraperitoneal bleeding that occurs during pregnancy or up to 42 days postpartum[1]. The incidence ranges between 4 – 4.9 per 100.000 births[2]. Although seen rarely, it is associated with perinatal morbidity and mortality due to maternal hemodynamic instability.

Case
A 30-year-old primigravid woman with a spontaneous conception, at 29 weeks of gestation, presented to our obstetrics and gynecology department with complaints of abdominal and back pain. In terms of her medical history, a laparoscopic cystectomy was performed one year ago due to a 90mm X 50mm endometrioma in the right ovary. Deep endometriosis and adenomyosis were not observed.

Ultrasound revealed a single fetus with a positive heartbeat, increased amniotic fluid volume, and an estimated fetal weight consistent with gestational age. The placenta was visualized as normal on the posterior uterine wall, and the cervical length measured 22mm. No abundant free fluid or bleeding was observed, ruling out uterine rupture as a concern. After decelerations appeared on the non-stress test; the repeat hemoglobin values dropped to 7.2 g/dL, blood pressure at 70/50 mm Hg and a pulse rate of 95/min; the decision was made for laparotomy and delivery of the baby. Upon entering the abdomen, 1000cc of blood and coagulum was observed. An active bleeding site, displaying a decidual appearance, was identified on the left side of the uterus near the broad ligament. Bleeding was successfully controlled. The newborn was discharged from the hospital on the 48th day with no complications.

Conclusion
It is crucial to consider spontaneous hemoperitoneum in pregnancy, especially in pregnant patients with a history of endometriosis surgery. Managing such high-risk cases in specialized centers and easily identifying predisposing factors for spontaneous hemoperitoneum can lead to improved outcomes, despite its rarity and poor prognosis.

Key words
Pregnancy, hemoperitoneum, endometriosis.

CAUSAL RELATIONSHIP BETWEEN ABORTION AND ENDOMETRIOSIS: A BIDIRECTIONAL TWO-SAMPLE MENDELIAN RANDOMIZATION STUDY

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Country where research was undertaken:
China

Introduction/Background
To examine the causal relationship between abortion and endometriosis.

Materials and Methods
We performed Mendelian Randomization (MR) analysis using GWAS data to assess genetic links between medical/spontaneous/other abortions and endometriosis, leveraging FinnGen and UK Biobank datasets. Primary analyses applied IVW random-effects models, supplemented with weighted median/mode and MR-Egger. Sensitivity analyses included Cochran's Q (heterogeneity), MR-PRESSO (pleiotropy), and Leave-One-Out stability testing.

Results
The IVW method revealed no statistically significant causal association between various types of abortion and endometriosis. Specifically, the odds ratios (ORs) were as follows: medical abortion, spontaneous abortion, and other types of abortions, indicating no significant effects on the risk of endometriosis. Similarly, analysis in the reverse direction showed no significant causal effects of endometriosis on the likelihood of experiencing any type of abortion, with ORs for medical abortion, spontaneous abortion, and other abortions. Sensitivity analyses supported these findings, demonstrating no evidence of horizontal pleiotropy or significant heterogeneity.

Conclusion
Our MR results do not support a causal relationship between abortion and endometriosis. Further research is necessary to explore additional genetic and environmental factors that could influence these conditions.

Key words
Endometriosis, abortion, mendelian randomization

ENDOMETRIOSIS AND CARDIOMETABOLIC DISEASE RISK (ENDCAM): ARE DOCTORS AND PATIENTS AWARE OF THE RISKS?

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Country where research was undertaken:
Australia

Introduction/Background
There is growing evidence to support that endometriosis increases a person's risk of cardiometabolic disease (a group of common conditions e.g., hypertension, heart disease and stroke) (1,2,3). Our aim is to assess the current history-taking practices and knowledge of clinicians involved in caring for clients with endometriosis and/or cardiometabolic disease.

Materials and Methods
An anonymous online survey has been developed by our investigators and consumer representative, to be administered to both patients with endometriosis and/or cardiometabolic disease, and clinicians who care for such patients. It will utilise both dichotomous and Likert scale questions to assess basic demographics, current clinical knowledge and current history-taking practices. This has been designed as an exploratory study and recruitment will occur through various national clinics and external promotion.

Results
Four groups will be surveyed. Two clinician groups (gynaecologists and cardiologists/other medical specialists), and two patient groups (those with endometriosis and those with cardiometabolic disease). Clinicians must be practicing in Australia and involved in the care of female, or assigned female at birth, patients with either endometriosis or cardiometabolic disease. Patients must be aged 18-45yo, with a diagnosis of either endometriosis or cardiometabolic disease and residing in Australia. A minimum of n = 35 participants will be sought per group, for a total of n = 140 participants. All survey responses will be de-identified. Statistical analyses will be conducted using standard statistical software and group differences will be analysed by appropriate regression methods.

Conclusion
We anticipate that the outcome of this project will help provide the evidence to implement better education for clinicians and patients on the importance of early monitoring for cardiometabolic risk in patient with endometriosis; which in turn will improve patient care and aid disease prevention.

Key words
Endometriosis, cardiometabolic disease

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IMPAIRED WNT4 EXPRESSION ASSOCIATED WITH PREGNANCY LOSS WITH ENDOMETRIOSIS

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Country where research was undertaken:
China

Introduction/Background
Endometriosis, a prevalent gynecological disorder, has been associated with increased risk of pregnancy loss in various nationwide population studies. However, the underlying mechanisms remain unclear. WNT4 is a crucial factor in the process of decidualization. This study aims to investigate the relationship between WNT4 expression and pregnancy loss in patients with endometriosis.

Materials and Methods
We obtained 24 cases of endometriosis eutopic endometrium, meantime 71 normal endometrium from our center. All patients have a history of pregnancy, and a laparoscopically verified diagnosis of endometriosis or non-endometriosis.The paraffined tissue sample collection used in this study was approved by ethics committee. Immunohistochemistry was employed to investigate association between WNT4 expression and pregnancy loss before first trimester in endometriosis.

Results
The age of participants ranged from 30.7 ± 3.9 years in the endometriosis group and 30.6 ± 6.0 years in the control group, with no statistically significant difference in age between the two groups. In terms of pregnancy loss, we observed that 7 out of 24 patients (29.2%) in the endometriosis group experienced pregnancy loss in the first trimester, compared to 18 out of 71 patients (25.3%) in the control group. This difference was statistically significant. Immunohistochemistry (IHC) was conducted on samples from the pregnancy loss cohort. WNT4 expression was observed 5 out of 7 (71.4%) cases in the endometriosis group showed low WNT4 expression, which was more prominent compared to the control group, where 7 out of 18 (38.9%) showed low WNT4 expression.

Conclusion
Our results suggest a potential link between WNT4 dysregulation and impaired decidualization in pregnancy loss cases associated with endometriosis.

Key words
WNT4, Endometriosis, pregnancy loss

THEME: EXPERIMENTAL MODELS OF ENDOMETRIOSIS

IN-VITRO MODEL FOR EARLY INITIATION AND ESTABLISHMENT OF PELVIC ENDOMETRIOSIS USING PRIMARY CELLS

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Countries where research was undertaken:
Brazil and United Kingdom

Introduction/Background
Retrograde menstruation is one of the most accepted theories for the etiopathogenesis of endometriosis. Peritoneal lesions could be established by the seeding of menstrual endometrial fragments and cells in the areas of peritoneal fluid stasis. These processes could be mimicked by *in vitro* matrix-free tridimensional models.

Materials and Methods
We have developed a matrix-free three-dimensional *in vitro* model for studying the early initiation of peritoneal endometriosis. It includes the formation of spheroids of primary endometrial cells in a liquid environment using ultra-low attachment plates. These spheroids were then transferred to plates containing a layer of mesothelial cells. Fluorescent labeled spheroids and mesothelial cells were observed by microscopy for 48h in a living cell assay. Also, attached spheroids were fixed and observed by microscopy.

Results
Spheroids can be assembled with different amounts of stromal and epithelial endometrial cells. The spheroids are able to attach to different coated surfaces, including those covered by mesothelial cells. The living cell assay showed that the mesothelial cell layer (actin labeled) interacts with the cells in the spheroids (tubulin labeled), opening space for the establishment of endometrial cells. This open space is also clearly observed in the fixed slides. Cell lines such as St-1b and LP9 behave similarly to primary cells. The model allows many types of evaluations, such as, *inter alia*, time to adhesion, area of invasion, identification of specific markers, inclusion of different compounds as medium supplementation such as hormones and drugs.

Conclusion
It is possible to mimic the peritoneal lesions' early initiation *in vitro* using primary endometrial cells and mesothelial cells. This model can contribute to the better understanding of the mechanisms involved in peritoneal endometriosis initiation and establishment.

Key words
Matrix free three-dimensional model, retrograde menstruation, etiopathogenesis

IMMUNE SYSTEM AND EXPERIMENTAL ENDOMETRIOSIS: ROLE OF DENDRITIC CELLS

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Country where research was undertaken:
Brazil

Introduction
Considering recent findings on dendritic cells (DC) in the pathophysiology of endometriosis, this study aims to investigate whether peritoneal DC in a mouse model behave similarly to peritoneal DC of women with endometriosis. We also analyzed the concentration of regulatory T cells, M1 and M2 macrophages comparing with control.

Materials and Methods
Sixteen Foxp3EGFP-Cre female mice underwent laparotomy under general anesthesia for endometriosis induction or Sham procedure. After the six weeks, animals were sacrificed and we inspected their abdominal and pelvic cavity, identifing the lesions and collecting the peritoneal fluid for analysis by flow cytometry of Treg lymphocytes, DC, M1 and M2 macrophages. Leukocytes were acquired in FACSCanto II and analyzes were performed using FlowJo software. Statistical analysis was performed and a P-value < 5% was considered.

Results
We observed statistically significant difference (p=0.0315) between Sham and Endometriosis group in the subpopulation of DC (CD11c+), with higher concentration of DC in Endometriosis group (42.45±20.37 Vs. 20.04±4.57). The subpopulations of regulatory T cells (15.58±14.64 Vs. 10.98±10.51), macrophages M1 (78.82±8.69 Vs. 69.84±10.62) and M2 (12 .08±9.56 vs. 6.20±3.76) showed no difference when comparing Sham and Endometriosis group.

Conclusion
These findings suggest that endometriosis induction in mice impact peritoneal fluid cell population, which might contribute to lesions progression. Some of these changes are similar to those identified in women with endometriosis, especially the increment in DC population.

Key words
Experimental endometriosis, immune response, dendritic cells

ASSESSING ENDOMETRIAL HORMONAL RESPONSE OF WOMEN WITH ENDOMETRIOSIS USING ENDOMETRIAL ORGANOIDS AND ASSEMBLOIDS

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Country where research was undertaken:
France

Introduction/Background
Around 30% of endometriosis patients suffer from infertility. Many factors can be involved, notably an altered endometrial receptivity. While progesterone resistance is described, precise mechanisms of dysfunctional receptivity are poorly understood. Furthermore, the steroid hormones quantity the endometrium is exposed to is not well controlled when directly using endometrial biopsies.

Materials and Methods
We used two 3D endometrial models derived from human endometrial biopsies from women with endometriosis (n=5) and unaffected controls (n=3). First, organoids, established from epithelial glands, then « assembloids » made from epithelial organoids mixed with stromal cells. These structures have been exposed to hormones to replicate the proliferative and the mid-secretory phase of the endometrium. To assess hormonal response in these models, we followed their growth by live-imaging and measured gene expression by RT-qPCR

Results
Our results indicate an altered response of our organoids to hormones in the endometriosis group. After estrogen treatment, there is a tendency towards a lower rate of establishment in organoids derived from patients with versus without endometriosis. Furthermore, key genes involved in endometrial hormonal response, decidualization and interaction with the embryo, have been assessed. These experiments showed an altered gene expression in the endometriosis group for some of these genes.

Conclusion
This work shows some interesting insights for endometriosis-related infertility, with a more precise assessment of differential steroid hormone response in key cell types. We will confirm our results by immunofluorescence. RNAseq will be performed on the assembloid model. This will allow a deeper characterization of hormonal response in well-controlled environments.

Key words
Endometrium, organoids, infertility

THEME: FERTILITY AND INFERTILITY IN ENDOMETRIOSIS

PERINATAL AND INFANT OUTCOMES FOLLOWING ART TREATMENT FOR ENDOMETRIOSIS ALONE COMPARED WITH OTHER CAUSES OF INFERTILITY: A DATA LINKAGE STUDY

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Country where research was undertaken:
Australia

Introduction/Background
To evaluate whether perinatal and infant outcomes differ between singleton births following assisted reproductive technology (ART) in women with endometriosis alone and those with other causes of infertility in a large population-based cohort.

Materials and Methods
This study included 29,152 ART-conceived singleton births from 24,116 mothers in New South Wales, Australia, born between 2010 and 2017. Endometriosis was identified from multiple sources, with cause of infertility categorized as: endometriosis alone (stratified by phenotype); endometriosis plus additional cause; non-endometriosis cause; and unstated cause of infertility. Generalized estimating equations were used to investigate associations between endometriosis and preterm birth (<37 weeks), very preterm birth

(<32 weeks), small-for-gestational-age (SGA), large-for-gestational-age (LGA), admission to neonatal intensive care unit, perinatal death, and infant hospitalisation up to age 2 years.

Results
Of the ART-conceived singleton births, 19.9% (5,806/29,152) were from mothers with endometriosis: 23.8% (1,379/5,806) from mothers with endometriosis alone and 76.2% (4,427/5,806) from mothers with endometriosis plus additional cause of infertility. There were 74.8% (21,795/29,152) births from mothers with infertility other than endometriosis and 5.3% (1,551/29,152) from mothers with an unstated cause of infertility. After adjusting for maternal age at the time of birth, parity, ART treatment characteristics, gestational hypertension and diabetes, smoking, and socioeconomic status, there was no overall association between cause of infertility and perinatal and infant outcomes. However, compared to women without endometriosis, those with deep endometriosis had a higher risk of preterm birth (adjusted relative risk [aRR] 1.75, 95% confidence interval [CI] 1.12–2.75) and SGA (aRR=1.58, 95% CI 1.05–2.37).

Conclusion
Reassuringly, perinatal and infant outcomes are generally comparable for ART-conceived infants born to mothers with endometriosis alone and those with other causes of infertility. For patients with deep endometriosis undergoing ART, the risks of preterm birth and SGA may be increased. Clinicians should be aware of these potential risks.

Key words
Assisted reproductive technology, endometriosis, perinatal outcome

FIRST BIRTH AND TOTAL FERTILITY RATE AFTER SURGICALLY VERIFIED ENDOMETRIOSIS – A NATIONWIDE REGISTER STUDY OF 9590 WOMEN

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Country where research was undertaken:
Finland

Introduction/Background
Endometriosis is associated with sub/infertility. However, data is scarce concerning birth rate after verified endometriosis at population level, especially among different endometriosis subtypes. We studied first birth rate and total fertility rate (TFR) after surgically diagnosed endometriosis according to different endometriosis subtypes.

Materials and Methods
A retrospective register-based study of nulliparous women aged 15-49 years, with surgically diagnosed endometriosis (n=9590) during 1998-2012 in Finland. We formed sub-cohorts of ovarian (n=3020), peritoneal (n=3146) and deep (n=659) endometriosis; other endometriosis (n=2765) comprised combined diagnoses, and rare forms of endometriosis. Follow-up started from the surgical diagnosis of endometriosis until first birth, emigration, sterilization/bilateral oophorectomy/hysterectomy, 50-years-of-age or December 31st 2019 – which ever came first. Main outcomes were first birth rate and TFR.

Results
Altogether 5184 (54.1%) women had first birth after surgically diagnosed endometriosis during 15.0 years of follow-up (median, interquartile range 11.5, 18.0). Women with peritoneal endometriosis had the highest (62.4%) and women with ovarian endometriosis (45.7%) the lowest first birth rate compared to other sub-cohorts (p<0.001). We plotted Kaplan-Meier curves of first birth and assessed restricted mean time survival

time (RMST) and RMST difference of first birth between the sub-cohorts. Adjusting RMST with age over 35 years, education, municipality, calendar time and prior IVF did not change the results.
TFR of parous women was significantly lower in women with combined/other endometriosis (1.78, SD 0.78) than peritoneal (1.84, SD 0.81), p<0.001. However, complete TFR among women achieving 50 years-of-age did not differ significantly between sub-cohorts.

Conclusion
Over half of the women in the cohort had first birth after surgically diagnosed endometriosis. Women with peritoneal endometriosis had the highest rate of first births. Complete TFR at 50 years-of-age did not differ between endometriosis subtypes.

Key words
Endometriosis, first birth, fertility rate

THE ENDOMETRIOSIS LONGITUDINAL FERTILITY STUDY (ELFS): PRE-PREGNANCY TREATMENT DECISIONS FOR WOMEN WITH MODERATE OR SEVERE ENDOMETRIOSIS WHO ARE TRYING TO CONCEIVE

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Countries where research was undertaken:
Australia and Israel

Introduction/Background
Endometriosis is associated with reduced pregnancy rates in women attempting both spontaneous and assisted conception. At present, the effect of surgery on the fertility outcomes of women with moderate/severe endometriosis remains unanswered. Treatment decisions are complex, particularly in those without pain symptoms seeking to optimise fertility outcomes.

Materials and Methods
The Endometriosis Longitudinal Fertility Study (ELFS) is a prospective cohort study aiming to measure and compare monthly fertility outcomes in women with evidence of moderate/severe endometriosis. Comparisons are planned between participants undertaking surgical or conservative management pre-pregnancy, who attempt conception naturally or with assisted reproductive technologies (ART). This interim report aims to assess outcomes for participants recruited during the first 36months of the study. Survey data is collected via the purpose-built ELFS App, with questionnaire timing dependent on a learned logic within the App.

Results
Following 36months of recruitment, there are 229 patients enrolled in ELFS. 154(67%) participants are in the surgical cohort (of which 86(56%) have undergone planned surgery) and 75(33%) are in the conservative cohort. Participants <35yrs and >35yrs of age have similar rates of pre-pregnancy surgical management. 59(26%) participants have indicated that they were actively trying to conceive during the study period and 279 survey cycles have been recorded for these participants. Of these, 80(29%) cycles utilised ART compared to 199(71%) cycles of natural conception attempts. A total of 33 pregnancies have been recorded, 19(58%) from the surgical cohort and 14(42%) from the conservative cohort. To date, there have been eight live births recorded, 5 from the surgical cohort (63%) and 3 from the conservative cohort (37%).

Conclusions
ELFS plans to continue recruitment for a further 24months. Additional long-term data is required to determine if fertility and pregnancy outcomes are influenced by surgical management of moderate to severe endometriosis.

Key words
Endometriosis, fertility, assisted reproductive technologies

EFFECTIVENESS OF SURGERY FOR INFERTILE WOMEN WITH ADVANCED STAGE ENDOMETRIOSIS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Objective
Advanced-stage endometriosis can significantly impact women's fertility. There is ongoing debate on whether surgery for advanced stage endometriosis improves spontaneous conception and in vitro fertilization (IVF) outcomes. Therefore, we aimed to compare pregnancy rates in women with advanced-stage endometriosis suffering infertility undergoing surgery vs IVF treatments.

Materials and Methods
Following prospective registration with PROSPERO and adherence to PRISMA guidelines, MEDLINE, Embase, and Cochrane databases were searched for comparative studies investigating the effects of surgical treatments on fertility in patients with advanced-stage endometriosis. Advanced-stage endometriosis was defined as moderate-to-severe endometriosis as per the ASRM classification and/or presence of deep infiltrating endometriosis. Comprehensive meta-analysis software was utilized for meta-analysis and heterogeneity assessment. The risk of bias in non-randomized studies was evaluated using the Newcastle-Ottawa Scale (NOS).

Results
Of the 120 reviewed abstracts, we screened 86 full-text articles. Five studies comparing pregnancy rates following surgical treatment to IVF alone met the inclusion criteria for the meta-analysis. No statistically significant difference was observed between pregnancy rates following surgery and pregnancy rates following IVF alone (RR, 1.34 [95% CI, 0.91-1.57, p= 0.24). High heterogeneity among studies was observed. Four studies preferred surgery pre-IVF, while one indicated no benefit and had the lowest NOS score.
In a separate analysis including 49 observational studies, spontaneous pregnancy rate post-surgery was compared with IVF treatment outcomes. The event rate for spontaneous pregnancies after surgery was 0.315 (95% CI, 0.274-0.358), whereas the event rate for IVF pregnancies post surgery was 0.264 (95% CI, 0.234-0.296).

Conclusion
A meta-analysis of comparative studies found no significant difference in pregnancy rates between surgery and IVF. However, a meta-analysis of observational studies showed higher spontaneous pregnancy rates post-surgery compared to IVF. Randomized controlled trials are needed to clarify surgery's effect on spontaneous and IVF conception in advanced-stage endometriosis.

CHRONIC ENDOMETRITIS AND ENDOMETRIOSIS: TWO SIDES OF THE SAME COIN?

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Country where research was undertaken:
Switzerland

Introduction/Background
Both chronic endometritis and endometriosis are common entities in infertile patients. The association and the co-existence of these two entities are poorly evaluated. The aim of this systematic review and meta-analysis was to examine the association between chronic endometritis and endometriosis and to find the prevalence of chronic endometritis in women with endometriosis.

Materials and Methods
A systematic electronic search was conducted using the MEDLINE, Scopus and Cochrane databases up to May 2022. Observational studies which examined the prevalence of CE in women with endometriosis were included. Newcastle-Ottawa Scale was used for the quality assessment. Odds ratios (OR) with

95% confidence intervals (CIs) for dichotomous outcomes and pooled prevalences with 95% CIs were calculated.

Results
855 studies were identified, of which six studies were included in the systematic review and five in the meta-analysis. The prevalence of chronic endometriosis in women with endometriosis was 28%, with higher frequency observed in women with endometriosis rASRM stage III-IV (43%) in comparison to women with endometriosis rASRM stage I-II (25%). The meta-analysis showed a significantly higher chronic endometritis in women with endometriosis in comparison to the control group (five studies, 264 endometrioses vs. 435 control, OR=2.07; 95% CI 1.11-3.84, I2 43%, p=0.02).

Conclusion
The present meta-analysis showed a significantly higher risk of chronic endometritis in women with endometriosis in comparison to the control group. These findings contribute to a better understanding of the causes and consequences of endometriosis and chronic endometritis and may help in the development of more efficient treatment strategies for women with associated infertility.

Key words
Endometriosis, chronic endometritis, infertility

DISTINCT DIFFERENCES IN THE GUT MICROBIOME COMPOSITION IN PREGNANCIES AFFECTED BY ENDOMETRIOSIS

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Country where research was undertaken:
Australia

Introduction/Background
Endometriosis impacts both natural and assisted conception. The gut microbiome has been implicated in both endometriosis and infertility and is emerging as a potential biomarker for these conditions. However, there are currently no studies on the gut microbiome of women with endometriosis who can and cannot conceive.

Materials and Methods
Stool samples were collected *preconception* from three cohorts: *n*=28 fertile healthy controls (control-fertile), *n=17* fertile women with endometriosis (endo-fertile), *n*=11 infertile women with endometriosis (endo-infertile). Further stool samples were collected at trimesters 1, 2 and 3 in the control-fertile and endo-fertile cohorts. Shotgun metagenomic sequencing was performed to analyse the composition of the microbiome. We compared the alpha-diversity and beta-diversity between the two cohorts then used differential abundance analysis approaches to detect for specific taxonomic differences.

Results
The mean ages of women within the three cohorts were 32.82 (control-fertile), 32.24 (endo-fertile), 33.55 (endo-infertile), and the mean Body Mass Index of women within the same three groups were 25.35, 24.63, and 24.36, respectively. Of the 56 participants, 51 women identified as white in ethnicity (Australian, American, Canadian and European). We compared the preconception gut microbiome from women diagnosed with endometriosis to control-fertile and observed significant differences ($p < 0.05$) in alpha- and beta-diversity. Further differences were also observed in the preconception gut microbiome when segregating women with endometriosis into endo-fertile and endo-infertile. Differential abundance analysis revealed potential markers emerging in trimesters 1 and 2 when comparing pregnant women, with or without endometriosis (endo-fertile vs control-fertile).

Conclusion
The results of this study reveal that the gut microbiome composition is different in pregnant women with endometriosis compared to pregnant women without endometriosis. This research could open new avenues for improving fertility and pregnancy outcomes for women affected by endometriosis.

Key words
Endometriosis, infertility, microbiome

COMPARATIVE EFFICACY OF COMBINED FSH AND LH VS. FSH ALONE IN OVARIAN STIMULATION AND FERTILITY OUTCOMES FOR ENDOMETRIOSIS PATIENTS

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Country where research was undertaken:
Israel

Introduction/Background
Endometriosis, commonly linked with infertility, often leads to lower IVF success rates compared to other infertility cases. This study examines differences in embryologic and clinical outcomes between pure follicle-stimulating hormone (FSH) and combined FSH plus luteinizing hormone (LH) treatments to determine optimal ovarian stimulation protocols for endometriosis patients.

Materials and Methods
This retrospective cohort study evaluated endometriosis patients who underwent IVF cycles for egg/embryo freezing or pregnancy from 2013 to 2023 at a tertiary medical center. Patients were grouped by ovarian stimulation protocol: pure FSH or combined FSH and LH. Primary outcome was oocyte retrieval, with secondary outcomes of pregnancy and live birth rates following embryo transfer. Statistical analysis included t-tests, chi-square tests, and multivariate analyses, adjusting for gonadotropin dose, BMI, age, and endometriosis characteristics.

Results
A total of 411 oocyte retrieval cycles among 238 endometriosis patients (mean age 32.3 years) were analyzed. Of these, 231 cycles (56.2%) used pure FSH for ovarian stimulation, while 180 cycles (43.8%) used combined FSH+LH. Ovarian stimulation outcomes were significantly improved in pure FSH cycles, with higher numbers of retrieved (9.33±5.9 vs. 7.41±5.3; P=0.003) and fertilized oocytes (3.23±3.6 vs. 2.32±2.6; P=0.013). Clinical pregnancy rates, however, did not differ significantly between groups. Multivariate analysis identified younger age (P=0.02; 95% CI, -0.22 to -0.01), antagonist protocol (P=0.02; 95% CI, -4.4 to -0.33), and overall gonadotropin dose (P=0.043; 95% CI, -0.02 to -0.001) as positive predictors of outcomes. Endometriosis characteristics, including prior surgical intervention, showed no significant association with IVF success.

Conclusion
This study suggests that pure FSH yields superior ovarian stimulation outcomes for endometriosis patients compared to combined FSH + LH. Tailoring stimulation protocols may enhance IVF success and provide insights into endometriosis's effects on fertility. Further prospective studies are warranted to substantiate these findings.

Key words
Endometriosis, ovarian stimulation, IVF outcomes

DIFFERENTIAL GENE EXPRESSION AND CELL TYPES IN ENDOMETRIUM AND BLOOD DURING WINDOW OF IMPLANTATION (WOI) IN PATIENTS WITH ENDOMETRIOSIS

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Country where research was undertaken:
United States of America

Introduction/Background
Studies that investigated single-cell differences in the endometrium of endometriosis patients have yet to focus on WOI or explored systematic factors during this menstrual phase. We applied single-cell transcriptomics and spatial-omics to the endometrium and blood in WOI to understand local and systemic factors that altered implantation in endometriosis.

Materials and Methods
Endometrial biopsies and peripheral blood were collected from subjects with and without endometriosis during WOI. Single cell RNA sequencing (sc-RNAseq) was performed on endometrial and peripheral blood mononuclear cells (PBMC). Additionally, we profiled the endometrial biopsies by high resolution, imaging based in situ spatial transcriptomics (Xenium) to spatially locate cells. Results were compared between samples obtained from endometriosis vs control subjects as well as

during vs. outside of WOI.

Results
We recruited 15 participants for WOI endometrium and blood collection, across both control and endometriosis cohorts. We generated a single cell dataset of ~100,000 cells across PBMC and endometrium. Differential analysis revealed unique transcriptional profiles in the WOI in endometriosis vs control subjects. These differential changes in cell types and gene expression were then confirmed by mapping the endometrium using Xenium 5k probeset.

Conclusion
Through this study, we created a transcriptomic and spatial atlas of the WOI endometrium in endometriosis and profiled systemically peripheral blood at the single cell level. This study will help us understand how endometriosis impacts implantation and pregnancy in patients with endometriosis.

Key words
Receptivity, implantation, endometriosis

THEME: GENETIC AND -OMICS TECHNOLOGIES

THE VAGINAL MICROBIOME IN ENDOMETRIOSIS: INSIGHTS FROM THE ISALA CITIZEN-SCIENCE PROJECT

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Country where research was undertaken:
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Introduction/Background
The vaginal microbiome, characterized by Lactobacillus dominance in health, is crucial to women's health and reproduction. Yet its ecology in debilitating diseases like endometriosis remains poorly understood. Here, we analysed the vaginal microbiome in women with and without endometriosis that participated in Isala, world's largest co-creational citizen-science project centered on studying the vaginal microbiome [1].

Materials and Methods
We analysed health questionnaires from participants with (n=106) and without endometriosis (n=3345) to assess the prevalence of various conditions, applying Fisher's exact test for each condition followed by multiple testing adjustment. To explore potential microbial associations, we examined the participants' vaginal microbiome profiles ($n_{endometriosis}$=73, $n_{controls}$=3265) using V4 16S rRNA gene sequencing, performing diversity and differential prevalence and abundance analyses followed by multiple testing adjustment to identify taxa potentially linked to endometriosis.

Results
Participants with endometriosis showed a higher prevalence of multimorbidity, including conditions such as subfertility, migraine, polycystic ovarian syndrome, bacterial vaginosis, dyspareunia, pelvic pain during menses, and irritable bowel syndrome (IBS), compared to participants without endometriosis. Notably, the prevalence of IBS was almost three times higher among participants with endometriosis compared to the control group. V4 16S rRNA gene sequencing revealed no significant differences in bacterial diversity and *Lactobacillus* dominance between both groups. However, *Finegoldia* was significantly more prevalent and abundant in vaginal samples of participants with endometriosis. Interestingly, *Fusobacterium* was significantly more prevalent and abundant in samples from healthy participants, raising questions about the molecular heterogeneity of *Fusobacterium* and its role in reproductive health, as recent studies have linked *Fusobacterium* to endometriosis.

Conclusion
Citizen science proves to be a powerful tool to improve our understanding of understudied diseases like endometriosis. This study highlights a higher prevalence of multimorbidity in women with endometriosis and suggests a potential link with the vaginal microbiome, opening avenues for mechanistic research, diagnostics and therapeutics.

Key words
Vaginal Microbiome, Citizen science, Multimorbidity

Reference
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11, pp. 2183–2195, Oct. 2023, doi: 10.1038/s41564-023-01500-0.

THEME: LIVED EXPERIENCES AND QUALITY OF LIFE IN ENDOMETRIOSIS

EFFECTS OF FREQUENT COLLECTION OF PATIENT-REPORTED OUTCOME MEASURES (PROMS) USING AN EXPERIENCE SAMPLING METHOD IN PATIENTS WITH ENDOMETRIOSIS

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Country where research was undertaken:
The Netherlands

Introduction/Background
Pain severity depends on physical pathology and maladaptive coping, with a possible important role of pain insight. We aimed to study the effect of intensive real-time symptom assessment by an experience sampling method (ESM) on pain, psychological symptoms and quality of life. For clinical implementation compliance needs to be investigated.

Materials and Methods
This prospective single-arm cohort feasibility study was conducted in an endometriosis expertise center. Women with deep endometriosis and at least one pain symptom NRS ≧ 4 could be included. Participants used an ESM application to measure endometriosis complaints 10 times daily for 3 days per week over 6 weeks. Change in pain score as primary and affective symptoms and quality of life as secondary outcomes were assessed via validated questionnaires at baseline (week 0) and week 7. In addition, application compliance was measured

Results
Twenty-two eligible patients were recruited between October 2023 and February 2024. After realistic counseling only 9 patients were willing to participate. Analyses on pain scores and secondary outcome measures showed no effects on the use of the ESM-app. Average, real-time pain scores with the ESM-app were significantly lower compared to the retrospective, follow-up pain score for chronic pelvic pain (mean difference 1.8). Compliance, as measured with the number of filled in questionnaires per day with the ESM-app declined significantly over the study period. Participants reported generally positive experiences with the app, despite encountering some technical issues.

Conclusion
Six weeks of intensive symptom assessment does change pain or QOL. Real-time pain scores are lower than the retrospective scores. Despite positive participant feedback, app-compliance declined over time. We need to find out the optimal intensity of scoring complaints and the willingness of the women to fully participate.

Key words
Pain, real-time assessment

MENSTRUAL DISTURBANCE FROM ADOLESCENCE TO ADULTHOOD: A 7-YEAR FOLLOW-UP OF THE MENSTRUAL DISORDER OF TEENAGERS (MDOT-2) STUDY

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Country where research was undertaken:
Australia

Introduction/Background
Menstrual disturbance is a common healthcare presentation. Symptom overlap between primary and secondary dysmenorrhea (e.g., endometriosis) contributes to diagnostic delays. Young women are not receiving timely management resulting in physical, psychosocial, and reproductive consequences. Whilst impact during adolescence is well established, there is limited research looking at persistence into adulthood.

Materials and Methods
This study aimed to conduct a follow-up of the 2016 MDOT study to determine if adolescents who were screened for menstrual disturbance sought medical intervention and received a diagnosis. (1) Through conducting a quantitative questionnaire with Australian women aged 22 to 25 (n=40), data was collected on self-reported menstrual disturbance, medical intervention, menstrual-related life interference, and patient-provider management experiences. Descriptive

analysis was performed. Fisher's exact test and Mann-Whitney tests were used as appropriate.

Results
Whilst nearly all participants (87.5%) presented to a health professional regarding their menstrual disturbance, less than half received a formal diagnosis (47.5%). Diagnoses included endometriosis (n=9) and polycystic ovarian syndrome (n=8), with marked delays in time to diagnosis from initial presentation. For participants with endometriosis, 33.3% had an increase and 55.6% had no change from their 2016 Period ImPact and Pain Assessment (PIPPA) screening tool score. A strong and consistent symptom profile (pain, gastrointestinal and mood symptoms) was found to persist into adulthood. Participants reported substantial interference with life activities, including work, tertiary studies and sport/exercise. Many participants felt unsatisfied with healthcare interactions regarding their menstrual health concerns, with gaps identified in clinician attitudes and patient education.

Conclusion
Menstrual disturbance-associated pain and symptoms are still prevalent into adulthood, with many not receiving a diagnosis. Menstrual disturbance, including endometriosis, was reported to negatively impact many daily life activities and experiences in adulthood, notably work attendance and performance. The patient-provider experience for menstrual presentations needs to be improved in Australia.

Key words
Menstrual disturbance, dysmenorrhea, endometriosis

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"MY BODY CONTROLS MY LIFE." UNDERSTANDING THE MOST PERTINENT AREAS OF LIFE FOR AUSTRALIAN PEOPLE LIVING WITH ENDOMETRIOSIS.

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Country where research was undertaken:
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Introduction/Background
Endometriosis impacts 11% of reproductively-aged women. People with endometriosis experience physical, emotional, relational, and mental well-being outcomes that contribute to their quality-of-life, exacerbating feelings of being, unheard, or isolated. A clinical questionnaire designed to understand the impacts of endometriosis on quality-of-life and optimise support for people with endometriosis is overdue.

Materials and Methods
A survey using REDcap was undertaken in August 2024, recruiting via social media and Endometriosis support platforms for people diagnosed with endometriosis, aged 18 years and over and living in Australia. The survey included demographics, endometriosis history and symptomology, as well as the Schedule for the Evaluation of Individual Quality-of-Life (SEIQoL). Qualitative data was derived via content analysis. Primary findings included a variety of themes arising from the SEIQoL questionnaire.

Results
Of the study sample, 44% and 28% had a family history of endometriosis and fibroids, respectively. The most common symptoms of endometriosis reported were pelvic pain (96%), fatigue (92%), bloating (81%), ovulation pain (81%), heavy bleeding (80%) and lower back pain (78%). All participants reported at least one endometriosis symptom. A final cohort of 75 people identified five crucial areas of life impacted by endometriosis. These include relationships, career, family, health, and hobbies. Participants described relationship difficulties with their romantic partner, family and friends, issues with career stability and mental health. Unpredictable symptoms created exacerbated feelings of guilt and worry due to a continued lack of understanding in relationships, the workplace, family, and friendships.

Conclusion
Endometriosis impacts many pertinant life areas. The themes derived from this study will inform the development of a tool to assess quality-of-life in this population. Determining the most important areas of impact may provide a holistic understanding of endometriosis quality-of-life, not just the symptomology, which may assist clinical and social care.

Key words
Endometriosis, quality-of-life, assessment

THE EFFECTS OF BEING IN THE UNIFORMED SERVICES ON HEALTH-RELATED QUALITY OF LIFE IN PEOPLE WITH ENDOMETRIOSIS

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Country where research was undertaken:
United Kingdom

Introduction/Background
Endometriosis symptoms, especially pain and fatigue, often limit career growth, particularly in demanding roles. Nearly 40% of individuals report hindered career development, and 50% experience reduced work capacity. With limited research on workplace adjustments, this study aimed to examine HRQoL in those with endometriosis in the uniformed services.

Materials and Methods
Patients with endometriosis were recruited between 11 March 2021 and 31 July 2022 via social media, support groups, and the British Society of Gynaecological Endoscopy (BSGE)-approved centres. A total of 2056 individuals aged 16 and above participated in this mixed-method study, which included the Endometriosis Health Profile-5 (EHP-5) and Pelvic Pain Impact Questionnaire (PPIQ). The data from 7 interviews with people in careers in uniformed services was used for interpretative phenomenological analysis (IPA).

Results
EHP-5 scores show that participants who had resigned reported a significantly higher negative impact on HRQoL compared to those employed in uniformed services and non-uniformed roles. Navy participants (n=4 (M=40.00 **±** 2.71)) exhibited significantly higher scores than Fire & Rescue (n=5 (M=21.00 **±** 6.20, p<0.0001)), Healthcare & Medical Services (n=166 (M=24.95 **±** 7.82, p<0.0001), Air Force & Army (n=4 (M=26.75 ± 10.90, p<0.05)), and Police & Law Enforcement (n=37 (M=20.78 **±** 9.56, p<0.0001)) suggesting endometriosis had a greater negative impact on HRQoL in Navy personnel. PPIQ scores also showed statistically higher scores in the Navy participants (n=4 (M=97.32 **±** 1.79)). IPA identified 6 major themes including impact in the workplace, dismissal of pain or experiences, navigating physical health, and interpersonal relationship impact.

Conclusion
This study reveals substantial differences between groups, underscoring the importance of developing tailored, inclusive healthcare approaches for those with endometriosis. The identified IPA themes provide a valuable framework for recognising and addressing the unique and complex challenges faced by individuals in uniformed services, who often experience specific barriers to care.

Key words
Endometriosis, mixed-methods, uniformed-services

SILENT BATTLES: REVIEWING THE IMPACT OF WAR ON ENDOMETRIOSIS PATIENTS

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Country where research was undertaken:
Israel

Introduction/Background
On October 7, 2023, Israel faced a severe terror attack impacting Jewish and non-Jewish victims alike. Since then, Israel has been

involved in conflict on multiple fronts. This study examines the compounded effects of ongoing war on endometriosis symptoms, physical and mental health, and illness perception of women with endometriosis.

Materials and Methods
The study was conducted in August 2024 with 841 participants who completed an online questionnaire via Qualtrics. Participants were recruited through social media and QR codes in endometriosis clinics. Statistical analyses were performed using SPSS and R software. Participants assessed their health across three time points: pre-war, two months post-war onset, and one year later. The study was conducted in accordance with the Declaration of Helsinki and received ethical approval.

Results
82.8% of participants were directly affected by war-related stressors. Mental health deteriorated substantially, with anxiety rates increasing from 34.7% to 94.1% and depression from 39.6% to 89.3% ($p<0.001$).

Physical health was also affected, with 77.4% reporting worsening endometriosis symptoms and 62.5% indicating overall medical decline. All specific symptoms, including pelvic pain, digestive and urinary symptoms, dyspareunia, fatigue and more, showed significant deterioration ($p<0.001$). Additionally, 38.9% and 14.4% of participants reported increased usage of pain and hormonal medications, respectively, indicating higher symptom-management needs.

War-related stress levels significantly correlated with both medical condition ($r=0.24$, $p<0.001$) and anxiety/depression levels ($r=0.36$, $p<0.001$). Multivariable analysis revealed that war-related stress (aOR=1.57, 95%CI=1.26-2.00), number of war-related stressors (aOR=1.20, 95%CI=1.03-1.40), and participants' anxiety/depression level (aOR=1.57, 95%CI=1.17-2.11) were significantly associated with symptom exacerbation.

Conclusion
These findings underscore the profound impact of war-related stressors on both physical and psychological health in women with endometriosis. These results emphasize the importance of integrating mental health support and tailored medical care to improve outcomes during and after periods of conflict.

Key words
War, illness-perception, endometriosis

LIVED EXPERIENCES OF WOMEN WITH ENDOMETRIOSIS IN KENYA

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Country where research was undertaken:
Kenya

Introduction/Background
It is estimated that endometriosis affects approximately 1 in 10 women of reproductive age resulting in physical and mental ill health[1]. There is a paucity of data on the psychological impact and the quality of life of women with endometriosis in Sub-Saharan Africa.[2].

Materials and Methods
Women with endometriosis were recruited through an online Support Group. A questionnaire was administered for quantitative data and a web-based focus group discussion for qualitative aspect. Themes were adapted from the 36-Item Short Form Health Survey questionnaire (SF-36) tool to assess health-related quality of life in the areas of pain, physical and social function, role limitations due to physical or emotional problems and mental health[3].

Results
Thirty women aged between 22 and 44 years participated. Respondents reported painful periods (30, 100%), stress and anxiety (24, 80%) fatigue and sleep disturbances (18, 60%) depression and suicide (12, 40%) social and relationship impact (24, 80%) impact on productivity (24, 80%) and infertility concerns (15, 50%).

Overall, the combination of physical pain, emotional distress and the uncertainty about treatment options led to a decline in the participants' quality of life. The struggle to balance personal, social, and professional lives while managing a chronic and often misunderstood condition confirms the profound impact that endometriosis has on the well-being of the women. The participants recommended a multidisciplinary approach to treatment, employer support & peer support networks.

Conclusion
This study highlights the significant psychological and quality of life related burden of endometriosis. It also emphasizes the benefit women with endometriosis may get from having access to multidisciplinary care, employer understanding and peer support networks.

Key words
Quality of life; endometriosis; low/middle income country

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THE ROLE OF SELF-COMPASSION AND DAILY FUNCTIONING IN INDIVIDUALS WITH ENDOMETRIOSIS: A DIARY STUDY

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Country where research was undertaken:
New Zealand

Introduction/Background
Research highlights the negative impact on quality of life in those with endometriosis. Yet, there is currently no published research looking at daily experiences of those living with this condition. Research suggests that self-compassion is a positive resource in improving quality of life in those with chronic health conditions.

Materials and Methods
The study examined whether participants with high levels of self-compassion are protected from the negative effect of the experience of daily symptoms and pain on daily mood. 151 individuals with endometriosis completed an online questionnaire (assessing trait self-compassion) followed by daily 5-minute questionnaires at the end of the day for 28 consecutive days measuring pain, endometriosis symptoms experienced (number and severity), mood, and an open-answer question regarding what they believe impacted their symptoms that day.

Results
The data has been collected but not yet analysed. This will be analysed in time for the conference. It is hypothesised that participants' mood will be lower on days when they experience more symptoms and/or report high levels of pain, but this association is expected to be weaker for participants with high levels of self-compassion.

Conclusion
The findings are expected to confirm that those with higher levels of self-compassion are better protected from negative impact on mood when experiencing daily symptoms and pain. This highlights the potential role of self-compassion in improving daily functioning of individuals with endometriosis and for future research looking at self-compassion interventions.

Key words
Self-compassion, daily functioning

LIVED EXPERIENCES OF ENDOMETRIOSIS PAIN COMMUNICATION WITH GENERAL PRACTITIONERS IN THE DUTCH HEALTHCARE SYSTEM

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Country where research was undertaken:
The Netherlands

Introduction/Background
Pain normalization and the difficulty to assess pain have been considered as key hurdles for timely endometriosis diagnosis, resulting in long diagnostic delays. Pain communication can be crucial to comprehensively address the pain with general practitioners, especially when they have a gatekeeping position, such as in the Netherlands.

Materials and Methods
Eleven online in-depth interviews were conducted with participants diagnosed with endometriosis in the last five years in the Netherlands. The age ranged from 25 to 46 years. The data was analyzed with a thematic analysis using ATLAS.ti and the Excel software.

Results
This research provides insights into the complex and multifaceted nature of pain communication. Due to the societal perception of menstruation complaints and the subjectiveness of pain, the participants experienced challenges in verbalizing their pain experiences. They shared feelings of a lack of pain acknowledgement from general practitioners during the consultations. This eventually sparked a transformation from the search for medical help from experts to advocation for their pain, through research, pain diaries and detailed descriptions. They critiqued the short and standard solution-oriented conversations with general practitioners, as well as the limited referrals to gynecologists, which often caused a diagnostic delay. To enhance the pain dialogue, the participants highlighted the need for more questions and examples from general practitioners to ensure more detailed pain conversations.

Conclusion
To receive medical attention, the participants felt the need to advocate for their pain, which influenced the patient-doctor communication dynamic. To manage this perceived communication imbalance, there is a need for more in-depth pain conversations, holistic consultation approaches, as well as increased attention on gynecological health conditions, such as endometriosis.

Key words
Pain communication, pain normalization, diagnostic delay

WELCOME TO THE #ENDOHOOD: A REVIEW OF SOCIAL MEDIA SPACES FOR THOSE WITH ENDOMETRIOSIS

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Country where research was undertaken:
United Kingdom

Introduction/Background
Social media has significant capacity to influence healthcare delivery. The development of online communities is well documented for conditions including asthma and stroke. Less is known about social media use amongst those with endometriosis. This review explores internet groups as an under-recognized supplement to healthcare, prompting greater clinician engagement online.

Materials and Methods
This scoping review was conducted according to the methodology developed by Arksey & O'Malley. It is the first piece of work bringing together commentary on endometriosis-related social media use and existing frameworks used to analyze other online communities. Relevant studies were identified through searches of MEDLINE and EMBASE. As an exploratory piece there were no predetermined exclusion criteria, provided articles were in or translated into English. A total of 26 articles from 2024-2024 were included.

Results
The literature on social media posts about chronic conditions typically explores the accuracy of medical content or offers sociological commentary.

Nine articles assess the evidence base of endometriosis posts across various platforms. All raised concerns about the reliability of information shared and called for expert engagement in the dissemination of educational materials online.

Three key themes emerged from analysis of online communities. First, online groups are perceived as an antidote to unmet needs in endometriosis patients accessing traditional healthcare, including problem solving and psychosocial support.

Further, such groups cultivate a sense of kinship amongst affected individuals. The exchange of experiences and peer validation of symptoms contributes to a collective narrative.

Finally, social media can facilitate open conversation around sensitive topics through anonymity within these communities.

Conclusion
Endometriosis is a condition with potential for profound psychological and psychosexual impact. Social media communities create a

space in which private suffering can become public and taboo subjects exploded. Clinicians have a responsibility to engage both with factual content curation and in addressing unmet care needs expressed by patients online.

Key words
Endometriosis; social media

A QUALITATIVE INVESTIGATION OF TREATMENT DECISION-MAKING FOR ENDOMETRIOSIS IN THE CONTEXT OF PREGNANCY PLANNING

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Country where research was undertaken:
Canada

Introduction/Background
Endometriosis patients are at higher risk of infertility and adverse pregnancy outcomes. Research is still unclear about whether certain endometriosis treatments may decrease these risks, which may lead to difficulties deciding between treatments. This study aims to understand how people with endometriosis who desire a future pregnancy navigate treatment decision-making.

Materials and Methods
Data are being collected through semi-structured, in-depth, individual interviews. Participants must live in British Columbia, Canada, must have been diagnosed with endometriosis by a medical doctor, and must either (1) currently be navigating endometriosis treatment decision-making while keeping in mind desire for a future pregnancy, (2) have experienced infertility in the past 2 years, and/or (3) have been pregnant in the past 2 years. Four patient partners with endometriosis have been involved in this project.

Results
Preliminary findings suggest that some endometriosis patients follow the authoritative advice of their physicians, while others research options and read about other patients' experiences to inform their decision-making. Previous treatment experiences are highly influential in determining which future treatments they consider. Endometriosis patients often feel uninformed about their treatment options and want to receive more credible information directly from their physicians. Many feel they lack choice in their treatment plans and that physicians take a blanket approach to treatment rather than considering nuances of individual cases. Patients desire more holistic care, which includes being made aware of non-hormonal and non-surgical approaches to endometriosis management. Participants also wished their physicians had proactively discussed potential fertility and pregnancy challenges that can occur with endometriosis.

Conclusion
This study highlights that endometriosis patients are frustrated with available treatment options and their education around these treatments. They wish to be presented with both traditional medical approaches and alternative health management strategies. Family planning discussions should occur soon after diagnosis to prepare patients for potential challenges.

Key words
Pregnancy, fertility, qualitative

DISTRESSING MEDICAL EVENTS, MEDICAL TRAUMA AND EFFECTS ON CARE SEEKING IN ENDOMETRIOSIS

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Country where research was undertaken:
Australia

Introduction/Background
Medical trauma refers to an emotional reaction following a traumatic medical event, with some of those affected developing Post-Traumatic Stress Disorder (PTSD). To date, medical trauma in people with endometriosis has received little attention from researchers.

Materials and Methods
Overall, 468 Australian adults with

endometriosis completed a mixed-methods online survey. Participants were asked whether they have experienced medical trauma and whether the events affected their care or diagnosis seeking. Participants also self-reported PTSD diagnoses and whether these were associated with endometriosis-related experiences. Qualitative template analysis and content analysis were used.

Results
As many as 80% of the sample reported incidences of medical trauma, with the creation of six sub-themes: Doctor Knows Best; Acting in an Unprofessional or Unethical Manner; The Power of Words, Procedures Create Vulnerability; and Gender and Sexuality Based Discrimination. Within these themes, the most common events were gaslighting, dismissal and normalisation (57%), physically uncomfortable or painful procedures (19%), emotionally uncomfortable procedures (10%), medical misinformation (10%), attributing symptoms to mental illness (10%), gatekeeping (10%) and lack of informed consent (8%). Of those who experienced medical trauma, 80% reported that their care or diagnosis seeking was subsequently affected, through delaying further care. Overall, 21% of the sample were diagnosed with PTSD, with 7% due to endometriosis-related experiences and 63% partially related.

Conclusion
People with endometriosis experience concerning levels of medical trauma. Trauma informed care practices need to be incorporated into medical training and professional development programs for doctors.

Key words
Medical trauma, psychology

INFORMATIONAL NEEDS OF INDIVIDUALS WITH ENDOMETRIOSIS IN AUSTRALIA

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Country where research was undertaken:
Australia

Introduction/Background
Informational support is crucial for people living with endometriosis to cope with the consequences their condition has on their physical and mental health and its wider effects on their everyday life. The aim of the study was to understand the informational needs of individuals with endometriosis in Australia.

Materials and Methods
This cross-sectional study used an anonymous, mixed-methods online questionnaire. Participants were recruited through convenience sampling via Facebook advertisements, as well as newsletters and social media pages of women's health services. Eligible participants included individuals aged 18 or older, living in Australia, with a diagnosis or suspicion of endometriosis. The survey comprised nine sections, starting with demographics, followed by information needs, and concluding with a section on preferred information formats.

Results
A total of 265 participants from seven states were included in the analysis. Most participants were diagnosed with endometriosis in the last five years. Participants expressed a need for more information across all provided topics. A particular need was identified for more guidance on disease management and navigating the healthcare system. Financial challenges were also a recurring concern, as endometriosis often results in substantial out-of-pocket costs for diagnosis and treatment, creating a significant burden. Further, responses included experiences of dismissal and medical gaslighting by healthcare professionals, often accompanied by a lack of knowledge on the providers' part. Consequently, patients had to become their own advocates and experts in their conditions, a challenging task made more difficult by the scarcity of information.

Conclusion
Understanding the information needs of individuals with endometriosis is essential for providing adequate patient support and addressing the dismissal they often experience from healthcare professionals. This research can inform the development of more comprehensive information resources that directly respond to the specific needs of the endometriosis community.

Key words
Information needs, patient support, endometriosis

A REQUEST FOR UNDERSTANDING, EMPATHY, COMPASSION, AND ACCEPTANCE: LIVED EXPERIENCE RECOMMENDATIONS FOR ENDOMETRIOSIS HEALTHCARE PRACTITIONERS.

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Country where research was undertaken:
Australia

Introduction/Background
Difficulties associated with patient and healthcare practitioner interactions have been linked to insufficient access to medical support, information, feelings of mistrust, despondency, and fear. Qualitative findings suggest healthcare practitioners who validate patient experiences and respond with understanding and compassion foster a positive patient-practitioner alliance and greater engagement in healthcare systems.

Materials and Methods
Forty-one individuals participated in semi-structured interviews to explore their experiences accessing endometriosis-related healthcare, with a view to developing patient-centered recommendations for enhancing the positive patient-practitioner alliance. An interpretive phenomenological approach, with a pragmatic feminist lens, was used to understand the lived experience accounts, with a view to informing recommendations for change within healthcare practices. Reflexive thematic analysis was used to interpret the interview data, with researcher reflexivity to ensure data dependability.

Results
Participants called for a *Greater Understanding of the Whole-of-Person Impacts,* asking for greater acknowledgement of the variety, severity, and magnitude of endometriosis symptoms. Participants described *Negative Past Experiences with Medical Practitioners,* feeling unheard, dismissed, undervalued, or disrespected. They noted that practitioners failed to communicate and share important information regarding their body and healthcare options, removing their personal agency. Participants detailed the *Need for Better Medicare Care*, reporting a sense of “having to fend for themselves” in the face of diagnostic delays, limited appointment availability, and a reluctance to facilitate specialist engagement by general practitioners. Accounts also reflected *Positive Medical Practitioner Qualities,* underpinned by medical practitioners who were transparent regarding their knowledge of endometriosis, empathic, compassionate, proactive, and provided a space to be heard.

Conclusion
The lived experience of people with endometriosis provides valuable insights for refining healthcare relationships. Participants recommended increased access to interdisciplinary healthcare, endometriosis-related continuing professional development for practitioners, increased knowledge and understanding of less invasive testing and the psychological impacts of endometriosis, and a greater emphasis on developing positive patient-practitioner relationships.

Key words
Qualitative, practitioners, healthcare

ENDOMETRIOSIS AND CHRONIC PELVIC PAIN DIAGNOSIS AND MANAGEMENT IN AUSTRALIAN PRIMARY CARE SETTINGS: PERSPECTIVES OF GENERAL PRACTITIONERS, STAKEHOLDERS AND PATIENTS.

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Country where research was undertaken:
Australia

Introduction/Background
In Australia, 14% of women are diagnosed with endometriosis by 44-49 years old. Women experience significant delays in diagnosis of approximately 6-8 years. General Practitioners (GPs) are often the first point of contact in the healthcare system for patients and are the ‘gatekeepers’ to hospital services.

Materials and Methods
This study aimed to explore the perspectives of women with endometriosis or CPP (patients), GPs and stakeholders from endometriosis-based organisations regarding endometriosis and chronic pelvic pain (CPP) diagnosis and management in primary care settings. This was a qualitative descriptive study involving individual interviews with GPs

and stakeholders, and focus group discussions with patients. Interviews and focus groups were conducted online via zoom. Inductive thematic analysis was undertaken on each group separately to identify key themes.

Results
Ten GPs, eight stakeholders, and 17 patients from across Australia participated. All participant groups highlighted: the significant impact of endometriosis and CPP on patients' health and quality-of-life; limited access to and affordability of healthcare services; challenges in reaching a diagnosis due to the complexity of the conditions; benefits of multidisciplinary care; and the lack of community awareness about the conditions and what is normal menstruation. They perceived gaps in health professionals' knowledge and skills regarding endometriosis and CPP. GPs questioned if they could make a clinical diagnosis for endometriosis and CPP, expressing a desire for further guidance about these complex conditions. Stakeholders and patients highlighted how current management approaches do not meet patient needs.

Conclusion
GPs need further guidance to support diagnosis and management. Additional support for patients is required, particularly in improving healthcare access and affordability. We recommend the development of evidence-based tools for use by GPs and patients, to improve endometriosis and CPP healthcare in general practice settings.

Key words
Endometriosis, primary care, management

THEME: MODELS OF CARE IN ENDOMETRIOSIS

PERSPECTIVES AND PRIORITIES FOR ENDOMETRIOSIS MULTIDISCIPLINARY TEAM CARE IN AUSTRALIA: A QUALITATIVE MIXED-METHODS STUDY INVOLVING PATIENTS, CAREGIVERS AND HEALTH PROFESSIONALS

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Country where research was undertaken:
Australia

Introduction/Background
Multidisciplinary team (MDT) care is fundamental for managing endometriosis. There remains a lack of consensus on what a MDT care model should include in an Australian setting. This study evaluated both patient and health professional perspectives on MDT care models for endometriosis and pelvic pain in Australia.

Materials and Methods
A co-designed mixed-methods study was developed by an advisory group of 14 healthcare professionals, research academics and people with endometriosis. Online surveys capturing quantitative and qualitative data were disseminated to patients/carers and healthcare professionals. Thematic analysis was performed on qualitative data. Consensus statements were developed based on the themes generated in the qualitative analysis. Consensus statements were refined, agreed upon and ranked during 2 focus group meetings, for each consumer group.

Results
Participants included 29 healthcare professionals and 24 patients/carers.

When asked to prioritise services, patients ranked gynaecologists, general practitioners, and imaging as top priorities, and healthcare professionals ranked gynaecologists, pain specialists, and pelvic floor physiotherapists as most essential.

The qualitative analysis resulted in 5 themes: clinic environments, staff interactions, services and care coordination, goal setting and resources. Patients valued empathetic, experienced clinicians and preferred options for face-to-face and telehealth interactions. Financial strain was a significant concern. Both groups stressed the importance of up-to-date, evidence-based information and personalised care.

Five consensus statements were developed and ranked, all participants agreed or strongly

agreed with these. The first statement related to “MDT meetings should be part of essential care for the development of treatment pathways for people with endometriosis.”

Conclusion
This study underscores the need for person-centred, holistic, and accessible MDT clinics for endometriosis and pelvic pain in Australia. The consensus statements provide a blueprint for developing such clinics. Implementing these recommendations may enhance endometriosis care quality, improving patient experiences and outcomes.

Key words
Multidisciplinary care, co-design, model of care

MODELS OF CARE IN ENDOMETRIOSIS: A PANEL DISCUSSION ON MULTIDISCIPLINARY APPROACHES IN AUSTRALIA’S “ENDO 22” CLINICS

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Country where research was undertaken:
Australia

Introduction/Background
This 3-year initiative established 22 Endometriosis and Pelvic Pain Clinics in primary care around Australia. It represents an innovative approach in multidisciplinary care. This presentation brings together representatives from clinics in Adelaide, Darwin, Perth and country NSW to evaluate the strengths, challenges, and lessons learned in these diverse settings.

Materials and Methods
Panellists from selected “Endo22” clinics will present case studies and practice insights, highlighting each clinic’s unique methods in managing pelvic pain through interdisciplinary collaboration. Emphasis will be placed on comparing strategies across regions, with a focus on clinical integration, allied health involvement, patient-centred care models, and adaptive practices based on each location’s experiences.

Results
The panel will discuss outcomes from diverse care pathways tailored to local needs, noting improvements in patient satisfaction, pain management, and quality-of-life measures. Strengths include enhanced access to expert care outside the hospital system, streamlined patient education, and region-specific clinical management. Challenges such as resource variability and clinician training needs will also be addressed, with recommendations for bridging gaps and advancing multidisciplinary endometriosis care across Australia.

Conclusion
This panel session provides attendees with actionable insights into the impact of multidisciplinary approaches within the “Endo22” framework, offering a roadmap for scalability, improved patient outcomes, and the future of collaborative models in varied healthcare environments.

Key word
Endometriosis, models of care, multidisciplinary

PEER EMPOWERED ENDOMETRIOSIS PAIN SUPPORT (PEEPS): RESULTS OF AN INTERDISCIPLINARY GROUP CARE PILOT CLINICAL TRIAL

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Country where research was undertaken:
United States of America

Introduction/Background
Traditional treatments for endometriosis-associated pain aim to treat the lesions; however, even the most definitive surgeries fail to prevent residual or recurrent pain. Patient-centered treatments aimed at pain management and overlapping conditions, such as pelvic floor dysfunction and mood disorders, have some efficacy, but are not broadly used or accessible.

Materials and Methods
We developed PEEPS, an interdisciplinary group care program comprised of eight, 2-hour weekly sessions of education, physical therapy, mindfulness, yoga, pain coping strategies, and peer support. In order to demonstrate feasibility in recruitment and retention and obtain preliminary data on efficacy, women with surgically diagnosed

endometriosis aged 18-48 were recruited to a single-arm feasibility pilot trial between February 2023 and December 2024. Descriptive statistics were performed for demographics, and mixed-effects modeling for patient reported outcomes.

Results
Of the 33 women who enrolled in PEEPS, 82% (n=27) attended ≥6 sessions. Median participant age was 33 years [range 22-45]. Majority of participants had 1 prior surgery for endometriosis (70%, n=21) and stage III/IV disease (53.3%, n=16). Pelvic floor dysfunction (45.4%, n=15), migraines (36.4%, n=12), and irritable bowel syndrome (30.3%, n=12) were the most frequent overlapping pain conditions. As compared to baseline, median pain interference decreased 1.5 points (p 0.34, post=54.2 post vs. pre=58.0) and pain intensity 1.6 points (p 0.22, post=58.1, pre=59.7). Quality of life measured by EHP-30 demonstrated 12.6-point improvement (p <0.005, post=44.2, pre=57.9). Participants showed improvement in the EHP-30 domains of: Pain (11.7 points), Control and Powerlessness (19.0 points), Emotional Well-being (11.9 points), Social Support (14.6 points) (p<0.005 for each).

Conclusion
PEEPS is a novel integrative group care intervention for women with endometriosis-associated pain that demonstrates excellent retention and shows promise in improving endometriosis-related quality of life.

Key words
Endometriosis, group care, integrative teams

THEME: MOLECULAR PROFILING AND HIGH THROUGHPUT TECHNOLOGIES

EXPLORATORY ANALYSIS OF THE MIRNOMA FROM MESENCHYMAL STEM CELLS ISOLATED FROM THE MENSTRUAL BLOOD OF ENDOMETRIOSIS WOMEN

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Country where research was undertaken:
Brazil

Introduction/Background
Understanding menstrual blood components uncovers molecular mechanisms in endometriosis. The presence of mesenchymal stem cells (MenSCs)[1], distinct miRNA profiles in endometriosis[2,3], and dysregulated miRNA biogenesis[4] and transcriptome[5] in endometriotic MenSCs reinforces that miRNome analysis in these cells may clarify MenSCs' role in endometriosis development.

Materials and Methods
This novel case-control study analyzed the miRNome of MenSCs from women with (n=10) and without endometriosis (III/IV ASRM, n=10), all without hormonal therapy, using Next Generation Sequencing. Differential expression of miRNAs (DEmiRs) was assessed via the nf-core/smrnaseq pipeline[6] and DESeq2 R[7]. Functional enrichment of genes and pathways regulated by DEmiRs was conducted with multiMiR[8], Cytoscape[9] and WebGestalt[10], providing insights into molecular mechanisms associated with endometriosis. Supported by FAPESP 2013/22431-3.

Results
We identified nine DEmiRs: hsa-miR-1271-5p, hsa-miR-125b-2-3p, hsa-miR-181a-2-3p, hsa-miR-185-5p, hsa-miR-182-5p, hsa-miR-337-3p, hsa-miR-1304-3p, hsa-let-7c-5p, and hsa-miR-337-5p. Through functional enrichment analysis, we found that at least seven of these miRNAs regulate the genes *LCOR*, *PLS3*, *INO80D*, and *TNRC6B*, which are involved in several cellular pathways. These include post-transcriptional silencing, PTEN and RUNX1 expression regulation, oncogene-induced senescence, modulation of MECP2 activity, activation of NMDA receptors, and glutamatergic synapse regulation. Dysregulation in these pathways may contribute to the etiopathogenesis of endometriosis, providing potential insights into disease mechanisms and therapeutic targets.

Conclusion
We identified miRNAs altered in endometriotic MenSCs, linked to cell maintenance, proliferation, and differentiation or fostering an inflammatory microenvironment for lesion formation. These findings highlight the role of mesenchymal stem cells in endometriosis,

where altered mechanisms could drive lesion formation and establish a pro-endometriosis niche upon reaching the peritoneal cavity.

Key words
Endometriosis; miRNome; MenSCs

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THEME: PAIN AND ENDOMETRIOSIS

ECOLOGICAL MOMENTARY ASSESSMENT OF ENDOMETRIOSIS PAIN AND PSYCHOLOGICAL EXPERIENCES OVER THE MONTH

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Country where research was undertaken:
Australia

Introduction/Background
Pain is the most common and impactful endometriosis symptom (Chalmers et al., 2017). There is a growing recognition of the importance of psychological factors in endometriosis pain experiences (Kalfas et al., 2022). Since endometriosis is hormone dependent (Vannuccini et al., 2022), pain can fluctuate with monthly hormonal fluctuations. Yet, how fluctuations in pain may relate to fluctuations in psychological experiences currently remains unknown.

Materials and Methods
In this online study, participants with endometriosis will complete a baseline survey followed by daily ecological momentary assessment of endometriosis-related pain severity and interference, and other key psychological constructs (interpretation bias, pain imagery (frequency, intrusion and distress), invalidation, bodily threat monitoring and fear of disease progression) for 30 days.

Results
Data collection for this study has just commenced and as such, results are currently not available though we are confident all data will be collected and analysed well ahead of WCE 2025. We will analyse the data using multilevel modelling (including moderations) by participant and diary session to assess the momentary relationships between pain outcomes (severity and interference), fear of progression, interpretation bias, bodily threat monitoring, invalidation, and imagery. Based on our prior research (Pickup et al., 2023; Todd et al., 2023), we anticipate that greater interpretation bias, fear of progression, body threat monitoring, invalidation and pain-related imagery frequency, intensity and distress will be associated with worse pain outcomes.

Conclusion
These findings will shed light on the momentary psychological experiences that

may be the antecedents or consequences of endometriosis pain outcomes. These findings will therefore help to 1) understand potential treatment targets and 2) determine whether there is an optimal time in the month to target certain psychological mechanisms for enhanced endometriosis care.

Key words
Pain, EMA, biopsychosocial

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PREVALENCE AND IMPACT OF PERIOD AND PELVIC PAIN IN AUSTRALIAN ADOLESCENTS: THE PPEP TALK® SCHOOLS PROGRAM

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Country where research was undertaken:
Australia

Introduction/ Background
Pelvic Pain Foundation of Australia's Periods, Pain and Endometriosis (PPEP Talk®) Program was expanded with the world's first National Action Plan for Endometriosis[1]. This study investigated students assigned female at birth (AFAB) and the prevalence and impact of period and pelvic pain, interaction with healthcare services and knowledge of endometriosis.

Materials and Methods
This study is a retrospective cross-sectional analysis of survey data collected from 13,208 students AFAB aged 15 – 18 years who received the PPEP Talk® in the 22-23 financial year. Anonymous, paper surveys were completed immediately prior to and post PPEP Talk®. Responses from four questions pertaining to the impact of period and pelvic pain and engagement with health professionals were analysed. Descriptive statistics compared predictive demographic variables including regionality, school type and socio-economic advantage.

Results
52.7% of students reported regular severe period pain, and 23.0% of students reported regularly missing school or work with their period. 21.6% of students had presented to a health professional for pain, and 5.7% had presented to an Emergency Department. 5.3% of students reported pelvic pain for more than 10 days per month. The impact of period and pelvic pain is greater in non-metropolitan, Government, and low socioeconomic schools. The proportion of students who knew what endometriosis was rose from 46.9% to 94.1% after the program.

Conclusion
The NAPE's objective to enhance education and awareness of endometriosis and period/pelvic pain was met. PPEP Talk® delivered a program that 100% of schools found age-appropriate, interactive and informative. Wide discrepancies in the prevalence of pain within different demographics were identified, providing previously unknown data to improve and direct services.

Key words Endometriosis, Pain, Education

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CANNABIDIOL IN THE TREATMENT OF WOMEN WITH CHRONIC PELVIC PAIN SECONDARY TO ENDOMETRIOSIS: A RANDOMIZED CLINICAL TRIAL

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Country where research was undertaken:
Brazil

Introduction/Background
Endometriosis often is associated with chronic pelvic pain, and 20-30% of women find no relief after surgery. Additionally, at least 20% experience symptom recurrence within two years. This study assesses cannabidiol's effectiveness in alleviating chronic pelvic pain in women with endometriosis who previously had surgery and are on hormonal therapy.

Materials and Methods
A single-centre, randomised, parallel, triple-blind, placebo-controlled trial enrolled women with surgically confirmed endometriosis, treated and on hormonal blockade, but still experiencing refractory pelvic pain. Participants received cannabidiol or placebo for 10 weeks. Primary outcomes included changes in pain intensity (visual analogue scale, categorical scale) and proportions achieving ≥30% and ≥50% pain reduction. Secondary outcomes covered pain sensitivity thresholds, psychiatric symptoms, functional impairment, quality of life, and cannabidiol-related adverse effects.

Results
Pain intensity, assessed using the Visual Analogue Scale (VAS), significantly decreased in both groups over time, with no statistically significant difference between them (effect estimate = -0.080, p = 0.991). A reduction in pain intensity of at least 30% was observed in 60% of participants in both groups, while 40% experienced a 50% reduction by the end of the trial. Notably, 72% of the placebo group reported substantial clinical improvement, compared to 60% in the cannabidiol group; however, this difference was not statistically significant (p = 0.370). Secondary outcome analyses revealed no significant intergroup differences in pain sensitivity thresholds, psychiatric symptoms, functional impairment, or quality of life. Participants receiving cannabidiol experienced more frequent mild side effects, including nausea, increased appetite, and taste changes, with similar improvements in functional capacity and quality of life across both groups.

Conclusion
Pain reduction was significant across all weeks in both groups, demonstrating consistent decreases over time. However, our findings indicate that, at the tested dosages, cannabidiol was not superior to placebo during the follow-up period of this study, highlighting the need for further research on its efficacy.

Key words
Cannabidiol; chronic pelvic pain; endometriosis.

THE ROLE OF CYCLOOXYGENASE2 (COX2) IN ENDOMETRIOSIS PAIN MANAGEMENT

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Country where research was undertaken:
Germany

Abstract
Endometriosis is an estrogen dependent a chronic inflammatory condition characterized by the presence of endometrial material outside the uterus. The symptoms normally include chronic pelvic pain, dyspareunia, and infertility. Currently, surgical laparoscopy followed by histological classification remains the gold standard for diagnosis.
Cyclooxygenase (COX) is an enzyme that facilitates the bioconversion of arachidonic acid (AA) to inflammatory prostaglandins (PGs). Up to date, three distinct isoforms have been identified namely, COX-1, COX-2 and COX-3. The regulation of COX-2 in endometrial epithelial and stromal cells by estrogens and/or progesterone or by hormone withdrawal is unresolved. Thus, in this study we aimed to analyse COX-2 protein levels in endometrial stromal and epithelial cells with and without hormones in vitro

Introduction/Background
Endometriosis is a chronic disease affecting approximately 6-10% of all women during their child-bearing ages worldwide (Gu *et al.,* 2020). It is an estrogen-dependent disorder that manifests through chronic pelvic pain, dyspareunia, and infertility affecting 30-40% of women in the USA (Mwenda *et al.,* 2007). The gold standard for endometriosis diagnosis include surgical laparoscopy followed by histological confirmation of viable glands and stroma..

Cyclooxygenase (COX; syn. Prostaglandin Endoperoxide Synthase, PGHS) is an enzyme that facilitates the bioconversion of arachidonic acid (AA) to inflammatory prostaglandins (PGs). Cox exists in three distinct isoforms namely, COX-1, COX-2 and COX-3 (Pasero & McCaffery, 2001; Lai *et al.,* 2019). The regulation of COX-2 in endometrial epithelial and stromal cells by estrogens and/or progesterone or by hormone withdrawal is unresolved and therefore , there is an urgent need to investigate the roles of estrogen and progesterone in the pathogenesis of human endometriosis

Materials and Methods
To address this objective, primary endometriosis epithelial and stromal cells were stimulated with and without estrogen and progesterone hormones and afterwards the hormones were withdrawn and Prostaglandins (PG) secretion was quantified. The results showed that treatment of both stromal and epithelial cells with estrogen and progesterone led to increased secretion of PGE2 and PGF2 while their withdrawal led to reduced secretion of the two prostaglandins

Results
We observed co-cultures of epithelial cells and stromal cells had a high secretion of PGE2 and PGF2 upon treatment of cells with both the two hormones in comparison with monocultures

Conclusion
This underscores the need for a model of co-cultures in understanding the pathophysiology of pain generated during menstruation and endometriosis.

Key words
Endometriosis, cyclooxygenase, prostaglandins

EFFECTIVENESS OF CONSERVATIVE THERAPIES IN WOMEN WITH ENDOMETRIOSIS-ASSOCIATED PAIN: A SYSTEMATIC REVIEW

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Country where research was undertaken:
Australia

Introduction/Background
Non-pharmacological conservative therapies include a range of biological, psychological or social interventions and have a growing evidence base in the treatment of persistent pain conditions, yet are under-investigated for alleviating endometriosis-associated pain (EAP). A synthesis of existing evidence of the effectiveness of conservative therapies for women with EAP is needed.

Materials and Methods
Five electronic databases were searched. We included study designs with a comparator arm

that evaluated the effectiveness of conservative therapies in women of reproductive age with a surgical or imaging diagnosis of endometriosis who experienced pain. Two reviewers performed study screening, data extraction and risk of bias appraisal. This protocol was prospectively registered in PROSPERO.

Results
Twenty-two studies provided pain outcome data from 1,107 women diagnosed with EAP. Conservative therapy interventions included: acupuncture (6), electrotherapy (3), exercise (3), manual therapy (2), mindfulness (2) virtual reality (2), hypnotherapy (1), sensate focus (1), psychotherapy with somatosensory stimulation (1) and dietary changes (1) Results of the effectiveness of the different types of conservative therapies in alleviating endometriosis-associated pain will be meta-analysed and GRADE results will be available in May 2025.

Conclusion
This systematic review highlights the wide range of conservative therapies aimed at reducing pain in women with EAP. The results of the meta-analysis and GRADE results will indicate current evidence for the effectiveness of different conservative therapies to treat EAP. Findings will inform clinical practice guidelines and future research.

Key words
Conservative therapies, endometriosis, pain

PAIN PERCEPTION IN YOUNG WOMEN WITH DYSMENORRHEA: OBSERVATIONS IN A NOVEL MULTIPROFESSIONAL TREATMENT SETTING

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Country where research was undertaken:
Germany

Introduction/Background
This observational study explores pain perception in young women with severe dysmenorrhea using a multiprofessional treatment framework. Over six months, patients consult with a gynecologist, nutritionist, psychologist, and physiotherapist. By assessing pain levels across these disciplines, the study seeks to identify factors influencing pain perception and improve pain management strategies.

Materials and Methods
This study aims to deepen understanding of pain perception by assessing pain levels reported to different healthcare professionals throughout treatment. We hypothesize that pain levels decrease over time and vary by professional focus (gynecology, physiotherapy, psychology, nutrition). Fifteen patients will report menstrual pain levels (VAS) over six months. Data analysis via SPSS will compare pain levels between initial and final sessions and across professionals using Wilcoxon and Friedman tests.

Results
Pain perception varied significantly across professionals, reflecting the distinct focus of each discipline. Patients discussing experiences with psychologists often highlighted emotional aspects, while sessions with physiotherapists emphasized physical tension and mobility. The multimodal approach enabled tailored responses, equipping patients with self-care and pain management strategies like relaxation and mobilization. Specific sequences of emotional support, nutritional guidance, and physical therapy can improve coping strategies, particularly for managing dysmenorrhea-related chronic pain. Multimodal interventions offer a promising strategy for treating complex pain conditions like endometriosis.

Conclusion
Healthcare professionals recognize distinctions in pain types, such as nociceptive, neuropathic, and nociplastic pain, which are not always reflected in patient responses. Multimodal care allows to address both physical and psychological pain dimensions and can optimize understanding and management of pain perception, highlighting the importance of education for both patients and providers.

Key words
Pain perception, dysmenorrhea, multimodal treatment

ENDOMETRIOSIS: EXPLORING NOVEL THERAPEUTIC AVENUES, GUT MICROBIOTA AND THE ENDOCANNABINOID SYSTEM IN SYMPTOM MODULATION

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Country where research was undertaken:
Australia

Introduction/Background
Endometriosis, affecting up to 10% of women and those assigned female at birth, involves endometrial-like tissue outside the uterus. Symptoms include chronic pelvic pain, dysmenorrhea and fatigue, significantly impacting quality of life. Treatment costs reach up to AUD $30,000 annually, often due to lost productivity.

Materials and Methods
Current treatments for endometriosis primarily include analgesics and surgery, though these are often inadequate due to limited efficacy and recurrence. This review explores the potential roles of the endocannabinoid system (ECS) and gut microbiota modulation as emerging therapeutic targets in endometriosis management.

Results
Research indicates that ECS activation, especially of CB1 and CB2 receptors, offers analgesic effects in preclinical models. However, clinical trials show mixed outcomes, as seen in pain reduction for HIV-associated neuropathy but not in multiple sclerosis with THC-CBD sprays. Meanwhile, gut microbiota dysregulation may influence symptom severity, with probiotics showing potential to reduce inflammation and improve gastrointestinal symptoms. Although preliminary, these findings suggest ECS and microbiota as promising adjunctive approaches to improve quality of life in endometriosis.

Conclusions
ECS modulation and gut microbiota are promising areas of endometriosis treatment. Further studies could elucidate their roles and optimise therapeutic strategies to enhance symptom management and patient quality of life.

Key words
Endometriosis, gut microbiota

"PAIN, PAIN, EVERYWHERE": ASSESSING THE ROLE OF SURGICAL EXCISION OF ENDOMETRIOSIS IN IMPROVING CENTRAL SENSITISATION IN AUSTRALIAN WOMEN

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Country where research was undertaken:
Australia

Introduction/Background
In women with persistent pelvic pain (PPP) secondary to endometriosis, alterations in pain thresholds and/or heightened sensitivity to pain are indicative of central sensitisation (CS). Despite its significant burden, CS is often unnoticed in endometriosis evaluation. There is limited evidence for treatment modalities for CS of the endometriosis patient (1).

Materials and Methods
A prospective cohort study of Australian woman was conducted to investigate the change in the CS and symptom score using the CS inventory (CSI) and BSGE (British Society for Gynaecological Endoscopy) questionnaire following surgical excision of endometriosis. Australian women aged 16-51 with PPP/endometriosis undergoing laparoscopic excision of endometriosis were recruited, completing questionnaires at baseline, 3, 6, and 12 months post-surgery. Statistical analysis was performed using Stata 17, with linear regression with robust standard errors utilized.

Results
Ninety-four participants were recruited. Forty patients had stage 3/4 endometriosis.

Complete demographics and CSI were obtained for 59 participants. The difference in mean CSI between baseline and six months was statistically significant at 4.79 (p=0.03), however not significant between baseline and 3 months.

BSGE data was completed for 57 patients. When comparing to baseline pre-menstrual pain, there was a statistically significant decrease in means at three months (-1.52, p=0.02) and six months (-3.07, p<0.001). The same was found for menstrual pain (mean decrease at 3 months = -2.09, p=0.003; mean decrease at 6 months = -2.62, p<0.001) and non-cyclical pelvic pain (mean decrease at 3 months = -1.22, p=0.006; mean decrease at 6 months = -1.75, p<0.001).

Conclusion
In participants who underwent surgical excision for endometriosis, preliminary results (pending 12 month results) demonstrate a statistically significant reduction in CSI at six months with reduction in pre menstrual, menstrual and non-cyclical pelvic pain at three and six months post-operatively.

Key words
Endometriosis, central sensitisation, surgery

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PAIN ORIENTATED SENSITIVITY TESTING (POST) IN YOUNG PEOPLE WITH DYSMENORRHOEA, PELVIC PAIN AND ENDOMETRIOSIS

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Country where research was undertaken:
Australia

Introduction/Background
Testing for Pressure Pain Threshold (PPT) and allodynia have been used to differentiate pain phenotype[1]. The study aimed to determine correlations between PPT in young people (YP) (ages 10-18) and their female parent/guardian (PG) while examining the influence of BMI, menstrual cycle stage, and survey data on objective POST results.

Materials and Methods
PPT was measured using a manual algometer and allodynia was measured by applying a cotton ball to nine abdominal sites. POST measurements were taken from the thenar eminence, foot arch, and paraspinal areas for YP and hand and foot for PG. For YP, we also assessed BMI, menstrual cycle stage, comorbidities and medication use. Pain, depression and anxiety were evaluated using the Periods Survey, electronic Persistent Pain Outcomes Collaboration (ePPOC), PHQ9 and GAD7 tools.

Results
We assessed 78 YP (mean age 15.7 years) and 72 PG. Mean PPT values ranged from 2.5 to 3.5 kg/force for YP across sites, while PG showed slightly higher PPT values, from 2.9 to 4 kg/force. Wilcoxon signed-rank test indicated a similarity only at the arch of the foot. No correlation was found between PPT and BMI, or diagnoses of adenomyosis, endometriosis or adhesions. Chronic pain and fibromyalgia were associated with lower PPT across all sites. Anxiety (GAD7) correlated negatively with PPT, especially at the thenar eminence. YP using pain modulators had lower PPT at the foot arch and thoracic spine (p=0.0044, p=0.0256), though the small sample size warrants cautious interpretation. Other medications and menstrual cycle stages showed no significant influence on PPT or allodynia.

Conclusion
Our findings suggest that anxiety and pain modulators may influence PPT, though these associations vary in strength. The lack of PPT and allodynia variation across the menstrual cycle is notable and could guide future research design and interpretation. A larger sample may be needed to draw more definitive conclusions.

Key words
Quantitative sensory testing; pelvic pain; Endometriosis

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CHRONIC PELVIC PAIN IN MEDICAL EDUCATION: A NEEDS ASSESSMENT OF BRITISH COLUMBIAN HEALTH CARE PROVIDERS-IN-TRAINING

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Country where research was undertaken:
Canada

Introduction/Background
Chronic pelvic pain (CPP) affects 15% of women and gender diverse people. Despite the significant negative burden of CPP, it is often dismissed by health care providers in part due to lack of medical education. We aimed to assess knowledge needs on CPP among medical and nurse practitioner students.

Materials and Methods
Cross-sectional survey study undertaken at the University of British Columbia (UBC). The anonymous online survey was open between April-November 2023 and included both closed and open questions. The survey was sent through emails and social media posts in closed groups to recruit UBC medical or nurse practitioner (NP) students. Knowledge and comfort level on CPP were explored in the survey. We also asked students about their perspectives on the current curriculum.

Results
69 participants completed the survey (57 medical students; 12 NP students). Only 30.4% correctly selected the prevalence of CPP. Over 80% of students identified endometriosis as a pain contributor in CPP. Gastrointestinal and musculoskeletal factors were less commonly identified as possible contributors to CPP. For an initial approach to imaging, only 56.5% of students said they would order a pelvic ultrasound for their patient with CPP. Students indicated that a lack of knowledge and training about CPP, stigma surrounding CPP, and differences in cultural attitudes towards pelvic pain, may contribute to healthcare providers feeling uncomfortable discussing CPP. 69.5% of students indicated that they learned very little/learned nothing about CPP in their curriculum.

Conclusion
This survey identified that current medical trainees felt inadequately prepared to manage CPP. Resources tailored to the diagnostic workup and treatment of CPP are needed in medical education. The role of medical education is key in dismantling gender-based barriers to timely medical diagnosis and adequate treatment for patients with CPP.

Key words
Chronic pelvic pain; medical education; needs assessment

PELVIC FLOOR MUSCLE TENDERNESS IN WOMEN UNDERGOING SURGERY FOR ENDOMETRIOSIS: A RELIABILITY STUDY

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Country where research was undertaken:
Australia

Introduction/Background
Pelvic floor muscle (PFM) tenderness is observed in a wide range of women with persistent pelvic pain (PPP) (14 - 79%) and the prevalence in people with confirmed endometriosis is unknown.[1,2] PFM function is commonly assessed through digital palpation, however this method lacks objective metrics and clear therapeutic thresholds. Gynaecologists and physiotherapists assess PFM function and make decisions regarding therapies to treat dysfunction, yet these two clinical groups may not rate these findings consistently.[3]

Objective
This study aims to assess inter-rater reliability between gynaecologists and physiotherapists in digital examination of PFM tenderness and tone, and to determine the value of PFM

algometry and pressure investigations alongside routine clinical assessment.

Materials and Methods
This was an observational single-cohort reliability study. Participants completed a baseline demographic and pain questionnaire. They were subsequently examined by a gynaecologist and physiotherapist to assess PFM tenderness and tone using a digital examination. An additional algometry and pressure assessment using a Femfit® device was performed during the physiotherapist assessment. Participants then completed a survey on the acceptability of the assessments.

Inter-rater reliability in assessing PFM tenderness and tone between gynaecologists and physiotherapists will be measured using the intra-class correlation coefficient (ICC), assessing consistency in rating for site and participant. Prevalence and severity of PFM tenderness measured by the Femfit® device will also be reported.

Results
Recruitment for this study has just been completed with a total of 30 participants. Data cleaning and analysis are underway and results will be ready to present at the conference should this abstract be accepted.

Conclusion
This study demonstrates the inter-rater reliability of digital PFM examinations between gynaecologists and physiotherapists. These data will guide a future study on the prevalence and severity of PFM tenderness and increased tone in women with endometriosis-associated pelvic pain and the impact of endometriosis surgery on these variables.

Key words
Persistent pelvic pain, pelvic floor dysfunction, pelvic floor assessment

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RETROPERITONEAL FIBROSIS: THE CAUSE OF DEEP ENDOMETRIOSIS-RELATED CHRONIC PELVIC PAIN

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Country where research was undertaken:
Thailand

Introduction/Background
Fibrosis is an important pathological feature of endometriotic lesions. Cyclical bleeding of endometriotic implants act as a repetitive tissue injury, activating myofibroblastic differentiation and causing excess fibrosis. This results in pain and infertility. Laparoscopy with removal of retroperitoneal fibrosis can aid in diagnosis and relief of pain.

Materials and Methods
This is a surgical VDO of a 46-year-old, para-2 woman who had two cesarean deliveries. Initially, she presented with pelvic pain and dyspareunia for 6 months and was unsuccessfully treated for pelvic inflammatory disease. Subsequent PV findings by another gynecologist reported CDS tenderness and resistance, favor pelvic endometriosis, which was treated with a 3-month GnRH agonist, followed by Dienogest. Partial pain improvement was observed with intolerable vasomotor symptoms. She then decided to undergo operative laparoscopy.

Results
Intraoperative findings revealed normal sized uterus with small adenomyoma and post-cesarean adhesions at lower uterine segment. Sigmoid was adhered to left infundibulopelvic ligament and left pelvic brim. No definite endometriotic lesions were visualized but generalized fibrosis and retraction on pelvic sidewall peritoneum. Sigmoid was mobilized exposing left pelvic sidewall. Retroperitoneal dissection found stiff adherence between ureters and surrounding tissue causing difficulty in ureterolysis. With expertise dissection skills, tissue interphase was clearly identified. Retroperitoneal fibrosis was thoroughly excised, and bladder was safely

mobilized from lower uterine segment. Finally, uterus with both tubes were successfully removed. Hyaluronic acid gel was applied to prevent adhesion reformation. The patient could be discharged from the hospital on postoperative day 2. At 6-week follow-up, pelvic pain and dyspareunia were significantly improved.

Conclusion
Retroperitoneal fibrosis is an important pathological feature of deep endometriosis-related chronic pelvic pain. Hysterectomy alone without removal of retroperitoneal fibrosis is considered inadequate, resulting in persistent pain. Although extensive resection is effective, this mandates meticulous and expertise skills in retroperitoneal surgical dissection to achieve safe and optimal patient outcomes.

Key words
Retroperitoneal fibrosis, deep endometriosis, chronic pelvic pain

WOMEN'S CAUSAL BELIEFS ABOUT THEIR PELVIC PAIN: A SYSTEMATIC REVIEW AND META-ETHNOGRAPHY

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Country where research was undertaken:
Australia

Introduction/Background
Investigating beliefs women hold regarding the cause of their persistent pelvic pain can identify misconceptions that may be helpful to address as part of management. The aim of this systematic review was to identify and synthesise the current literature on women's beliefs about the cause of their persistent pelvic pain.

Materials and Methods
Seven electronic databases and relevant grey literature sources were searched from their inception to June 2023 with an English language limiter. We included primary, qualitative studies that explored the beliefs held by women regarding the cause of their persistent pelvic pain. Studies underwent screening, data extraction, and risk of bias appraisal in duplicate. Study quality was assessed using the Critical Appraisal Skills Programme qualitative checklist. A meta-ethnography was used to synthesise results and generate themes.

Results
The quality of reporting and demographic diversity of included studies was limited, often lacking consideration of researcher-participant relationships, and primarily including Caucasian, cis-gender, heterosexual women from Western countries. Four themes were generated: 1) It's happening to me because I'm a woman, 2) It's happening to me in my body, 3) It's happening to me due to my actions, and 4) It's happening to me due to my life. Within these themes, women's causal beliefs ranged from biomedical to biopsychosocial, and women ranged from feeling that their pain was completely out of their control, to feeling that they had some control over their pain narrative. A conceptual model was developed to represent the spectrum of beliefs women hold about the cause of their pelvic pain.

Conclusion
Women largely expressed either being unsure about the cause of their pelvic pain or held predominantly biomedical beliefs about the cause of their pelvic pain. Women who framed the cause of their pelvic pain in a biopsychosocial manner felt more in control of their pain.

Key words
Pain, beliefs, biopsychosocial

REVERSIBLE MECHANICAL TUBAL BLOCKAGE FOR ENDOMETRIOSIS TREATMENT USING STIMULI-RESPONSIVE HYDROGELS

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Countries where research was undertaken:
Switzerland and Czech Republic

Introduction/Background
Endometriosis affects 10% of women of reproductive age, characterized by endometrial tissue outside the uterus (1). Current treatments have limited efficacy and recurrence risks. This study introduces a hydrogel-based implant to prevent retrograde menstruation by blocking fallopian tubes, offering a new mechanical approach to managing endometriosis.

Materials and Methods
A stimuli-responsive hydrogel system composed of acrylamide-based polymers was designed for reversible occlusion of the fallopian tubes. The hydrogel's swelling properties allow it to block menstrual flow mechanically. Biocompatibility and degradability were evaluated in vitro and in vivo using a porcine model. The implant was tested for its ability to prevent the passage of endometrial cells, simulating retrograde menstruation.

Results
In vitro studies demonstrated that the hydrogel implant effectively occluded the fallopian tubes, preventing the passage of both endometrial cells and live sperm, showcasing its potential for contraception and endometriosis prevention. In vivo trials conducted in a porcine model confirmed that the implant remained stable and biocompatible for up to three weeks, with no signs of significant inflammation or tissue damage. The hydrogel system was easily removed within 30 minutes, either through light irradiation or the application of a glutathione solution, proving its reversible nature.

Conclusion
The hydrogel implant offers a novel mechanical approach to preventing retrograde menstruation and endometriosis progression. Its reversible nature and biocompatibility present a promising alternative to current treatments, with the potential for wider adoption pending further clinical validation.

Key words
Implant, reversible occlusion

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CANNABIS USE IN ENDOMETRIOSIS: PATIENTS AND PHYSICIANS' PERSPECTIVES THROUGH QUESTIONNAIRE STUDIES

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Country where research was undertaken:
Germany

Introduction/Background
Endometriosis affects around 10% of women of reproductive age, with conventional treatments often proving inadequate or causing severe side effects. Since 2017, medical cannabis has been available for severe cases, but its use in gynecological conditions such as endometriosis remains under-researched in German-speaking countries.

Materials and Methods
This cross-sectional study comprised three online surveys: one from March 2017 to 2022 gathering data from physicians prescribing cannabis on treatment indications, side effects, and outcomes; another from November 2023 to February 2024 focusing on physicians' experiences with medical cannabis as a treatment for gynecological conditions; and a third from August to December 2022 targeting endometriosis patients (≤18) in Germany, Austria, and Switzerland to assess self-management, symptom improvement, medication reduction, and safety measures.

Results
Among 16,809 mandatory datasets, 28 were included with endometriosis as the primary diagnosis. More than 50% of patients had previously been treated with NSAIDs, opioids, or antidepressants. 89.3% of physicians reported improvements in patients' quality of life and symptoms, with side effects ranging from 10.7% to 25.0%. The second part of the study included 17 datasets from German physicians, where scientific journals and conferences were the main sources of knowledge on cannabis use. 64.7% identified a lack of knowledge and training as challenges. 82.4% would prescribe more often if more guidelines were available. The patient survey yielded 912 valid responses, with 75.4% using self-management strategies. 114 patients found cannabis the most effective for symptom relief, reducing pain medication by 90% with minimal side effects.

Conclusion
Medical cannabis is rarely prescribed due to complex requirements, but it is a popular self-management method for endometriosis, improving symptoms. Further research is needed on administration, dosage, THC/CBD ratios, side effects, and long-term effects. Physicians are open to prescribing cannabis, but lack of guidelines and training hinders its use.

Key words
Medical cannabis, self-management, chronic pain

PALMITOYLETHANOLAMIDE AND POLYDATIN EFFECT ON PELVIC PAIN IN WOMEN PRE LAPAROSCOPIC TREATMENT OF POSSIBLE ENDOMETRIOSIS: DOUBLE BLIND RANDOMISED CONTROLLED TRIAL

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Country where research was undertaken: Australia

Introduction/Background
This double-blind randomised trial evaluates the combination of Palmitoylethanolamide (PEA), an anti-inflammatory, and Polydatin (PLD), an antioxidant with pain-inhibiting properties, for treating persistent pelvic pain in endometriosis. The goal is to determine if PEA/PLD improves pain compared to placebo.

Planned number of participants is 260 in total.

Materials and Methods
Patients awaiting endometriosis surgery will be offered joining the study without affecting their care plan. After consent, randomisation occurs to receive either PEA/PLD supplements or a placebo for 8 weeks pre-surgery. Endometriosis is confirmed or excluded during surgery, and participants will complete surveys on pain and quality of life at baseline, after 8 weeks treatment, and 4 months post-surgery. The study will compare changes in pain and quality of life between groups.

Results
As of November 8, 2024, a total of 110 patients have been recruited for the study, with 92 actively participating and 18 withdrawn. Seven study sites have ethics approval.

Current participants have a mean age of 30.5 years (SD 7.0), with 64 (69.5%) undergoing surgery to date.

Among 64 participants who completed the 8-week pre-operative period, compliance with the treatment was 81.3% (52 participants), non-compliant 10.8% (7), mainly due to surgery schedule changes or personal reasons. 7.8% (5) did not complete the survey correctly to indicate compliance.

No adverse events have been recorded among those who completed the supplement regimen.

Conclusion
In this study, early results suggest that the PEA/PLD supplement regimen is well-tolerated, with high compliance rates and no adverse events reported. Ongoing participant recruitment and data collection will further clarify the potential of PEA/PLD as a preoperative treatment for persistent pelvic pain in endometriosis.

Key words
Endometriosis, pelvic pain, PEA/PLD

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THEME: PATHOGENESIS AND AETIOLOGY OF DISEASE

DOES GLYCOLYSIS AND HYPOXIA CONTRIBUTE TO ENDOMETRIOSIS: A SYSTEMATIC LITERATURE REVIEW

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Country where research was undertaken:
United Kingdom

Objective
This systematic review examines glycolytic enzymes and hypoxia in endometriosis to understand their roles in disease pathogenesis and diagnostic potential.

Introduction/Background
Endometriosis is a chronic condition involving the ectopic growth of endometrial-like tissue, affecting 10% of reproductive-age women. Diagnosis often requires invasive laparoscopy, delayed by the heterogeneity of symptoms. Retrograde menstruation and hypoxia, which modulates gene expression, are key to current pathophysiology theories. This review explores the roles of glycolytic enzymes, particularly PDK1, LDHA, and TGF-B1, in endometriotic tissue growth.

Materials and Methods
Following PRISMA guidelines, we searched CINAHL, PubMed, Scopus, and Web of Science for primary studies on glycolysis and hypoxia in endometriosis. Inclusion criteria focused on studies assessing gene expression under hypoxic conditions, with exclusions for chemical hypoxia induction and lack of healthy controls. Quality was assessed via a modified NOS score, and meta-analysis was conducted using REVMan5.

Results
From 36 studies, LDHA was found to increase under hypoxia through HIF-1α, leading to lactate production, which supports endometriotic cell survival. PDK1 emerged as one of the most promising proteins, with 12 studies identifying it as significantly upregulated in endometriotic tissues ($p<0.05$). PDK1's inhibition of pyruvate entry into the TCA cycle, instead converting it to lactate, enhances glycolysis. TGF-B1, elevated in endometriosis, correlates with higher lactate in the peritoneum and induces a Warburg-like metabolism by promoting glycolysis and upregulating HIF-1α, LDHA, and PDK1.

Conclusion
Findings suggest a glycolysis-hypoxia axis in endometriosis pathogenesis, with PDK1, LDHA, and TGF-B1 playing crucial roles. Understanding these pathways could lead to non-invasive diagnostic approaches and targeted treatments.

Key words
Endometriosis, glycolysis, hypoxia

THE SUCCESSES OF ESTABLISHING AN ENDOMETRIOSIS BIOBANK, FOLLOWING THE WERF GUIDELINES – AN EVALUATION

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Country where research was undertaken:
Australia

Introduction/Background
Biobanks are an essential resource that increases the scale of clinical research (1). An endometriosis specific biobank was established in 2023 with the aim of collecting comprehensive patient and surgical information, in conjunction with a variety of biospecimens, to reinforce future collaborative research opportunities (2).

Materials and Methods
Designed as a single centre prospective study, the biobank recruits patients aged ≥18 years, pre-menopausal, not pregnant, and planning surgery for suspected endometriosis or other benign gynaecological conditions. After consent, participants complete a pre-op baseline questionnaire. Biospecimens are collected during surgery and surgeons complete a questionnaire post-surgery. Histopathology and surgical reports are also obtained post-surgery. All processes are adapted from the World Endometriosis Research Foundation Endometriosis Phenome and Biobanking Harmonization Project (3, 4, 5).

Results
The biobank has recruited 122 participants (from 07 August 2023 to 14 November 2024). Of which, we have 119 participant baseline surveys and 113 surgeon surveys completed. 76 participants had histology confirmed endometriosis (66.1%) and 39 participants (33.9%) were negative on histology (controls) (7 histology reports are currently pending). From endometriosis cases, we have 59 blood samples, 15 peritoneal fluids, 19 peritoneal washings, 60 endometrial and 11 myometrial tissues, and 19 endometrioma and 113 endometriosis lesions (from 56 patients). From non-endometriosis controls, we have 33 bloods, 32 endometrium, 15 myometrium, 7 peritoneal fluid and 11 peritoneal washings.

Conclusion
We hope that our biobank will facilitate the discovery of new biomarkers, targeted therapies, and improved diagnosis and treatment of endometriosis. Ultimately, our biobank will enable large-scale, collaborative research that aligns with international harmonisation criteria, driving progress in improved health outcomes for people with endometriosis (4, 5).

Key words
Biobank, biospecimen, endometriosis

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IN VITRO STUDY ON THE PRESCRIPTION OF CLEARING HEAT AND REMOVING BLOOD STASIS TO INHIBIT ENDOMETRIOSIS BY REGULATING MACROPHAGES

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Country where research was undertaken:
China

Introduction/Background
The study aims to explore molecular mechanisms of endometriosis treatment of Traditional Chinese Medicine, focusing on the estrogen function on macrophage and endometriosis (EMs) progression, then to clarify the regulatory mechanism of the Clearing Heat and Removing Blood Stasis prescription on macrophage polarization and their inhibitory effects on EMs progression.

Materials and Methods

1. Network pharmacology research: predicting active ingredients and targets of the prescription and EMs, with common targets and a network diagram, and then core targets for GO and KEGG obtained.
2. HESCs from EMs patients: a cell co-culture model was established to evaluate effects of estradiol on proliferation and polarization.
3. Medicated sera preparation: The cell co-culture model was used to verify the prescription affecting macrophage polarization via estradiol/ER regulation.

Results

1. he study demonstrated that the prescription was involved in estrogen signaling, IL-17 signaling, JAK-STAT signaling, HIF-1 signaling, and TNF signaling pathways.
2. he co-culture microenvironment dominated by M2 macrophages will promote the progress of EMs. Additionally, E2 stimulates changes in the immune microenvironment in co-cultures and induces polarization of M1 macrophages to M2 macrophages via ERβ, and then promotes the progression of EMs.
3. The serum with the prescription reduced the polarization of M2 macrophages in co-culture microenvironment by down-regulating ERβ to inhibit the progress of EMs. Serum with a partial prescription aimed at removing blood stasis or clearing heat has comparable regulatory effects to that with the whole prescription.However, the whole prescription's effects are significantly better.

Conclusion

The therapeutic method of clearing heat and removing blood stasis exhibits a unique characteristic of "multi-components-multi-targets-multi-pathways", which mainly acts on EMs through estrogen and immune cell regulation. The serum containing the prescription reduces the polarization of M2 macrophages by down-regulating ERβ in co-culture microenvironment, thus inhibiting the progress of EMs.

Key words

Clearing heat and removing blood stasis; endometriosis; macrophage; estrogen

CHALLENGING PRIOR ASSUMPTIONS: DOES A CORRELATION BETWEEN POLYCYSTIC OVARIAN MORPHOLOGY AND ENDOMETRIOSIS EXIST?

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Country where research was undertaken: Canada

Introduction/Background

Endometriosis and Polycystic Ovarian Morphology (PCOM) are common conditions impacting well-being of individuals assigned female at birth. Though different pathophysiologies, they may co-occur, challenging prior claims that they are discrepant diseases. Aim of the present study is to investigate a possible correlation, by analyzing PCOM prevalence in patients with endometriosis.

Materials and Methods

This retrospective cohort examined patients undergoing endometriosis ultrasound at a specialized gynecologic ultrasound clinic. Endometriosis was categorized as ovarian (OE), deep (DE), or superficial (SE). PCOM was defined by ≥20 follicles (2-9 mm) and/or ovarian volume >10 ml without dominant follicles/cysts. PCOM prevalence among patients with an endometriosis scan and patients with endometriosis diagnosis was calculated. Baseline characteristics were compared between groups with PCOM and endometriosis vs endometriosis alone, employing two-sample t-test and Chi-square test.

Results

Out of 166 patients sent for an endometriosis scan because of “endometriosis symptomatology”, 66 (40%) had PCOM on at least one ovary, and 101 (60%) had an endometriosis diagnosis. Among patients with an endometriosis diagnosis, 37 % had PCOM. In particular, 24/48 (50%) had PCOM and SE; 2/5 (40%) had PCOM and OE; 7/31 (23%) had PCOM and DE; and 4/17 (24%) had a combination of PCOM + DE and OE. Patients with endometriosis were significantly older (p < .001), with higher weight (p = .020) and BMI (p = .040) compared to those with endometriosis and PCOM. Gravida and parity

counts were lower in patients with endometriosis + PCOM ($p < .001$). Moreover, there were endometriosis phenotype differences between patients with and without PCOM.

Conclusion
This study highlights for the first time that PCOM is incredibly common in patients who present with endometriosis, or with endometriosis symptoms. Further studies are needed to understand whether PCOM is a contributing factor for pelvic pain, or if it can be considered a risk factor for endometriosis.

Key words
Endometriosis, PCOM, PCOS

THEME: PERSONALISED MEDICINE AND ENDOMETRIOSIS

TREATMENT OF ENDOMETRIOSIS – FOCUS ON IMPROVING QUALITY OF LIFE

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Country where research was undertaken:
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The whole world community of gynecologists is concerned about the problem of endometriosis, and the question of the etiopathogenesis of the disease remains open. According to the UBP-WRS study, 67% of women with endometriosis have impaired quality of life, i.e. they need long-term therapy. Gestagens are most often used in medical practice in the territory of the Russian Federation, which in the clinical recommendations of RSOG (2024) are referred to as first-line therapy for endometriosis Not all gestagens are the same. Differences in chemical structure led to differences in their receptor binding selectivity, efficacy, and bioavailability. Many progestogens act on androgenic, glucocorticoid, estrogenic and mineralocorticoid receptors. The use of progestogens with affinity for receptors other than progesterone can lead to the development of side effects. The patient's refusal of hormone therapy due to undesirable effects and/ or misunderstanding of the importance of the stage of drug treatment after surgery may lead to a recurrence of endometriosis. 39.3% of women with endometriosis independently canceled dienogest due to undesirable effects or ineffective therapy.

Among patients with endometriosis (approximately 1 million Russian women) who need hormone therapy, only about 25% of the total number receive it. One of the factors of refusal of therapy is the fear of patients of hormone therapy and its side effects in the form of depressive states, mood swings, weight gain, decreased libido, etc. In this regard, patients independently refuse the prescribed treatment, which contributes to the recurrence of endometriosis. According to the ESHRE consensus on endometriosis therapy, modern therapeutic approaches to treatment should consider the effectiveness, safety, and personalization of therapy. Initial comorbid conditions, the duration and severity of endometriosis, as well as a woman's desire to maintain hormonal balance have a direct or indirect effect on the development of side effects from taking Dienogest.

Introduction/Background
In a group of women who underwent surgery for endometriosis and took dienogest, to retrospectively analyze several factors leading to early abandonment of therapy and possible schemes for correction of therapy. The relationship between the disease, the therapy and the mental health of patients with endometriosis is discussed.

Materials and Methods
Observation, retrospective analysis. 48 women who underwent surgery for endometriosis and were prescribed dienogest 6-month therapy course. The age of the studied patients 35-50 years. Two groups were identified: Group I - 38 (79.17%) completed course and did not have any side effects, and Group II - 10 (20.83%) patients who developed side effects, due to which it became necessary to discontinue the therapy. The change in QoL was assessed according to the Short Form-20 and VAS.

Results
In the study groups, among the patients in Group II, the highest percentage of all side effects was attributed to depressive episodes (30%), followed by metrorrhagia (60%) and

migraine (50%). However, no statistically significant differences were found between the two study groups in other categories. Ehe presence of concomitant diseases was not a determining factor influencing the need to discontinue dienogest therapy.

Conclusion
Endometriosis therapy with dienogest is associated with depressive and anxiety symptoms, as well as with impaired quality of life. In the presence of risks of endometriosis-associated complications, switching to dydrogesterone is recommended, since the presence of only a continuous regimen in dienogest limits its capabilities in terms of overcoming several undesirable effects. Group 2 patients were more likely to have endocrine and neurological diseases, which could possibly have influenced the occurrence of side effects and the need for early discontinuation of dienogest therapy.

Key words
Endometriosis, dienogest, dydrogesterone

THEME: PUBLIC HEALTH POLICY AND GLOBAL CHALLENGES

EVALUATING THE LANDSCAPE OF ENDOMETRIOSIS PUBLICATIONS BETWEEN 1990-2024

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Country where research was undertaken:
Australia

Introduction/Background
Endometriosis is an important health problem. Understanding medical literature trends helps identify research gaps, prioritize future research agendas, and enhance the planning and execution of studies. We studied trends in published endometriosis research between 1990-2024, including geographical distribution and the type of research.

Materials and Methods
We systematically searched for articles on endometriosis from 1990 to 2024 in Dimensions.AI, a database containing comprehensive meta-data. Using text-mining in 'R', studies were categorized into 'Basic and Animal Research', Randomised Controlled Trials (RCTs), 'Non-Randomised Clinical Studies' (NRCTs) and Meta-Analyses/Systematic Reviews. 'Country of standardized research organisation', as provided by Dimensions.AI, was used to extract country of first author information and plot the distribution of publications globally.

Results
We identified 25471 articles, growing from an average of 308 publications per year in the 1990s to 1,763 on average per year between 2020-2023. 'Basic and Animal Research' was the most common category of studies, accounting for 6,973 (27%) studies compared to 577 (2.3%) RCTs, 5461 (21%) NRCTs and 779 (3.1%) Systematic Reviews/Meta-Analyses. RCTs had the slowest growth rate in publications over time. The US and China led independent country output, with 3,589 (17.1%) publications from the US, 2,919 (13.9%) from China followed by 5,599 (26.7%) from European Union countries. Much of China's output follows a recent surge, with an increase of over 7,500% in 5-year-rolling average publications per year since 1990. Additionally, Turkey and Iran have recently emerged as top 15 endometriosis publishing countries.

Conclusion
Endometriosis research has increased more than five-fold in the last 35 years. 'Basic and Animal Research' and 'NRCTs' account for a substantial portion of endometriosis research with comparative limited growth seen in publication of RCTs over time.

Key words
Meta-research, research evaluation, endometriosis

EVALUATING THE LANDSCAPE AND POWER OF ENDOMETRIOSIS RANDOMISED CONTROLLED TRIALS

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Country where research was undertaken:
Australia

Introduction/Background
Randomised Controlled Trials (RCTs) are the cornerstone of evidence-informed medicine. We evaluated the geographical distribution and, crucially, sample size of endometriosis RCTs published between 1990-2024.

Materials and Methods
We searched Dimensions.AI for endometriosis articles published between 1990-2024. RCTs were identified, whilst follow-up trials or secondary analyses of RCTs were excluded. Country of author information was extracted using Dimensions.AI. Sample sizes of RCTs were determined from abstracts. Conventional sample size calculations were utilised to determine minimal detectable difference of RCTs, using extracted sample sizes, conventional power targets of 80% and 90%, an assumption of two groups per trial and statistical significance threshold of 0.05.

Results
A total of 577 RCTs were included. Europe, China and the US published 150, 73 and 71 RCTs, respectively. Iran, Egypt and Turkey were also productive with 34, 13 and 10 RCTs, respectively.

Of 577 RCT abstracts, 533 provided a sample size. The most common sample size was between 40-60 participants (N = 113), with most RCTs (N = 314, 58.9%) reporting on less than 80 participants. Of included RCTs, 34% (N = 179) would require a 'large' (Cohen's D of 0.8-1.2) in standardized mean difference to have statistical power of 80% to detect a statistically significant difference between the two study groups. For 90% statistical power, this increased to 49.7% (N = 265) of RCTs.

Conclusion
Almost half of RCTs had sample sizes rendering them insufficient to detect treatment effect unless it was 'large' or 'very large'. This may indicate significant wastage of resources. As endometriosis has limited satisfactory management options, future trials should be adequately powered to detect modest but clinically relevant effects.

Key words
Randomised controlled trials, meta-research, endometriosis

ENDORISE: A MULTIDISCIPLINARY ENDOMETRIOSIS PROGRAM EMPOWERED BY COMMUNITY OUTREACH AND LEGISLATIVE ADVOCACY

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Country where research was undertaken:
United States of America

Introduction/Background
Endometriosis Research Innovation Support and Education [EndoRISE] is a multidisciplinary, state-funded data and biorepository program aimed at transforming endometriosis care, and creating sustainable models to addressing this complex disease in the state of Connecticut [CT].

Materials and Methods
EndoRISE creates centralized resources to enhance public awareness and community outreach, advocates for policy changes and legislative funding, and provides targeted education for healthcare providers. The initiative also includes building a statewide specimen and data biorepository, supported by a custom designed REDCap Office of Research Computing and Analytics [ORCA] specimen and data tracking instrument, that enhances sample and data traceability. The biobank aims to advance academic and biotech/pharma research.

Results
EndoRISE program led to significant outcomes since its creation in 2022:

- Awareness campaigns through the creation of a webpage and content distribution fostered significant community and legislative engagement.
- Legislative outreach led to passing two laws prioritizing endometriosis in the state of CT.
- Educational events targeting nurses, including school nurses provided resources for endometriosis sufferers, starting with school age individuals.
- EndoRISE program hosted continuing medical education events for professional health care providers such as live imaging of gynecologic conditions for diagnosis preoperative conditions.
- Since biorepository enrollment opening in April 2024, 1700+ specimens with linked clinical, demographic and survey data

have been biobanked from multiple healthcare institutions across CT and representative of a diverse population. Sample quality was validated through cutting edge technologies, such as single cell transcriptomics, and sample distribution to researchers is well underway.

Conclusion
EndoRISE demonstrates how strategic integration of public awareness, policy advocacy, provider education, and innovative research tools can address endometriosis care gaps. This multidisciplinary model offers a roadmap for advancing diagnosis, treatment, and research, paving the way for broader implementation and improved outcomes for endometriosis patients in CT and beyond.

SLIPPERY KNOWLEDGE: ECOLOGIES AND ENVIRONMENT IN ENDOMETRIOSIS FRAMING

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Country where research was undertaken:
United Kingdom

Introduction/Background
Despite a growing body of literature linking endometriosis with environmental toxins (primarily endocrine disrupting chemicals including PCBs, dioxins, BPA, and phthalates), including recent systematic reviews, environmental issues make only occasional appearances in public, patient, and specialist conversations about endometriosis. They hover at the edges, but do not gain traction.

Materials and Methods
This work is based on 15 months of ethnographic research in Scotland 2020-2021, including nineteen open-ended online and in-person interviews with clinicians and clinical staff and people with endometriosis or suspected endometriosis, as well as participant observation at local support groups. Ethical approval was sought obtained. Interviewees provided written informed consent. Interviews were transcribed and anonymized. Transcriptions and field notes were analyzed via thematic and content analysis using an abductive approach.

Results
Most people I spoke with only mentioned environmental factors in response to direct questioning, and many had nothing to say on the topic. I argue that environmental concerns are elided because differently situated people feel powerless to act on environmental etiologies. This presentation develops a concept of “slippery” knowledge as that which evades action. Ignorance of environmental or ecological etiologies is less a dearth of information as a dearth of possibilities for action. The presentation elaborates two ways of grasping environmentally or ecologically driven disease: the exposure model predicated on harmful external factors “getting in” to damage individuals or communities, and the embodied ecologies model which posits inevitable and ongoing mutual imbrication among living and non-living entities. Knowledge regarding endometriosis is “slippery” in both models.

Conclusion
What is not found, not known, not talked about, and not looked for is politically determined and important. The slippery knowledge this presentation describes is inextricable from deep-seated power dynamics related to colonialism, gender, and race, which perpetuate ways of knowing (and acting) on endometriosis that are troublingly durable.

Key words
Anthropology, epistemology, decolonizing

PATTERNS OF CARE FOR PATIENTS WITH ENDOMETRIOSIS IN THE NATIONAL ENDOMETRIOSIS CLINICAL AND SCIENTIFIC TRIALS (NECST) REGISTRY

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Country where research was undertaken:
Australia

Introduction/Background
Data on patterns of care for endometriosis is limited[1] but important for healthcare providers, and policy makers to better direct effective healthcare resources and treatments and lessen the health economic burden. This study aims to describe patterns of care of those with endometriosis in Australia.

Materials and Methods
Clinical and health data were sourced from the NECST Registry and assessed for completeness between 2020-2024. Women and people over 18 years, diagnosed or experiencing endometriosis-related symptoms were recruited from hospitals, private clinics or social media across Australia. Demographics, presenting and medical history using a shortened Endometriosis Phenome and Biobanking Harmonisation Project (EPHect) patient questionnaire (EPQ) at baseline, with follow-up at 6-, 12-, 24- and 36-months, were included.

Results
Analyses of 1693 participants revealed the symptom burden experienced by participants was 5.8 symptoms (SD=1.74, range=1-10); and overall distress (visual analogue scale) rating of 6.0/10 (SD=1.50, range=1.5-10). Of those with endometriosis (n=1,539, 90.9%), surgery (n=1,224, 79.5%) was the most common route of management. Other management options included analgesics (n=889, 57.8%), hormonal therapies (n=670, 43.5%), other medications (n=608, 39.5%) and allied health/complementary therapies (n=626, 40.7%); with the most common paracetamol (n=329, 20.0%), levonorgestrel intrauterine system (n=271, 31.9%), other medications (n=514, 59.1%) and physiotherapy (n=230, 22.0%), respectively. Combination therapy for pain management was common (47%). Using Pearson’s correlation, there is a significant relationship between overall symptom burden and overall distress, total number of hormonal, pain, other medications and allied health/complementary therapies used (all $p<0.001$).

Conclusion
Patients with a greater number of symptoms are more likely to utilise a combination of therapies to manage pain. Detailed mapping of geographic variability and economic evaluations using these data will help drive healthcare policy on the provision of appropriate, effective and accessible care for endometriosis patients.

Key words
Endometriosis, public health policy, patterns of care.

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MULTDISCIPLINARY APPROACH IN ENDOMETRIOSIS IN A PUBLIC HOSPITAL

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Country where research was undertaken:
Argentina

Introduction
Endometriosis is a chronic and complex disease, often underdiagnosed, leading to treatment delays of several years. This results in a negative impact on patients' quality of life and inefficient use of health resources. This study outlines the establishment of an Endometriosis Care Unit (ECU) to enhance early diagnosis and equitable multidisciplinary management.

Materials and Methods
The ECU brings together consultations by gynecologists, nutritionists, psychologists, and kinesiologists to provide comprehensive care. Clinical protocols were developed for medication management, and multidisciplinary surgical teams, including proctologists and urologists, were formed. Health care personnel were trained for accurate diagnosis and referral, while the community was encouraged to seek early consultations.

Results
The ECU aims to reduce diagnostic delays from an average of 6–8 years to under 2 years, improving outcomes with personalized care plans. Institutionally, it is expected to enhance resource allocation by reducing repetitive consultations and emergency service inefficiencies. The ECU seeks to set a

standard in public hospitals, improving women's quality of life and serving as a replicable model for inclusive and efficient health care in other regions.

Conclusions
The ECU represents a significant milestone, introducing a multidisciplinary, equitable model tailored to the public sector's needs. This initiative serves as a benchmark for replication nationwide, promoting improved standards of care and fostering a more inclusive health system.

Key words
Endometriosis, multidisciplinary care, diagnosis optimization

THEME: SURGICAL MANAGEMENT

HYSTERECTOMY SHOULD NOT BE DESCRIBED AS THE 'DEFINITIVE' PROCEDURE FOR TREATING PATIENTS WITH ENDOMETRIOSIS

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Country where research was undertaken:
Australia

Introduction/Background
Surgical treatments - both conservative and extirpative - are frequently sought by people with endometriosis. The aim of the current study is to explore and compare outcomes following conservative surgery alone with hysterectomy as an additional treatment on pain and quality of life (QoL) for women presenting with endometriosis.

Materials and Methods
Data from the National Endometriosis Clinical and Scientific Trials (NECST) Registry has been interrogated to evaluate pain and QoL at baseline, 6- and 12-months post-operatively. Pain has been evaluated using visual analogue scale (VAS) scores for menstrual and non-menstrual pain. QoL has been assessed using the validated instruments of Endometriosis Health Profile 30 (EHP-30) and EuroQol 5-dimensional (EQ-5D). The statistical analysis plan includes between-group comparisons using a one-way analysis of variance (ANOVA) and Cohen's d.

Results
An analysis on 379 women was conducted with 40 participants having hysterectomy and with 339 participants having conservative surgery (153 'resection' and 186 'ablation'). At 6- and 12-months post-surgery, pain and QoL scores had improved from baseline in both groups. A statistically significant between group difference in QoL at 12-months in favour of participants who underwent hysterectomy only for EHP-30 measures of emotional wellbeing (Cohen's d=0.58, 95% CI [0.22-0.94]; p<0.001), self-image (Cohen's d=0.49, 95% CI [0.14-0.85]; p=0.007) and social support (Cohen's d=0.39, 95% CI [0.04-0.75]; p=0.024) compared to participants having conservative surgery. No other significant differences were found between groups at 6- or 12-months post-surgery. Longer term data are being prepared and will be updated and presented.

Conclusion
Preliminary results suggest that few significant differences exist between hysterectomy and conservative surgical procedures in the context of pain and QoL. With both outcomes showing improvement over a 6- and 12-month period, it is crucial that hysterectomy no longer be regarded as the 'definitive' procedure in the treatment of endometriosis.

Key words
Endometriosis, surgery, hysterectomy

FERTILITY AFTER ENDOMETRIOSIS SURGERY: A COMPARISON OF PRIMARY VS MULTIPLE SURGICAL INTERVENTIONS

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Country where research was undertaken:
Australia

Introduction/Background
Endometriosis, with its global impact, is often inadequately managed. Surgery is a common management, but the impact of multiple surgeries, particularly the role of post-surgical adhesions on recurrence and fertility remains unclear. This systematic review compares the fertility outcomes in patients who underwent one versus multiple surgeries for endometriosis.

Materials and Methods
We searched Embase, Medline, PubMed, and Web of Science for studies published between 2003 and 2023. Eligible studies included reproductive-age women who underwent at least one surgery for endometriosis. Participants were divided into two groups: primary surgery (one surgery) and multiple surgery groups (two or more surgeries). We assessed spontaneous pregnancy, live birth, and abortion rates as primary outcomes, and pregnancy per embryo transfer (ET), cumulative live birth, and miscarriage rates following assisted reproductive technology (ART) as secondary outcomes.

Results
The protocol was registered with PROSPERO (ID: CRD42024506530). Five cohort studies involving 1724 participants met inclusion criteria. Four studies assessed spontaneous fertility outcomes. For the primary surgery group, spontaneous pregnancy rates ranged from 40% to 71.7%, while the multiple surgery group showed lower rates between 20% and 55.9%. However, spontaneous live birth rates were similar in both groups (66% vs. 66.9%), as were miscarriage rates (5.8%–8% vs. 3.3%–9.8%). Three studies evaluated ART outcomes, showing higher pregnancy rates per ET in the primary surgery group (47.9%) compared to the multiple surgery group (25.1%). However, cumulative ART live birth rates were similar (41.7% vs. 39.4%), and miscarriage rates were comparable (16.7%–22.2% vs. 15.2% - 24.2%).

Conclusion
Overall, multiple surgeries for endometriosis appear to reduce spontaneous and ART pregnancy rates. However, live birth and miscarriage rates were similar between the primary and multiple surgery groups. The limited number of studies suggests a need for further research to clarify the long-term impact of multiple surgeries on fertility.

Key words
Endometriosis, surgery, fertility

MANAGEMENT OF THE APPENDIX IN ENDOMETRIOSIS: A PRISMA-SCOPING REVIEW

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Country where research was undertaken:
Australia

Introduction/Background
The assessment & management of the appendix during concomitant surgical treatment for endometriosis remains controversial. The appendix may be directly affected by endometriosis, either contiguously with advanced pelvic disease or as an isolated site for extra-pelvic endometrial deposits. The appendix's role & management in chronic pelvic pain is poorly characterized.

Materials and Methods
The Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) methodology was utilized to systematically capture published data relating to the appendix in the management of endometriosis. A Patient/Problem, Intervention, Comparison, Outcome (PICO) technique was utilized to develop a broadly inclusive search strategy. Screening, selection, and data extraction was performed by multiple authors. A narrative categorical and Centre for Evidence-Based Medicine: Levels of Evidence (CEBM) methodology was selected for describing results.

Results
160 articles were identified in the initial search and 53 were included in the final analysis following exclusions / removal of duplicates. 22 articles were narrative clinical reviews without systematic literature search, 13 articles were case reports, 13 articles were observational studies (cohort or case control), and 5 were review articles with some degree of systematic literature review. Articles were primarily categorized into one of four domains: endometriosis of the appendix, appendicectomy at the time of surgery for endometriosis, the role of the appendix in the surgical management of chronic pelvic pain, and the radiological assessment of the appendix in the context of endometriosis and/or chronic pain. There was a high degree of overlap between the domains in most papers.

Conclusion
There is an extreme paucity in high quality evidence supporting the assessment and management of the appendix in the context of endometriosis, or other gynaecological conditions presenting as chronic pelvic pain. Management of the appendix should be included in future studies on the surgical management of endometriosis.

Key words
Endometriosis, appendix, surgery

LINEAR RESECTION OF BOWEL ENDOMETRIOSIS: A CASE REPORT AND LITERATURE REVIEW

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Country where research was undertaken:
Australia

Introduction/Background
Endometriosis involving the bowel is a challenging condition that often necessitates surgical intervention for symptomatic relief. This case report presents a unique instance of linear resection for bowel endometriosis, highlighting its benefits, such as reduced surgical duration and nerve preservation, alongside a review of relevant literature.

Materials and Methods
A 40-year-old woman with a history of severe pelvic pain and dyschezia was diagnosed with bowel endometriosis, primarily affecting the anterior surface of the sigmoid colon and rectum. Linear resection was performed using an Eschelon 60 mm stapler, avoiding the need for complete lateral bowel mobilization and thereby preserving the nerves. We utilized this technique for a linear lesion up to 4 cm in length. A literature review was conducted using databases like PubMed and Cochrane Library.

Results
The patient underwent a successful linear resection, which significantly reduced the surgical duration compared to disc or segmental resection. The technique proved effective for anterior lesions of the sigmoid and rectum, preserving nerve function and resulting in discharge within 24 hours. This approach was successfully applied in two cases with similar outcomes. While the technique appears to be a promising alternative to shaving, disc, and segmental resection, careful case selection is essential. It is particularly suitable for longer anterior surface lesions, with no size limitations observed for lesions up to 4 cm. However, further long-term data are needed to assess lumen narrowing and post-resection leak rates.

Conclusion
Linear resection offers a valuable surgical option for bowel endometriosis, especially for anterior lesions of the sigmoid and rectum, reducing operative time and preserving nerve function. It serves as a good alternative to traditional techniques, but careful case selection is critical. Future studies are required to evaluate long-term outcomes, including potential risks such as lumen narrowing and anastomotic leak rates.

Key words
Bowel endometriosis, linear resection, surgical technique

THE EFFECT OF TEMPORARY ABDOMINAL WALL OVARIAN SUSPENSION DURING LAPAROSCOPIC ENDOMETRIOSIS SURGERY FOR ADHESION PREVENTION

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Country where research was undertaken:
Israel

Introduction/Background
Pelvic adhesions, particularly between ovaries and pelvic sidewall, frequently complicate endometriosis surgery. Despite various interventions, no widely accepted solution exists. Small studies suggest temporary ovarian suspension may reduce adhesion formation. This technique, which temporarily elevates ovaries postoperatively, shows promise but requires further investigation to confirm its efficacy and long-term outcomes.

Materials and Methods
This prospective, single-blinded, randomized controlled study compares adhesion formation in endometriosis patients at risk for ovarian adhesions. Participants are randomized to undergo laparoscopic surgery with temporary ovarian suspension or standard care without ovarian suspension. Pain and suture removal

eagerness are assessed via daily questionnaires. Blinded ultrasound experts evaluate adhesions at 6 and 13 weeks postoperatively. No anti-adhesive barriers are used to minimize confounding factors

Results
This ongoing study aims to evaluate the efficacy of ovarian suspension in reducing adhesions following laparoscopic endometriosis surgery. Based on previous research, we hypothesize a reduction in adhesion rates from 50% to 20%. To achieve 95% confidence and 80% power, a sample size of 76 ovaries (38 suspended, 38 non-suspended) is required in women with moderate to severe endometriosis.

Secondary objectives include analyzing patient symptoms, adherence to ovarian suspension, and requests for early suture removal (before one week postoperatively). We anticipate 5-10% of patients may request early suture removal.

The study is currently in progress, and results are pending. These findings will contribute to our understanding of ovarian suspension as a potential adhesion prevention technique in endometriosis surgery.

Conclusion
Temporary ovarian suspension represents a potentially valuable, cost-effective approach to mitigate postoperative ovarian adhesions following laparoscopic endometriosis surgery. If ongoing research confirms its efficacy, this straightforward technique could become a standard component of surgical protocols, potentially improving outcomes for patients undergoing endometriosis treatment

Key words
Adhesions, ovary, suspension

THEME: SURGICAL VIDEOS

VAGINAL ENDOMETRIOSIS RESECTION GUIDED BY INTRA-OPERATIVE TRANSVAGINAL ULTRASOUND

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Objective
Vaginal endometriosis is a common condition occurring in 3.5-14.5% of patients with endometriosis (1-3). Complete resection of vaginal endometriosis is important as aggressive resection may lead to unnecessary colpotomy which may be associated with increased risk of rectovaginal fistula (4), while an incomplete resection may result in residual disease and possibly increase rate of recurrence. The aim of this study is to demonstrate the use of intra-operative ultrasound to guide safe and complete vaginal wall endometriosis resection.

Design
A video article demonstrating a surgical technique.

Setting
A patient with previous history of hysterectomy, presenting with symptomatic rectal deep-infiltrating endometriosis nodule invading the vaginal wall, an academic affiliated health care center.

Interventions
This is a case of a 33-year-old patient with chronic pelvic pain, dyspareunia, constipation, and dyschezia. Patient was previously undergone laparoscopic hysterectomy and bilateral salpingectomy due to abnormal uterine bleeding and adenomyosis. Imaging investigation including advanced ultrasound scanning and magnetic resonance imaging, showed an atypical right ovarian endometrioma, a rectal deep endometriosis nodule, and a posterior vaginal fornix endometriosis that is tethered to the bowel endometriosis nodule.

The patient underwent a laparoscopic right oophorectomy, colorectal anterior resection, and excision of vaginal vault endometriosis under transvaginal ultrasound guidance.

In this procedure, after performing cystectomy and pelvic adhesionolysis, we identified the recto-vaginal endometriosis nodule which was then confirmed with a intraoperative transvaginal ultrasound scan. The rectum segment affected with endometriosis was then isolated and mobilized. A suture was placed on the vaginal endometriosis nodule to mark its location and to allow proper traction to facilitate its resection.

The vaginal vault was re-assessed with both palpation and TVS for residual disease. Although, the residual vaginal endometriosis

was not clearly identified by palpation alone, intra-operative TVS scan revealed residual disease that was then surgically removed. We subsequently proceeded with the anterior resection that was performed by our colorectal surgeon team.

Conclusion
Intraoperative ultrasound- guided vaginal endometriosis resection is an effective technique that allows a better intraoperative visualization of vaginal endometriosis and may facilitate a safe and complete resection of vaginal endometriosis.

Key words
Endometriosis, vaginal endometriosis, intraoperative ultrasound

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COLORECTAL SURGERY FOR ENDOMETRIOSIS: A COMPREHENSIVE STEP-BY-STEP APPROACH OF THE DISC EXCISION TECHNIQUE

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Countries where research was undertaken:
Switzerland and France

Introduction/Background
The aim of this video is to present the systematic approach of the disc excision technique for patients suffering from colorectal infiltration of endometriosis.

Materials and Methods
We are presenting the case of a 27-year-old woman experiencing dyschezia and dyspareunia. Preoperative magnetic resonance imaging (MRI) revealed a 3 cm endometriotic nodule in the rectosigmoid colon. We opted for a discoid resection.

Results
This technique can be used if the endometriotic nodule in the rectum is not too large, with a diameter of 3 cm most commonly considered the limit. However, if shaving is performed before resection, lesions up to 4–5 cm can be treated using the disc excision technique.

No special preoperative bowel preparation is required. The surgery consists of the following six steps: 1. Adhesiolysis and ureterolysis, 2. Dissection of the mesorectal space, 3. Transection of the endometriotic nodule, 4. Superficial shaving of the nodule, 5. Transrectal insertion of the circular stapler, and 6. Resection of the anterior rectal wall with enclosure of the affected area. Patients can receive early enteral nutrition following the ERAS concept (Enhanced Recovery After Surgery).

Conclusion
According to our experience and to a prospective study (1) the disc excision technique is a reproducible and safe procedure with a low complication rate, good functional outcomes, and significant symptom reduction, particularly in cases of dyschezia.

Key words
Deep endometriosis, rectum, laparoscopy

Reference
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COMBINED ROBOTIC-TRANSANAL-TRANSECTION-SINGLE-STAPLER (TTSS) RECTAL RESECTION AND COLO-ANAL ANASTOMOSIS FOR DEEP ENDOMETRIOSIS OF LOW RECTUM, VAGINA AND PARAMETRIUM

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Country where research was undertaken:
France

Objective
To describe a combined robotic and transanal technique used to treat deep endometriosis infiltrating the vagina, both parametria and ultralow rectum in a 27-year-old patient with deep dyspareunia, right sciatic pain, bladder dysfunction and severe dyschezia.

Introduction/Background
The achievement of bowel anastomosis in low rectal endometriosis is challenging owing to technical and anatomic limitations. By allowing a right angle rectotomy with a single-stapled anastomosis, the transanal transection single-stapled technique overcomes these technical difficulties ensuring a good-quality anastomosis with an easier correction of postoperative anastomotic leakage when it occurs.

Interventions
The surgical strategy is splitting the nodule in 3 components according to different anatomic structures involved (parametrium, vagina, and rectum), then removing each one separately. The rectal involvement is approached following several steps: 1) opening of the rectovaginal space, 2) transection of the mesorectum and mesocolon; 3) section of inferior mesenteric vessels to obtain a proper colon mobilization; 4) start of the transanal step and transanal distal section of the rectum at 4-5 cm above the anal verge; 5) extraction of the specimen through the anus, 6) proximal bowel segment transection 1 cm above the upper limit of the nodule under ICG control; 7) placement of circular stapler anvil into the sigmoid colon which is secured by a purse string suture; 8) running suture of the distal edge; 9) connection between the anvil and the shoulder of the transanal circular stapler, which is then fired with coloanal anastomosis formation; 10) stapled line reinforcement by stitches and integrity anastomosis test. No preventive diverting stoma was performed in accordance with our policy. Operative time averages 3 hours.

Conclusions
Although data from other centers are scarce in patients with ultralow rectal endometriosis, the use of TTSS technique is an interesting approach in young patients, with favorable functional outcomes.

Key words
Rectal endometriosis; ultralow rectum; coloanal anastomosis; TTSS.

ROBOTIC COLORECTAL RESECTION USING ONLY CIRCULAR STAPLER - SURGICAL VIDEO

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Country where research was undertaken:
India

Introduction/Background
Rectal endometriotic nodules can cause significant symptoms and are often challenging to detect, especially in patients with a history of hysterectomy. This video demonstrates a robotic-assisted colorectal resection technique using a circular stapler for anastomosis without the use of a linear stapler, providing an organ-preserving and precise approach to excise a missed rectal endometriotic nodule.

Materials and Methods
In this surgical video, a robotic colorectal resection is performed on a post-hysterectomy patient presenting with symptomatic rectal endometriosis due to a previously missed

bowel nodule. The approach avoids the use of a linear stapler, instead employing a circular stapler for the anastomosis. Key steps highlighted include precise robotic dissection, careful excision of the endometriotic nodule, and an anastomosis completed with the circular stapler, facilitated by robotic suturing tools.

Results
The video illustrates the successful excision of the rectal endometriotic nodule with clear margins using the robotic-assisted approach and circular stapler anastomosis. The patient's postoperative recovery was smooth, with immediate symptom relief, no anastomotic leaks, and normalized bowel function. This technique provided comparable outcomes to traditional methods while reducing the need for multiple stapling instruments.

Conclusion
This video showcases the effectiveness of a robotic approach for resecting rectal endometriotic nodules using a circular stapler for anastomosis, particularly beneficial in complex cases following hysterectomy. This approach improves symptom management, preserves bowel integrity, and optimizes resource use, supporting further exploration of this technique in endometriosis-related colorectal surgery.

Key words
Rectal endometriosis, robotic colorectal resection, circular stapler

THEME: TRANSLATIONAL SCIENCE/MEDICINE

EFFECT OF INTRAUTERINE ADMINISTRATION OF CXCL12 OR MESENCHYMAL STEM CELLS ON PREGNANCY OUTCOMES IN MICE WITH INDUCED ENDOMETRIOSIS

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Country where research was undertaken:
Brazil

Introduction/Background
Probably women with endometriosis have impaired embryo implantation, likely due to a potential decrease in stem cell trafficking for endometrial repair. This project aims to evaluate the effect of uterine administration of CXCL12 or mesenchymal stem cells (MSCs) on pregnancy rates and placental characteristics in subfertile mice with induced endometriosis.

Materials and Methods
Wild-type C57BL/6 mice underwent endometriosis induction by suturing uterine fragments from a donor onto the abdominal wall; while sham group received the same sutures without uterine tissue. Four weeks later both groups were subdivided to receive: intrauterine injection of 1. CXCL12 or 2. MSCs (from GFP+ donors) or 3. placebo. These female mice were put to mate with proven males. Pregnancy was terminated by C-section near term for collection ofplacenta, adjacent uterus and umbilical cord.

Results
Reproductive outcomes showed a 100%pregnancy rate in all three Sham groups (ShamCX, ShamMSC, and ShamPl)($p > 0.05$). In the EndoPl group, only a 50% pregnancy rate was observed($p=0,016$) compared to all other five groups, confirming subfertility in these animals. However, fertility was completely restored (100% pregnancy rate) in both the CXCL12(EndoCX) and MSC(EndoMSC) treated groups. Also, the offspring size was similar between sham groups and Endo treated groups ($p>0.05$). However, beside the improve in implantation and in pregnancy rates, immunofluorescence analysis did not identify MSCs in the placental-decidual endometrial complexes of the MSC-treated groups, indicating they were not composing the placenta tissue as differentiated cells. No significant histomorphometric differences were found in the placenta structural characteristics between the study groups ($p > 0.05$).

Conclusion
Probably MSCs, whether attracted byCXCL12or injected directly into the uterus, had a favorable effect on placental development without directly being incorporated into it. We speculated it might secrete some substance or trigger some processes in a molecular level, not evaluated in this study, improving endometrial receptivity for embryo implantation.

Key words
Endometriosis mice model; mesenchymal stem cells (MSC); placenta

DEVELOPING NOVEL THERAPIES AGAINST ENDOMETRIOSIS THROUGH INHIBITION OF OXIDATIVE PHOSPHORYLATION

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Country where research was undertaken:
United States of America

Introduction/Background
Maximum amount of cellular ATP is produced by oxidative phosphorylation (OXPHOS). Several inhibitors of this pathway trigger the production of oxygen radicals that reduce cell viability. Here we provide evidence, that the clinically-approved anti-malarial drug, atovaquone and other inhibitors of OXPHOS are novel drug candidates for clinical management of endometriosis.

Materials and Methods
Viability, oxygen radical formation and DNA damage in the endometriosis cell line 12Z and patient-derived endometriotic cells in response to atovaquone, plumbagin and other OXPHOS inhibitors was tested using live/dead assays, flow cytometry and fluorescence microscopy, respectively. Oxidative damage and glutathione and other antioxidant molecules were monitored by ELISA and western blotting. Seahorse analyzers were used to monitor oxygen consumption and extracellular acidification. 6-Phosphogluconate and other metabolites were analyzed by ELISA and other bioanalytical techniques.

Results
Treatment of 12Z and patient-derived endometriotic cells with atovaquone, plumbagin and other OXPHOS inhibitors resulted in significant decrease in cell viability at IC50 concentrations between 1-50 µM. Exposure to these drug candidates resulted in a rapid increase in intracellular oxygen radicals that caused downstream damage to nuclear DNA and nuclear integrity. This triggered activation of ATM/ATR pathway. Moderation of the oxidative damage reversed the adverse effects of the OXPHOS inhibitors on cell viability. The OXPHOS inhibitors inhibited oxygen consumption by the endometriotic cells and an increase in extracellular acidification suggesting a metabolic shift to aerobic glycolysis. Additionally, an increase in 6-phosphogluconate suggested an increase in pentose phosphate pathway to neutralize the oxygen radicals through the production of glutathione.

Conclusion
Our studies suggest that OXPHOS is a druggable pathway in endometriosis. Atovaquone is extensively used to treat malaria in humans and is therefore an excellent agent to consider for the treatment of endometriosis. The metabolic adaptations by the OXPHOS inhibitor-treated endometriotic cells may provide additional targets for drug development.

Key words
Oxidative phosphorylation, drug development, metabolism

AIDEN-STUDY(II): EXPLORING THE IMPACT OF AN ANTI-INFLAMMATORY DIET INTERVENTION ON ENDOMETRIAL AND SYSTEMIC IMMUNE SYSTEM IN PATIENTS WITH ENDOMETRIOSIS

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Country where research was undertaken:
The Netherlands

Introduction/Background
Endometriosis is characterized by inflammation, contributing to chronic pain and lowered health related quality of life (HRQoL). An anti-inflammatory (AIDEN) intervention may reduce inflammation, potentially alleviating pain and increase HRQoL (abstract I). This study examines whether AIDEN intervention impacts endometrial and systemic immune system in endometriosis patients.

Materials and Methods
Eighteen patients with endometriosis completed the 12-week intervention, while nine healthy women served as controls. Pain levels in patients were assessed using the Numeric Rating Scale (NRS) before and after the AIDEN intervention. Plasma samples from patients, and controls were analyzed for 92 inflammatory markers. Additionally, a 42-marker flow cytometry panel characterized immune cell subsets in menstrual (MB) and peripheral blood (PB). Both manual and unsupervised methods were employed to analyze the high-dimensional flow-cytometry data.

Results
Seven inflammatory markers-CDCP1, CXCL10, IFN-γ, IL6, IL18, MCP-3, and MMP-10 were significantly elevated ($p < 0.05$) in endometriosis patients compared to controls. Immunophenotyping showed significantly higher frequencies of regulatory/transitional $CD24^{high}CD38^{high}$ B cells in MB ($p = 0.023$) and PB ($p = 0.001$) in the endometriosis group. Additionally, lower frequencies of terminally differentiated effector memory $CD4^{+}T_{TEMRA}$ ($p = 0.002$) and $CD8^{+}T_{TEMRA}$ cells ($p = 0.010$) in PB indicated impaired effector responses. While the intervention significantly reduced pain levels of endometriosis patients, it did not decrease inflammatory marker levels. However, it led to a significant reduction in $CD24^{high}CD38^{high}$ B cell percentages ($p = 0.049$) and a significant increase in Th2-type $CD4^{+}$ ($p = 0.0065$), $CD4^{+}T_{TEMRA}$ ($p = 0.027$), and effector-memory $CD4^{+}$EM cells ($p = 0.046$) in PB.

Conclusion
Our study identified significant differences in inflammatory markers and immune cell profiles between endometriosis patients and controls. The AIDEN intervention influenced immune cell subsets in PB. Currently the data is further analyzed to explore the relationship between diet, pain, and immune function in endometriosis.

Key words
Anti-inflammatory diet, immune system, high-dimensional flow cytometry

MUCOADHESIVE MASTERY: HYDROGEL USE IN DRUG DELIVERY

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Country where research was undertaken:
United Kingdom

Introduction/Background
Laparoscopic surgery for endometriosis has a 60% repeat rate[1], whilst hormonal therapies often cause systemic side-effects and inhibit desired conception. Developing a peptide hydrogel for localised low-dosage drug-delivery at disease sites may reduce endometriotic lesion regrowth and the need for repeat surgeries, causing fewer side-effects and allowing conception.

Materials and Methods
PeptiGels® are injectable self-assembling hydrogels[2]. The stability, mucoadhesive and degradation properties of PeptiGels® were assessed *in vitro* on a Visking membrane under continuous flow (2 ml/min) for 2 hours of bio-relevant 'peritoneal-fluid' media and under immersed conditions (10 ml) at 37°C for 28 days. Oscillatory and shear recovery rheology were performed to indicate the injectability of each PeptiGel®. Degradation was assessed using PeptiGels® tagged with fluorescein isothiocyanate (FITC).

Results
PeptiGels® remained on the visking membrane, demonstrating mucoadhesion and maintaining their shape over two hours under a continuous flow of bio-relevant media. The PeptiGels® remained affixed to the visking membrane for up to 14 days in immersed conditions and maintained their integrity and shape for up to 28 days. Degradation, as indicated by the FITC release, was minimal, with a cumulative release of 2.1% and up to 30.0% under continuous flow and immersed conditions, respectively. Findings show that altering peptide concentration improves mucoadhesion. Rheology testing indicated that PeptiGels® were injectable and recovered after shear stress.

Conclusion
PeptiGels® demonstrate stability and mucoadhesion under bio-relevant conditions. They present a promising localised delivery system at disease sites, enabling low drug-dosages over a longer period, thus enhancing conception chances while minimising side-effects. Adjustments to biomechanical and biochemical properties of PeptiGels® are continuing to be explored for controlling drug-

release.

Key words
Local-treatment, Hydrogel, Endometriosis

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PEROXISOME PROLIFERATOR-ACTIVATED RECEPTOR Γ (PPARΓ) PLAYS A ROLE IN THE BENEFICIAL EFFECTS OF VOLUNTARY EXERCISE IN AN ENDOMETRIOSIS ANIMAL MODEL

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Countries where research was undertaken:
Puerto Rico and United States

Introduction/Background
Voluntary exercise can reduce lesion development and inflammatory parameters in an animal model of endometriosis.[1] We hypothesized that this effect might be mediated by the ability of exercise to increase the expression of peroxisome proliferator-activated receptor γ (PPARγ) since we previously found PPARγ overexpressed in vesicles of exercised animals.

Materials and Methods
Female Sprague-Dawley rats were randomized to Endo Vehicle No-Exercise, Endo Vehicle Exercise, or Endo Drug Exercise (n=12/group). Following surgical endometriosis induction (day 0) exercise groups had access to a running wheel. Endo Drug Exercise received a PPARγ antagonist (GW9662; 10 mg/kg) using a 1:1 mixture of peanut butter and Cheez Whiz from day 8 until sacrifice (day 61). Developed vesicles were collected and measured. Colon, ileum, and mesenteric fat were stored for further histological analysis.

Results
Both exercise groups had a significantly higher food consumption ($p<0.001$) when compared to non-exercise, while no difference was observed in weight change or absolute weight at the time of sacrifice. The fat/body weight percentage was significantly decreased by exercise in the endometriosis animals ($p<0.0001$). Exercise reduced the percentage of developed vesicles compared to non-exercise (64.6% vs 85% respectively) as well as their size (area, length, weight), while this effect was reversed with the PPARγ antagonist (87.5%). Exercise significantly decreased the colonic macroscopic damage ($p<0.0001$), while that effect was reversed by the antagonist ($p<0.0001$). The same trend was observed in the microscopic analysis by hematoxylin and eosin staining. No significant differences were observed in mast cell infiltration, nor cytokine levels in serum or peritoneal fluid.

Conclusion
Our results indicate that PPARγ contributes to decreasing endometriosis presentation via voluntary exercise. These beneficial effects were reversed by administration of a PPARγ antagonist. Understanding how exercise improves endometriosis will help us design personalized non-pharmacological complementary patient interventions.

Key words
Endometriosis, Exercise, PPARγ

Reference
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