BIMDG

British Inherited Metabolic Disease Group

The British Inherited Metabolic Diseases Group (BIMDG) Annual Symposium

Abstract Booklet

Monday 29 June - Wednesday 1 July 2026

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Oral Presentations

Long-term safety and efficacy of pegunigalsidase alfa in patients with Fabry disease: results from the Phase 3 BRILLIANCE extension study

Prof Derralynn Hughes[1,2], Prof John Bernat[3], Prof Aleš Linhart[4], Prof Ozlem Goker-Alpan,[5], Dr Shoshi Tessler[6], Dr Meng Wang[7], Dr Giovanni Piotti[8], Joana Almeida[8]
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BRILLIANCE (NCT03566017; last patient/last visit 21-January-2025) is an international, single-arm, open-label Phase 3 extension study characterizing the long-term safety/efficacy profile of pegunigalsidase alfa 1 mg/kg every 2 weeks (E2W) in adults with Fabry disease (FD). Eligible patients had either completed the Phase 3 BRIDGE or BALANCE trials, or ≥48 months of the phase 1/2 PB-102-F03 trial. On enrollment to BRILLIANCE, patients continued receiving, or switched to, pegunigalsidase alfa (PA) 1 mg/kg; baseline was defined as last assessment prior to the first ever PA infusion. Ninety-seven patients were enrolled; 54.6% had classic FD, 61.9% were male. At baseline, most patients had received enzyme replacement therapy (71.1% agalsidase beta; 18.6% agalsidase alfa); 25.8% had anti-drug antibodies (ADAs) against PA, and median (range) baseline estimated glomerular filtration rate (eGFR) was 77.7 (24.4, 131.0) mL/min/1.73m². From first dose, cumulative population and median (range) patient-level exposure to PA were 529.1 years and 5.7 (1.3, 10.6) years, respectively. Treatment-related adverse events (TRAEs) occurred in 47.4% of patients, representing only 5.4% of all adverse events (n=134/2486). Serious TRAEs were rare (n=2; 2.1%, both infusion-related reactions [IRRs]), and only one patient (1.0%) discontinued due to a non-serious TRAE. IRRs were infrequent (0.6/100 infusions; 83 IRRs in 29 [29.9%] patients <24h post-infusion), with no withdrawals or deaths attributed to IRRs. Four deaths occurred, all unrelated to PA. Kidney function remained stable throughout the study (median [range] annualized eGFR slope –1.77 [–21.2, 4.2] mL/min/1.73m²/year) and low plasma globotriaosylsphingosine (lyso-Gb3) levels were maintained without re-accumulation. The proportion of ADA-positive patients remained consistent from baseline to the last visit (24.7%). These findings demonstrate that long-term treatment with pegunigalsidase alfa 1 mg/kg E2W offers a sustained safety and efficacy profile in adults with FD over a median of nearly six years, supporting its role as a viable long-term therapy.

Management of pregnancy in a patient with lysinuric protein intolerance complicated by immune dysregulation and severe thrombocytopenia

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Background: Lysinuric protein intolerance (LPI) is a rare autosomal recessive disorder of dibasic amino acid transport associated with secondary urea cycle dysfunction and immune

dysregulation. Pregnancy in LPI is rarely reported and presents significant metabolic, haematological, and obstetric challenges.

Case: We report a 25-year-old woman with genetically confirmed LPI complicated by prior haemophagocytic lymphohistiocytosis (HLH), systemic lupus erythematosus (SLE), and reduced bone mineral density, presenting with an unplanned pregnancy. She was managed in a specialist maternal inherited metabolic disorders (IMD) clinic within a multidisciplinary team. Early gestation was characterised by metabolic instability, including transient hyperammonaemia and elevated orotic acid, which improved with optimisation of nitrogen scavenger therapy, citrulline supplementation, and nutritional support.

The second trimester was complicated by progressive severe thrombocytopenia and anaemia, managed as presumed immune thrombocytopenia with corticosteroids and intravenous immunoglobulin, achieving partial response. Renal involvement progressed with increasing proteinuria despite preserved renal function.

In the third trimester, hyperammonaemia (peak 171 µmol/L) occurred following antenatal corticosteroid administration in the context of underlying metabolic vulnerability. This was managed with intravenous dextrose and nitrogen scavenger therapy. Delivery by elective caesarean section at 35 weeks resulted in a live infant requiring short-term neonatal support. Postpartum recovery was marked by resolution of thrombocytopenia and stable metabolic control. Breastfeeding was established with calcium supplementation and ongoing metabolic bone surveillance.

Conclusion: This case defines a previously unreported high-risk LPI phenotype characterised by immune dysregulation and severe thrombocytopenia. It highlights the importance of multidisciplinary management, including specialist maternal IMD care, in achieving favourable maternal and neonatal outcomes.

Pregnancy in maternal isovaleric acidaemia: management and outcome

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Background: Evidence to guide pregnancy care in women with isovaleric acidaemia is scarce. This cohort study reviewed metabolic and dietetic management, and maternal and neonatal outcomes in pregnancies supported by a single adult inherited metabolic diseases service.

Methods: Medical and dietetic records were reviewed for all pregnancies in women with isovaleric acidaemia managed from 2006 to 2026. Data captured diet and protein intake, carnitine and glycine use, key biochemical markers, intrapartum metabolic plans and maternal, obstetric and neonatal outcomes.

Results: Fifteen pregnancies occurred in five women (range 1–5 each). Seven pre-dated specialist follow-up and had limited data; eight pregnancies were analysed in detail, albeit complete data sets were not available for each pregnancy. No maternal metabolic decompensations or emergency regimen use were recorded. Intrapartum intravenous 10% dextrose was recommended in 5 pregnancies; intravenous carnitine was not recommended. Delivery mode was recorded for six pregnancies: elective caesarean (n=4), emergency caesarean (n=1) and instrumental vaginal (n=1); mode was unrecorded for two. All recorded births (n=5) were at term and no neonatal intensive care admissions were reported. Protein intake was recorded in five pregnancies and varied markedly: self-restricted intake (patient-initiated restriction despite a non-restricted clinical prescription) was lower (median 0.38

g/kg/day) than unrestricted intake (median 1.39 g/kg/day). No pregnancy used leucine-free amino acid or glycine supplements. In available trimester samples, isoleucine was within range in 8/9, valine 5/9, leucine 4/9 and glycine 8/8; vitamin B12 9/11, folate 11/11, and total homocysteine 7/10.

Conclusions: Pregnancy in women with isovaleric acidaemia was not associated with maternal metabolic decompensation and neonatal outcomes were favourable. Only 33% of deliveries were prophylactically supported with 10% intravenous dextrose. Lower protein intakes coincided with lower branched chain amino acids and vitamin B12 and higher total homocysteine levels. Wide variability in protein intake supports proactive, trimester-specific dietetic review.

Transition in urea cycle disorders from paediatric to adult services: a UK multi-centre mixed-methods service evaluation

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Background: Transition from paediatric to adult services is critical for patients with urea cycle disorders (UCDs), yet evidence on post-transition metabolic outcomes remains limited. This evaluation assessed whether transition affected ammonia control and hyperammonaemic crisis (HAC) frequency, and identified pre-transition risk factors for stratified care.

Methods: A retrospective convergent mixed-methods service evaluation was conducted across four English specialist metabolic centres (n=25; 14 female; median transition age 17 years; OTC deficiency n=13, ASL deficiency n=7, other n=5). Pre- and post-transition ammonia, glutamine, HAC frequency, and healthcare utilisation were compared using Wilcoxon signed-rank tests. Effects of sex, intellectual disability (ID), and UCD type were examined via Mann–Whitney U and Kruskal–Wallis tests. Spearman correlations identified pre-transition predictors. Clinician proformas captured qualitative data on transition and perceived success.

Results: Ammonia control was maintained post-transition (median 41.5 vs 48.0 µmol/L, p=0.851), with no change in HAC frequency (p=0.953) or emergency department visits (p=0.422). Male sex predicted higher post-transition ammonia (92.3 vs 35.0 µmol/L, p=0.004, r=0.61), HAC frequency (p=0.007), and emergency department visits (p=0.005). A sex-by-ID interaction (H=11.54, p=0.009) showed ID conferred risk predominantly in males; females with ID had the best control. Pre-transition HAC history was the strongest predictor of post-transition crises (rs=0.91, p<0.001). A three-factor risk score (male, ID, not independent) showed dose–response with post-transition ammonia (H=9.63, p=0.022). Clinicians rated 86% of transitions successful, but ratings were unrelated to biochemical outcomes; only 20% received formal readiness assessment.

Conclusions: Transition in urea cycle disorders can be achieved without deterioration in ammonia control or crisis frequency. Male sex combined with intellectual disability identifies a high-risk subgroup requiring intensified monitoring. Pre-transition crisis history and a three-factor risk score are actionable tools to stratify care. The disconnect between clinician-perceived success

and metabolic outcomes suggests formal readiness assessment and objective outcome measures should be incorporated into transition practice.

A service evaluation of patient initiated follow up – the experience of a large adult inherited metabolic disease service

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Background: The Mark Holland Metabolic Unit (MHMU) is the largest adult inherited metabolic disease (IMD) service in the UK. Patient numbers have increased by 70% since 2019, reaching 2,445 by March 2026, placing increasing pressure on outpatient capacity. Patient initiated follow up (PIFU) offers a solution, enabling stable patients to request review based on need rather than fixed intervals. Evaluation of PIFU in IMD services is limited.

Methods: A service evaluation was undertaken of all patients enrolled in PIFU in March 2026. Individuals are offered a deferred routine follow-up and the option to request earlier review based on patient need.

Results:A total of 143 patients (5.8% of the MHMU total cohort) were enrolled in PIFU with a median age of 39 years (IQR: 29-52). Patients have been enrolled in PIFU since 2022, but the majority (n=78, 54.5%) were recruited within the last 12 months providing a median time on PIFU of 10 months (IQR:7-19). Deferred follow-up appointments were scheduled at 59 months (IQR:23-86) with only 4 individuals (2.8%) requesting follow up prior to this. Assuming one appointment per year, an estimated 95 outpatient appointments were saved. The most frequent conditions in PIFU were low-risk PKU (n = 38, 26.6%), suspected metabolic myopathy (n = 27, 18.9%) and low-risk fatty acid oxidation defects (n = 26, 18.2%). 50 patients (35%) had a history of inconsistent attendance. Inconsistent attendance was most frequently seen in PKU (60.5%) and least frequently in metabolic myopathy (0.0%) and TMAU (0.0%). There were no emergency admissions due to metabolic decompensation.

Discussion: Early results demonstrate that PIFU has reduced routine outpatient demand with minimal need for early review, supporting its use as a safe and efficient follow-up model in selected IMD patients. Continued monitoring is required to understand long term effects on patient experience, safety, and outpatient capacity.

Heterogeneity in Sapropterin Administration Among Paediatric/Adult Patients with Phenylketonuria: Findings from a National Survey

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Background: Sapropterin dihydrochloride (sapropterin) is an established treatment for phenylketonuria (PKU) in responsive individuals, yet uncertainty persists regarding optimal dosing frequency, timing relative to meals, dietary influences, and formulation handling. Variation in clinical advice and patient practices may influence treatment effectiveness, tolerability, and adherence. Real-world administration behaviours have not previously been characterised. This study aimed to describe how sapropterin is administered in everyday practice and examine its association with changes in natural protein tolerance.

Methods: A 31-item questionnaire was disseminated via the NSPKU website and social media. Data collected included demographics, dosing schedules, formulation use, administration techniques, co-ingestion with food, and changes in natural protein tolerance following sapropterin initiation. Ordinal regression was used to identify predictors of protein tolerance change.

Results: A total of 129 individuals completed the survey, including 123 current sapropterin users. Most respondents were caregivers of children or adolescents (69% aged 0−18 years). Over half (55%) had been on treatment for two to three years. Once-daily dosing was most common (66%), typically taken with breakfast, followed by twice-daily dosing (33%). Tablets were the predominant formulation (93%), with 51% swallowed whole; 7% used powder sachets. Most respondents (75%) took sapropterin with food, including low-fat (37%) and high-fat (26%) meals. Natural protein tolerance increased significantly after treatment initiation ($p<0.001$), with reported increases ranging from 65% to >447%. Adults and individuals swallowing tablets whole experienced greater increases ($p=0.038$). 15% achieved an unrestricted diet. While 72% were satisfied with their increased protein allowance, many expressed a desire for further improvement.

Discussion: This is the first UK study to characterise real-world sapropterin administration in PKU. Substantial heterogeneity in formulation handling, and co-ingestion behaviours reflects the need for further standardised guidance. These findings highlight the need for further research to optimise sapropterin administration across patient age groups.

The authors acknowledges NSPKU for funding.

Undetectable Beta-lipoproteins in a Family with Definite Familial Hypercholesterolaemia

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Introduction: Familial hypercholesterolaemia (FH) is a common monogenic disorder characterised by elevated LDL-C and increased cardiovascular disease risk. Conversely, familial hypobetalipoproteinemia (FHBL) is a rare monogenic disorder characterised by defective production of beta-lipoproteins, due to APOB genetic variants. Low levels of ApoB and LDL-C

protect against cardiovascular disease; however, FHBL is associated with hepatic steatosis and rarely cirrhosis. We present an unusual case of a family where FH coexists with FHBL.

Case report: The index patient was a 53yr old male with baseline LDL-C 5.3 mmol/L. Genetic testing confirmed FH due to LDLR variant. Cascade screening found two children with the familial LDLR variant. Despite genetically confirmed FH, one son (13yrs) had LDL-C 0.7 mmol/L and ApoB <0.2 g/L. Another son (11yrs) had LDL-C <0.5 mmol/L and ApoB <0.2 g/L.

To help ascertain the cause of hypobetalipoproteinaemia, we tested the children's mother and found a low ApoB 0.41 g/L (0.60–1.17 g/L). Genetic testing for FHBL identified a heterozygous pathogenic variant in APOB (c.9344del) in the mother. The two sons had also inherited the FHBL variant (alongside LDLR variant).

The older son had a raised ALT with hepatomegaly and moderate-severe hepatic steatosis on ultrasound. The younger son had evidence of mild hepatic steatosis.

Discussion: To our knowledge, this is the only report of LDLR variant causing FH co-existing with heterozygous APOB FHBL. Previous case report of dual APOB variants causing FH and FHBL led to a normolipidaemic picture, while that of APOB (FHBL) and PCSK9 (FH) variants led to a similar picture seen in our family. The side effect of APOB inhibition may be variant dependent, and suggest a role of targeted therapy in APOB FH. Ongoing hepatic surveillance is needed given pre-existing liver disease. LDL-C may fluctuate during puberty and whether phenotype persists into adulthood remains to be seen.

The significance of CSF Glutamine

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Background: CSF amino acid concentrations are typically requested to investigate seizures. Concentrations of CSF amino acids are mostly low relative to those levels typically measured in plasma and it is generally accepted that CSF levels are highly influenced by plasma. Whilst this is undoubtedly true, we noticed that in contrast to most other amino acids, CSF glutamine levels can be unexpectedly high and could significantly surpass paired plasma concentrations. This work looked deeper into the frequency and causes of elevated CSF glutamine.

Methods: Laboratory CSF amino acid data over seven years was extracted and interrogated by looking at total CSF data and paired CSF/plasma results.

Results: From a total of 1291 analyses, 206 samples (16%) showed increased glutamine of >600 µmol/l and 29 samples (2%) showed glutamine >1000 µmol/l. When paired CSF and plasma data was reviewed, glutamine appeared to be the only amino acid that was commonly increased relative to its concentration in plasma. The frequency of this finding suggests that a mechanism for this is likely reflective of an adaptive process rather than being suggestive of a primary genetic cause. Indeed, when clinical details were reviewed from patients in whom CSF glutamine was high, the patient set was diverse rarely with a definitive diagnosis. However, the set did include 24 samples from patients with confirmed DHPR deficiency in which elevated CSF glutamine has been reported. Together this data suggests active glutamine synthesis/release/control in the brain. It is tempting to speculate that this may be mediated by astroglial cells and might also relate to clinical condition.

Conclusions: Full CSF amino acid profiles may reveal more information that we have previously been aware of. In this laboratory, elevated CSF glutamine is common but its cause and significance is unknown. If related to disease then it may be modifiable.

Flash Presentations

Flash presentations will have a supporting digital poster on the Symposium App

Rapid Reversal of Neurological Decline in Arginase 1 Deficiency: Pegzilarginase as a "Bridge" to Living-Donor Liver Transplantation

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Background: Arginase 1 Deficiency (ARG1-D) is an ultra-rare urea cycle disorder where enzyme deficiency leads to toxic arginine accumulation and debilitating neuroprogressive morbidity. Pegzilarginase (Loargys) is a first-in-class, licensed recombinant human enzyme replacement therapy (ERT) designed to normalize arginine levels.

Case Presentation: A pediatric patient, diagnosed at birth, maintained chronically elevated plasma arginine (mean 575 µmol/L; peak 699 µmol/L) despite strict dietary management. Following normal early development, she entered a rapid four-month neurological decline at age three. Progressive spasticity resulted in the total loss of independent ambulation, alongside severe dysarthria and regression to fragmented speech.

Management: After two years on the cadaveric liver transplant list, the patient was moved to the living-donor list to expedite surgery. While awaiting a donor, and as Loargys was not yet NHS-funded, the family secured access via crowdfunding. This licensed ERT was initiated as a vital neuroprotective "bridge" for one of the most severe young cases of ARG1-D treated to date. The patient received 16 weekly doses prior to liver transplant.

Results: Clinical and biochemical response was profound:

- Biochemical: Arginine normalized (116 µmol/L) after four doses (~83% reduction).
- Early Gains: Within three weeks, limb stiffness reduced and speech fluency improved.
- Neurological: By three months, speech returned to normal; dysarthria and stuttering resolved.
- Functional: At 4.5 months, the patient regained independent standing and began taking unassisted steps.

Conclusion: Pegzilarginase can rapidly reverse severe, acute-subacute neurological deficits in ARG1-D. This case underscores the necessity of early access to disease-modifying therapies to restore function in high-severity pediatric patients awaiting definitive transplantation.

An unexpected diagnosis in a child with cardiomyopathy and 3-methylglutaconic aciduria

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Background: An 11 month old female, previously fit and well, presented with a short history of pyrexial illness with vomiting and hypoglycaemia (blood glucose 1.9 mmol/L; ketones 1.6 mmol/L). She deteriorated clinically, necessitating escalation to intensive care. Echocardiogram demonstrated severe dilated cardiomyopathy.

Results: The initial plasma acylcarnitine profile showed free carnitine of 7µmol/L (13-52) and no diagnostic acylcarnitines. The accompanying bloodspot acylcarnitine profile showed normal free

carnitine. A urine organic acid profile was grossly ketonuric with increased 3-methylglutaconate (3-MGA) (confirmed in a subsequent sample). Variants in TMEM70, TAZ (Barth Syndrome) and DNAJC19 (3-MGA-uria type V) have been associated with 3-MGA-uria and cardiomyopathy. However, R14 sequencing revealed pathogenic variants in SLC22A5 (carnitine transporter deficiency, CTD). Mitochondrial genome sequencing was unremarkable. Urine organic acids repeated after 3 months of carnitine supplementation demonstrated resolution of 3-MGA-uria. Repeat echocardiogram demonstrated improved cardiac function.

Conclusions: CTD was an unexpected diagnosis, due to the normal bloodspot free carnitine, and plasma free carnitine was also not as low as expected for CTD. These findings were explained by a prior carnitine infusion the patient had received as part of a Cardiology protocol. 3-MGA-uria has been described in CTD carriers, but has not previously been associated with patients affected with CTD. A state of partial carnitine deficiency following carnitine infusion may have resembled the carnitine status of CTD carriers, providing a possible explanation for the 3-MGA-uria. Normalisation of 3-MGA following 3 months on carnitine would also be consistent with the 3-MGA-uria being secondary to partial carnitine deficiency.

This case illustrates the importance of being aware of prior carnitine supplementation when interpreting acylcarnitine profiles, and that carnitine deficiency should be considered as part of the differential diagnosis of 3-methylglutaconic aciduria.

From frustration to function: reimagining registry value with individual monitoring dashboards to visualise disease progression in Pompe disease

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Background: Pompe disease is progressive and can lead to irreversible muscle damage. This can impact breathing, movement, quality of life, and the ability to perform daily activities, placing a burden on individuals, families and caregivers. Industry registries often lack value to clinicians and patients. Monitoring longitudinal changes in, and the impact of treatment on, motor and respiratory function is essential in Pompe disease management. Raw data are frequently dispersed across electronic records, and clinicians often lack simple, integrated ways to visualise and interpret data to discuss with patients without additional time burden. We aim to address these challenges with a patient monitoring dashboard, which will be provided to enrolled participants at each site participating in the followME Pompe Journey registry (NCT06121011).

Methods: followME Pompe Journey is a global, prospective, observational registry assessing the real-world, long-term safety and effectiveness of Pompe disease treatments. It is being conducted at ~100 sites globally, with 500 anticipated participants (first participant enrolled: February 2024; estimated last patient last visit: September 2033).

Results: The dashboard will provide a one-page graphical summary of patient-level longitudinal data, updated at planned data cuts. Data will be shown for seven clinically relevant outcome measures, selected based on clinician and patient feedback: 6-minute walk distance, 10-metre walk test, forced vital capacity, maximal inspiratory and expiratory pressures, creatine kinase and Fatigue Severity Scale. Feasibility will be monitored, and the dashboard evolved accordingly, given the potential variability in standard clinical practice, existing monitoring systems and data

entry practices across registry centres, as well as possible incompatibility with selected endpoints.

Conclusions: The followME Pompe Journey registry dashboard is being designed to support multidisciplinary reviews, treatment evaluations, shared decision-making and patient–clinician conversations. Further research will assess its utility in supporting multidisciplinary care teams and patients in real-world clinical practice. Supported by Amicus Therapeutics, Inc.

Phenotypic spectrum and diagnostic evolution in GLUT1 deficiency syndrome: a single-centre adult cohort experience

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Background: Glucose transporter type 1 deficiency syndrome (GLUT1DS) is a rare neurometabolic disorder caused by pathogenic variants in the SLC2A1 gene. It is classically described as an infantile-onset condition; however, an expanding phenotypic spectrum is increasingly recognised, including diagnoses in adulthood. In this retrospective review of an adult cohort with GLUT1DS, we explore the phenotypic diversity and diagnostic evolution within this cohort.

Methods: This retrospective case series was a single-centre study conducted at the Mark Holland Metabolic Unit, Salford Royal Hospital and included adult patients with GLUT1DS confirmed via clinical, biochemical or genetic testing.

Results: Thirty-one individuals were identified with a median age of 27 years (IQR: 22-37). Median age at symptom onset was 3 years (IQR: 0-7). Median diagnostic delay was 4 years (IQR: 0-21.5) with a maximal delay of 47 years. 56% of individuals were diagnosed via genetic testing, most commonly by Sanger sequencing or targeted single-gene exon sequencing, with a shift towards whole exome and whole genome sequencing (WGS) in more recent cases. Individuals with a mixed phenotype (seizure and movement disorder) had the lowest median diagnostic delay (0.5 years, IQR: 0-6.75). The longest diagnostic delay was seen in movement-disorder predominant phenotypes (6 years, IQR: 0-40). Loss-of-function SLC2A1 variants tended to present earlier and with seizure-predominant or mixed phenotypes, whereas missense variants more commonly presented later with movement disorder-predominant phenotypes.

Conclusion: This case series demonstrates the marked phenotypic heterogeneity in GLUT1DS. It also charts the evolution in diagnostic methods over the last few decades, illustrating how the increased availability of WGS and cascade testing has identified milder and atypical phenotypes. Widespread adoption of cascade testing would help identify individuals with undiagnosed GLUT1DS and further define the full spectrum of GLUT1 deficiency.

Female heterozygous ornithine transcarbamylase deficiency: paediatric cohort review of presentation, disease course and treatment requirements

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Background: Ornithine transcarbamylase deficiency (OTCD), an X-linked urea cycle disorder, manifests variably in heterozygous females. We assessed a single-centre cohort aiming to review differing treatment requirements related to severity and disease course.

Method: 'Snapshot' data abstracted (March 2026) from medical notes assessed OTCD diagnosis mode/age, symptoms, biochemical manifestations, medication (nitrogen scavengers, arginine) and dietary management (unrestricted diet, self-selected protein restricted diet (SSD), prescribed safe intake protein diet (SIPD)).

Results: Seventeen heterozygous OTCD females were identified. N=3/17 presented symptomatically aged 1-3 years with hyperammonaemia (2 encephalopathy, 1 abnormal liver function). All required SIPD, arginine, sodium benzoate and phenylbutyrate. One proceeded to liver transplant.

N=14/17 were diagnosed after cascade testing. 10 were prospectively tested/managed at birth as at-risk neonates. Of these, n=3/10 remained well and asymptomatic with no hyperammonaemia and no treatment (medication, diet) except emergency regimen. N=7/10 had evidence of OTCD-related symptoms/ hyperammonaemia, of these: 2/7 continue SIPD, arginine and ≥1 nitrogen scavenger; 4/7 have a SSD of whom 2/4 have arginine and phenylbutyrate, 1/4 receives phenylbutyrate, 1/4 no medication; 1/7 has unrestricted diet and arginine.

N=4/17 were diagnosed after cascade testing later in childhood (9m-16y) following proband diagnosis (n=2 had younger male sibling with fatal neonatal-onset OTCD, n=1 had a younger male sibling with late-onset OTCD, and n=1 had a father diagnosed in adulthood with late-onset OTCD). 2/4 have unrestricted diet and no medication, 2 have SSD including 1 who receives phenylbutyrate.

Phenylbutyrate was given as glycerol phenylbutyrate (4.7-12.5g/m2/day, sodium phenylbutyrate dose-equivalence 226-646mg/kg/day), with highest doses in the symptomatic presentation group (mean 12.4mg/m2/day).

Conclusion: OTCD females have a variable disease course. Symptomatic presentations require treatment like male OTCD. Older asymptomatic females generally remain well and require little treatment. At-risk female neonates may later require treatment or remain asymptomatic. There is variability in dietary and medication management that warrants further standardisation.

Empowering our metabolic adolescent patients to be equipped for transition to adult care

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Background: Improvements in early metabolic diagnosis and treatment have enabled our adolescent cohorts within metabolic services to grow. Our patients have life-long diagnoses and research has shown that unsupported transition to adult services can not only lead to poorer

health outcomes, but can also negatively impact disease control, social participation and educational achievement. One of our responses to this has been to create an adolescent evening programme to support our young patients to gain skills needed for transition, as well as a parallel session for parents.

Methods: Our adolescent evening was attended by 9 young people with varying diagnoses. We split the group into three smaller groups and had them work through three stations over the evening. Memory skills, pharmacy simulation and healthy food choices were all discussed. Our parent evening discussed the principles of transition and the lifestyle aspects that could be supported in their young people.

Results: The evening achieved an average score of 9 out of 10 for usefulness for both parents and children. All parents felt that their knowledge has improved and the young people showed a good knowledge about their own medications and health needs. They all expressed that they enjoyed the event and would attend again.

Conclusions: This evening is part of the work that we are continuing in Leicester around transition. We have a dedicated transition service, which includes targeted transition clinics, use of the Ready-Steady-Go resources, and collated resources on making the choice for adult center to be referred to. We have started to improve our links with adult services, by attending joint MDT meetings. We hope that our combined approach across the MDT will help to equip and support our patients into adult care in the best possible way.

Headaches that kill? When to consider hyperammonemia in patients with headache and/or migraine

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Background: Headache is recognised in urea cycle disorders (UCDs) but may be overlooked because it is common and non-specific. Delayed diagnosis remains a major problem in late-onset disease, particularly in females with ornithine transcarbamylase deficiency (OTCD). Published reports describe headache phenotypes including migraine-associated vomiting, hemiplegic migraine and tension-type headache, often with vomiting, behavioural change, confusion or other neurological symptoms.

Case study / Methods: We describe a family with OTCD due to the OTC variant c.533C>T; p.Thr178Met, illustrating marked intrafamilial variability. A male infant died following hyperammonemia. Of two sisters, one had severe early-childhood disease with recurrent hyperammonemia (>600 µmol/L), repeated hospitalisations, and underwent liver transplantation; she remains well 4 years later. A second sister is more mildly affected, with a single hyperammonemic episode.

Their mother, a confirmed heterozygote, was initially considered asymptomatic but had recurrent severe migraine-like attacks. At age 36 years, during one episode with vomiting and poor response to migraine treatment, plasma ammonia was 275 µmol/L. She commenced sodium benzoate with marked improvement. At follow-up she was asymptomatic, ammonia was 36 µmol/L, and liver function was normal. We performed a focused literature review of headache/migraine presentations in UCDs and included collaborator-provided registry and real-world clinical data.

Results: This case suggests that severe headache in a female OTC heterozygote may represent symptomatic hyperammonemia rather than a primary headache disorder alone. Published reports describe delayed diagnosis in patients with recurrent headache plus vomiting, psychiatric symptoms, altered consciousness or protein aversion. Collaborator-provided data identified headache at presentation in 80% of late-onset registry cases, while 157/567 patients in a North American late-onset OTCD cohort reported headache.

Discussion/Conclusion: Headache alone is not a useful screening marker for hyperammonemia. However, headache or migraine with vomiting, confusion, behavioural change, lethargy, ataxia, protein aversion, catabolic triggers or relevant family history should prompt urgent ammonia measurement.

Infantile Brown-Vialetto-Van Laere syndrome unmasked after viral illness: a treatable riboflavin transporter deficiency

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Infantile Brown-Vialetto-Van Laere syndrome unmasked after viral illness: a treatable riboflavin transporter deficiency

Background: Brown-Vialetto-Van Laere syndrome is a rare, treatable riboflavin transporter disorder that may present in infancy with non-specific neurometabolic features before the classic cranial neuropathy phenotype becomes fully apparent. Early recognition matters because delayed treatment can lead to irreversible neurological injury.

Methods: We report a female infant with history of multiple presentations to different hospitals after intercurrent viral illnesses with lethargy and gross motor regression. Initial investigations, including an abnormal acylcarnitine profile and brain MRI changes, suggested a mitochondrial/metabolic disorder, prompting metabolic and genetic evaluation.

Results: Genetic testing confirmed a homozygous pathogenic SLC52A3 variant consistent with Brown-Vialetto-Van Laere syndrome. High-dose riboflavin was commenced promptly, with initial thiamine cover while the diagnosis was being clarified, and the child has shown developmental progress after treatment. At the time of review, she had not yet developed major bulbar or hearing deficits, but required multidisciplinary follow-up and reliable administration of riboflavin via nasogastric tube. Family counselling and sibling screening were arranged given the autosomal recessive inheritance and the potential for presymptomatic disease in relatives.

Conclusions: This case highlights an early, atypical presentation of Brown-Vialetto-Van Laere syndrome in which biochemical and radiological clues preceded the full neurological phenotype. The key transferable message is that clinicians should consider riboflavin transporter deficiency in infants with regression, respiratory difficulty, or unexplained metabolic abnormalities, and start riboflavin without delay when suspicion is high. Earlier diagnosis supports better neurological outcome and enables targeted family screening in a condition that is both genetic and treatable.

Case Report: Dietary modification in a patient with Maple Syrup Urine Disease (MSUD) to stabilise leucine throughout the menstrual cycle

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Maple Syrup Urine Disease (MSUD) requires lifelong restriction of leucine, valine and isoleucine combined with branched-chain free amino acid supplementation (BCAA-free PS). In our centre, leucine is monitored fortnightly via dried bloodspots, with dietary modifications made as necessary to maintain branch chain levels within target (leucine target range 200-400 µmol/L). This case describes a 24-year-old female diagnosed with MSUD through newborn screening. During menstruation, her leucine levels consistently rose above 400 µmol/L, necessitating frequent dietary adjustments — primarily protein restriction. These repeated changes negatively affected her quality of life and increased the psychosocial burden of her MSUD. Dietary assessment indicated reduced caloric intake during menstruation due to decreased appetite; this resulting catabolic state may have contributed to the observed rise in leucine levels.

Our centre initiated a pre-emptive rather than reactive plan to increase calorie intake from carbohydrates and BCAA-free protein through consumption of a glucose polymer and 10g BCAA-free PS (+435kcals) on the first day of menstruation. Earlier initiation is not possible due to unpredictable cycles. She then reverts to her established regimen at the end of her period.

This has resulted in a stabilisation of leucine levels [Pre: median 352 µmol/L, range: 135-690 µmol/L; Post: median 334 µmol/L, range: 142-612 µmol/L)] which consequently reduced the number of dietary modifications needed by 59% and repeat dried bloodspots by 64%. This decreased patient burden and bloodspot equipment as well as dietitian and laboratory resources.

Association between post-illness low leucine levels and illness type in Maple Syrup Urine Disease (MSUD)

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Background: Acute illness management in MSUD aims to prevent catabolism, causing high leucine levels and metabolic decompensation. Leucine intake is stopped, an emergency regimen of normal/high energy intake, BCAA-free protein substitute and L-isoleucine, L-valine given. Monitoring of blood spot BCAA surrounding illness guides leucine reintroduction. This study examined illness-type association with post-illness low leucine levels.

Methods: Data from January to December 2025, was abstracted from medical records of MSUD patients (BCAA results, leucine intake, illness type and dietetic management). Terms defined as: L1=Length of episodic high leucine levels (days >400µmol/L to <400µmol/L), L2=Length of episodic low leucine levels (days <200µmol/L to >200µmol/L), subdivided Group1: L2=0days, Group2: L21-20days, Group3: L2≥21days.

Results: Fifteen patients, median age 8years [2-18], had 799 BCAA results, median 58 each [19-68]. Sixty-three illness episodes occurred [1-7 per patient], 59 (94%) resulted in a leucine level >400µmol/L. Of total low leucine levels 92/157 (59%) were post-illness. Groups 1 and 3 are discussed.

Group1 = Thirty-four episodes. Primary illness: coryzal symptoms n=19, vomiting n=2, diarrhoea n=1, constipation n=6, other n=5, chest infection n=1. L1 median=11days [0-30], median peak leucine=570µmol/L [411-922]. During illness leucine was stopped and ER given, post-illness 'usual' leucine was re-introduced over median 4days [0-37].

Group3 = Twelve episodes. Coryzal symptoms n=1, vomiting n=6, diarrhoea n=3, chest infection and other n=2. L1 median=16days [2-62], median peak leucine=785µmol/L [515-1283]. L2 median=41days [21-77], median trough=51µmol/L [33-158]. Post-illness, leucine was re-introduced over median 10days [2-24]. In 9 episodes, post <200µmol/L, leucine was increased by median 131% [108-200%] of 'usual' over median 24days [6-53].

Conclusion: Low leucine levels were common post-illness with association to illness type. Vomiting and diarrhoea more commonly led to higher peak leucine level, longer L1 and time off/on reduced leucine, subsequent L2>21 days, and increased leucine requirement. Earlier reintroduction of leucine during illness recovery may shorten L2.

Screening for MCADD - False Positive or False Negative? Implications and learning from Generation Study

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Background: Newborn bloodspot screening (NBBS) for medium chain acyl CoA dehydrogenase deficiency (MCADD) has been established in the UK since 2009. It relies on elevated C8 and C8:C10 acylcarnitine ratios for cases to be identified. Since October 2024 MCADD and other conditions in the established newborn bloodspot screening program can also be identified by The Generation Study, a research study utilising whole genome sequencing for screening.

Case Description: A newborn enrolled in the Generation Study was referred following genomic identification of one copy of the common ACADM c.985A>G (p.Lys329Glu) pathogenic variant and a second ACADM variant classified as likely pathogenic. MCADD was reported as not suspected on NBBS. C8 at screening (day 5) was 0.30 µmol/L (above 99th centile but below screening cut off of 0.50 µmol/L). Follow up investigations were initiated to clarify biochemical significance.

Urine organic acid analysis detected only trace amounts of hexanoyl and suberylglycines, at the threshold of reportability. Repeat bloodspot acylcarnitines showed only borderline increases in metabolites associated with MCADD: C0: 25.3 µmol/L (reference 15−50), C8: 0.18 µmol/L (< 0.15), C10: 0.16 µmol/L (< 0.12), C8:C10 ratio: 1.2

Conclusions: This case illustrates the potential for discordant findings between the two screening programs. Despite the presence of two ACADM variants identified through genomic screening, biochemical markers remained low or borderline, falling below NBBS thresholds and displaying only subtle abnormalities on follow up testing. The findings reinforce the importance of case definition when developing screening pathways. Such cases provide insights into the spectrum of metabolic expression and will help refine and define expectations for genomic first screening pathways.

Protein and Micronutrient Intake After Two Years of Sapropterin Treatment in PKU

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Background: In patients responsive to BH4 in PKU, sapropterin may allow a natural protein intake and reduced dependence on protein substitutes. Protein substitutes provide essential fortified micronutrients, so reduction may increase the risk of nutritional insufficiency. Evidence describing detailed micronutrient intake in sapropterin treated children remains limited. Methods: This secondary analysis evaluated dietary protein and micronutrient intake after 24 months of sapropterin treatment in 21 responsive children enrolled in a prospective longitudinal study. Caregivers completed three-day food records, reviewed by dietitians. Records were analysed for energy, protein, and micronutrients(calcium, iron, zinc, vitamin D, vitamin B12). Intakes were compared with UK Dietary Reference Values (DRVs). Results: Mean total protein intake was 75±14 g/day, including 30 ± 16 g/day from natural protein and 45 ± 21 g/day protein equivalent from protein substitutes. Natural protein tolerance varied widely (8–66 g/day). Protein substitutes remained the main source of micronutrients, providing 80% (72–84) of calcium, 84% (72–88) of iron, 87% (82–92) of zinc, 96% (90–99) of vitamin D, and 78% (63–93) of vitamin B12. Median micronutrient intakes exceeded DRVs for most children; however, four had intakes below DRVs, almost exclusively when protein substitutes were reduced or omitted. One child consuming >40 g/day natural protein but no protein substitutes had low iron (51%), zinc (90%), and vitamin D (4%). A non adherent adolescent had low calcium (46%), iron (64%), zinc (41%), and vitamin D (60%) intake. Another child taking 60 g/day protein equivalent from protein substitutes had marginally low vitamin D (85%) intake due to reduced fortification in one product. Children who maintained regular protein substitute use consistently met micronutrient requirements. Conclusions: After two years of sapropterin treatment, dietary liberalisation increased natural protein intake but did not ensure micronutrient adequacy. Dietitian-guided adjustments to protein substitutes are essential to maintain micronutrient sufficiency as diets become more flexible.

Bloodspot phenylalanine monitoring frequency in adults with phenylketonuria: A service improvement project

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Background: Adults with phenylketonuria (PKU) are advised to monitor their blood phenylalanine (phe) concentration monthly, usually via dried bloodspot sample (van Wegberg et al. 2025). Regular monitoring is associated with more stable blood phe concentrations and better outcomes (Romani et al. 2017, Pinto et al. 2024).

At baseline, only 20% of adults with PKU in our metabolic centre sent monthly bloodspots, with forgetting to do so commonly reported. External reminders, such as text messages, support prospective memory and task fulfilment (Scarampi & Gilbert 2020), particularly in individuals with cognition or memory difficulties (Risko & Gilbert 2016) and have been shown to reduce non-attendance in healthcare settings (Rohman et al 2015).

This project aimed to improve bloodspot monitoring frequency in adults with PKU via the introduction of a text message reminder service.

Methods: A pilot text message reminder service with prospective data collection took place January - April 2025. 37 adults with PKU were included, age range 18-60 years. A reminder text was initially sent once (month one and two) then twice per month (month three). The number of bloodspots received per month was recorded, compared with baseline and displayed as a run chart. A validated questionnaire captured service user feedback.

Results: A 50% increase in the number of bloodspots received above the median was observed at month two, however the limited timeframe produced too few data points to claim causation. The improvement was sustained one month after reminders stopped then fell again. Acceptability was high and no one opted out of reminders.

Conclusion: The use of text messages reminders is a feasible and well accepted intervention to support improved bloodspot monitoring frequency in adults with PKU. Initatives such as this could assist timely and reflexive dietetic support and treatment adjustment, with the potential to improve symptom management and clinical outcomes.

Two cases of taurine transporter (SLC6A6) deficiency presenting with retinopathy and severe hypotaurinaemia

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Background: Taurine transporter (TauT) defect is a rare disorder caused by SLC6A6 variants leading to reduced taurine uptake, increased renal loss and defective transport across cell membranes. This disorder is particularly associated with retinal dysfunction (usually Leber congenital amaurosis), which has been seen in all reported cases, although cardiomyopathy has been reported in many patients.

Case Report: Two brothers, aged 7 and 13 years, presented to ophthalmology with rod/cone dystrophy and were referred to genetics, who identified homozygous SLC6A6 c.794del likely pathogenic variants in both patients. These were modelled to cause a premature stop codon and

likely full loss-of-function. All literature cases at time of diagnosis had some residual transporter activity, leading to uncertainty around prognosis and treatment in these patients.

Plasma amino acid analysis was requested, and the patients were found to have very low taurine (5 and 3 umol/L respectively, reference range 110-243). In addition to ophthalmological symptoms the 13-year-old patient had microcephaly, developmental delay, learning difficulties and hearing loss while the 7-year-old patient had relative microcephaly on presentation, and was later found to have learning difficulties. Neither patient has evidence of any cardiomyopathy. Intriguingly, many of these symptoms had not been reported in other cases but some have been seen in TauT knockout animal models.

Treatment using high dose taurine supplementation has proven effective in other patients, but as this mainly relies on residual TauT activity it is unclear whether this will be efficacious in these patients with full loss-of-function.

Conclusion: Very low taurine should not be ignored, particularly in the context of retinal dysfunction. It is important to consider the appropriateness of the lower end of the taurine reference range to enable diagnosis of these patients as taurine supplementation often halts retinal/cardiac disease progression and in some cases may improve cardiac function.

Elevated 2,3-dihydroxy-2-methylbutyric acid on urine organic acid analysis: a case series

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Background: 2,3-dihydroxy-2-methylbutyrate (2,3-DH-2-MB) is metabolised by enzymes involved in branched chain amino acid catabolism. Increased excretion of the erythro- isomer of this compound has classically been associated with 3-hydroxyisobutyryl-CoA hydrolase (HIBCH) deficiency, mitochondrial short-chain enoyl-CoA hydratase (ECHS1) deficiency, methylmalonic acidaemia (MMA) and propionic acidaemia (PA), although more recently pathogenic increases have been seen in several other disorders, many associated with mitochondrial dysfunction. We present 3 cases where elevated 2,3-DH-2-MB was identified on urine organic acid analysis and a review of previous MMA and PA patients.

Case Report: Case one presented at 11 months old with hyperlactataemia, seizures, hypotonia and global developmental delay. Further biochemical analysis initially only identified increased C4-OH carnitine, but re-examination of the urine organic acids also showed increased 2,3-DH-2-MB. A diagnosis of HIBCH deficiency was confirmed by enzyme analysis.

Case two presented at 3 months old, again with hyperlactataemia and seizures. White matter changes were also identified on MRI. In this case acylcarnitine analysis was unremarkable, and increased 2,3-DH-2-MB was the only abnormality seen on urine organic acid analysis. A diagnosis of pyruvate dehydrogenase deficiency was confirmed by genetic analysis.

Case three presented as a neonate, again with high lactate. Acylcarnitine analysis showed increased C5, C5-DC and medium chain acylcarnitines, and organic acids showed increased 2,3-DH-2-MB but no other significant abnormalities. A diagnosis of SLC25A4-related mitochondrial DNA depletion syndrome was confirmed by genetic analysis.

In addition, diagnostic samples from MMA and PA patients were reviewed for presence of this compound. 60% (3 of 5) PA patients and 84% (5 of 6) MMA patients had elevated 2,3-DH-2-MB.

Conclusion: 2,3-dihydroxy-2-methylbutyric aciduria has a wider differential diagnosis than has been historically thought. Our case of SLC25A4-related mitochondrial DNA depletion is the first reported with an increase in 2,3-DH-2-MB.

Galactose-1-phosphate uridyltransferase (GALT) testing for Classical Galactosaemia (CG): indications and impact on human milk feeding (HMF)

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Background: Symptoms of CG arise in the first days of life related to lactose exposure. In UK, infants are identified clinically, via NBS for PKU, or at-risk sibling screening. If CG is suspected as a cause of liver dysfunction, GALT testing is requested and lactose excluded until results reported. This cohort study reviewed indications for GALT testing and impact on HMF.

Methods: Data was abstracted from medical records (2019-2025) of patients, treated at a tertiary children's hospital, who underwent GALT testing including age, biochemical liver indices, blood transfusions, mode and type of feeding before/during/after testing and analysis turnaround-time (TAT).

Results: Forty-five patients had GALT testing (47 results), median age at sampling 58days [3-563], TAT median of 10days [1-21]. Patients admitted to intensive care (n=38) were later investigated for CG, 64% (n=37) received metabolic/liver team consultations. Main indications were raised ALT n=26, conjugated hyperbilirubinemia n=34, raised prothrombin time n=13. Nine had abnormalities of all 3 markers; six had none. On admission, 77% (n=36) received HMF. By time of testing, HMF (n=17), Parenteral nutrition /IV Fluids (n=13), lactose-free formula (n=10), standard/non-lactose-free specialist formula (n=7). During testing three had HMF excluded, one had lactose-containing formula excluded, three started HMF, 25 received lactose. Two re-established HMF when results reported (8,15d). All GALT results were negative, 62% (n=29) received blood transfusions <6weeks prior, invalidating initial results. After testing 49% (n=23) had HMF.

Discussion and Conclusion: No GALT test yielded a positive result. Clearer guidance is needed on indication for GALT testing and to raise awareness of alternative testing if blood transfusion has occurred. A risk stratification of either: high risk immediately GALT test and interrupt HMF, if lower index of suspicion, consider/send test but continue HMF will help reduce unnecessary testing and temporary cessation of HMF. A more rapid TAT would shorten time-off HMF.

Determinants of successful human milk feeding in inherited metabolic disorders (IMD) on dietary treatment

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Background: Human milk (HM) offers immunological, nutritional and developmental benefits. This study aimed to examine the effect of therapeutic dietary modification and early infant experience on HM feeding.

Methods: A ten-point scoring tool was developed to quantify determinants of successful HM feeding related to clinical (5) and physiological (5) factors. A higher score indicated greater probability for successful HM feeding. Data was abstracted from medical records of newly diagnosed infants (PKU and Galactosaemia excluded) on HM feeding and therapeutic diet from 2016 to 2026. Dietary modifications were classified as: protein restriction (PROT), amino acid restriction with protein substitute (AA), long-chain fat restriction (LF), frequent feeding (FF), high fat, high protein (HFHP).

Results: Fifty-two HM feeding infants (direct or expressed) had therapeutic dietary modifications: PROT in organic acidaemias and UCDs (n=18), AA in MSUD, tyrosinaemia, HCU, GA1 (n=23), LF in LC-FAOD, lipid disorders (n=6), FF in GSD1b (n=3), HFHP in Citrin deficiency (n=2). PROT v AA are discussed. PROT scored lower for clinical factors: PICU admission, median 5d [0-99d] v median 0d [0-14d], required intubation, median 3d [0-14d] v 0d [0-8d], time off oral feeding, median 8d [0-99] v 0d [0-69] and hospitalization, median 22d [1-111] v 7d [0-76]. Of physiological factors PROT v AA scored higher for skin-to-skin encouragement and prior experience of HM feeding but lower for maternal 22erbalized anxiety and HM availability.

Conclusion: The AA v PROT group had higher average score indicating greater probability of HM feeding. Duration of HM feeding was higher at 6-8 weeks (AA 48% v PROT 29%), and 6 months (AA 21% v PROT 6%), lower than UK statistics. Diet modification type and early infant experiences affected success and duration of HM feeding. Strategies to improve HM feeding are needed, to prevent metabolic instability causing delayed oral feeding and need for on-going expressing.

Protein Substitutes: challenges applying International Dysphagia Diet Standardisation Initiative standards (IDDSI) for an aging PKU community

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Since "diet for life" recommendations were introduced for those with Phenylketonuria (PKU), an increasing number of older adults with PKU follow low protein diets supplemented with protein substitute drinks. Ageing brings additional comorbidities including dysphagia, which may necessitate texture modified diets and thickened fluids. Dysphagia affects an estimated 8% of the global population. Current PKU guidelines do not address its management, and there is no published literature on the suitability of PKU protein substitutes for individuals requiring thickened fluids. The International Dysphagia Diet Standardisation Initiative (IDDSI) framework is widely implemented in the UK and internationally, yet PKU protein substitutes have not previously been evaluated against IDDSI criteria.

Methods: Members of the British Inherited Metabolic Diseases Group (BIMDG) dietetic group were questioned about their experiences using thickened protein substitutes. Manufacturers supplying PKU protein substitutes in the UK were contacted to determine whether IDDSI guidance existed for their products.

Results: Half of the six responding UK metabolic centres reported no experience with thickened protein substitutes. Across six different patients, five different protein substitutes were used. At the time of enquiry, none of the manufacturers had assessed their products for IDDSI suitability. Testing by some companies following contact indicated that most available substitutes corresponded to IDDSI Levels 0–1 in their standard form. Not all products were compatible with commercial thickeners due to acidity or formulation. These findings are informing the development of UK guidance to support clinicians in selecting appropriate substitutes across IDDSI levels.

Conclusions: Dysphagia requires greater consideration within PKU dietary management, particularly as the PKU population ages. Access to suitable, safely thickened protein substitutes is essential for maintaining nutritional adequacy. This work represents the first evaluation of PKU protein substitutes within the IDDSI framework and provides practical insights to guide clinical decision making.

An unusual presentation of Alpha-methylacyl-CoA racemase deficiency in a patient with elevated creatine kinase

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Background: Alpha-methylacyl-CoA racemase (AMACR) deficiency is a rare, autosomal recessive perioxismal disorder that results in accumulation of pristanic acid and toxic bile acid intermediaries. AMACR deficiency typically presents with neurological symptoms in adults or hepatic manifestations in children. We present an unusual case of AMACR deficiency presenting with raised ALT and elevated creatinine kinase (CK).

Case: 13 year old female presented with a long-standing history of lower limb discomfort. Examination was unremarkable. Initial investigations showed mildly elevated ALT 100 U/L (10-50) and CK 649 U/L (25-200). ALT elevation persisted and a liver biopsy was performed which was normal. A family history of juvenile arthritis prompted rheumatological investigation demonstrating negative autoimmune serology. CK was persistently elevated and genetic testing excluded muscular dystrophy.

Myalgia continued and CK rose to 5000 U/L. A broader genetic panel showed biallelic pathogenic AMACR variants. Very long chain fatty acids showed elevated pristanic acid at 60 umol/L (<1.4) confirming AMACR deficiency. MRI lower limb was subsequently suggestive of mild oedema or inflammation. Nerve conduction studies showed no evidence of peripheral neuropathy.

Patient has been started on a low phytanic diet and commenced cholic acid, a novel therapy in AMACR deficiency. Pristanic acid has dropped to 38.7 umol/L and symptoms have improved. Patient's twin brother was also found to have AMACR deficiency on cascade genetic testing. Although asymptomatic pristanic acid was elevated at 45.7 umol/L and has commenced treatment.

Discussion: This case demonstrates the importance of considering peroxisomal disorders in patients with myopathy of no clear cause. Very long chain fatty acids should be considered in

investigation of metabolic myopathy. When no clear cause of elevated CK can be identified, genetic testing can be beneficial. Cholic acid supplementation is used in peroxisomal disorders. This can be considered in AMACR deficiency and needs longer term follow-up to establish benefit.

PAH genetics and sapropterin responsiveness in paediatric NI patients

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Background: In 2021 NICE approved the use of sapropterin for responsive patients with PKU. Ahead of this approval the BIMDG developed a pathway for trialling sapropterin which considered gene mutations. In Northern Ireland all paediatric patients with PKU attend the Royal Belfast Hospital for Sick Children. We established a locally commissioned service for sapropterin and this included genetic testing of all known and new PKU patients to assist sapropterin roll out.

Methods: We have collated all genetic results and sapropterin trial outcomes of our PKU patients from the NI paediatric population. This includes known PKU patients from sapropterin roll out and so some are now under the care of our adult service. The correlation between genotype and responsiveness will be explored as part of a service evaluation project.

Results: In total 111 patients are included in this cohort taken at the end of March 2026. Genetic data was available for 108 patients. We have separated patients into those over now 18 years old, those not for sapropterin, those eligible for sapropterin who have had a trial and those eligible who have not yet trialled the drug. Most eligible patients have already had their trial, and a few are awaiting a trial as they are still too young to start, or the family have not been ready. Conclusion: We have a large cohort of patients with PKU and extensive genetic information with the opportunity to correlate this with sapropterin responsiveness. We are currently analysing this further and soon hope to have translatable data to inform likely responsiveness for future patients. A key finding in our clinical experience is that sapropterin responsiveness testing is challenging, requires good patient compliance and to date we have had some patients with unexpected outcomes.

followME Fabry Pathfinders registry: cardiac and renal effectiveness in a multi-national, multi-**centre cohort of patients on migalastat treatment for ≥5 years**

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Background: The ongoing, real-world followME Fabry Pathfinders registry (EUPAS20599) is designed to evaluate natural history and treatment outcomes in Fabry disease (FD). Here, we present ≥5--year effectiveness and safety data for migalastat in patients with FD.

Methods: Data were collected and analysed from patients ≥12 years of age with confirmed FD, migalastat-amenable GLA variants, an estimated glomerular filtration rate (eGFR) ≥30mL/min/1.73m² and who had received migalastat for ≥4.9 years.

Results: As of August 2025, 156 patients (64.1% male) were included. Median migalastat exposure was 5.7 years (range: 4.9–7.5). At enrolment, median age was 56.0 years (range: 16–77); p.N215S was the most common GLA variant (n=41; 26.3%). The Chronic Kidney Disease Epidemiology Collaboration equation was used to calculate eGFR. At baseline, 56 patients (35.9%) had eGFR (mL/min/1.73m²) ≥90, 54 (34.6%) ≥60–<90, 10 (6.4%) ≥30–<60 and 36 (23.1%) had missing values; 39 had a proteinuria category ≥1 and 27 had missing values. Female baseline median eGFR was 90.8mL/min/1.73m² (n=43; range: 57.7–128.1) with median annualised rate of change (ARC) –1.40mL/min/1.73m²/year (n=55; 95% confidence interval [95%CI] –2.04, –0.72); baseline median left ventricular mass index (LVMi) was 85.5g/m² (n=35; range: 47.0–232.5) and median LVMi ARC was –0.69g/m²/year (n=46; 95%CI –2.36, 1.68). Male baseline median eGFR was 85.8mL/min/1.73m² (n=77; range: 37.8–133.1) with median ARC –1.51mL/min/1.73m²/year (n=99; 95%CI –2.06, –0.68); baseline median LVMi was 132.3g/m² (n=55; range: 54.3–296.2) and median LVMi ARC was –1.53g/m²/year (n=67; 95%CI –4.72, 0.40). Combined, median eGFR ARC was –1.47mL/min/1.73m²/year (n=154; 95%CI –1.99, –0.98) and median LVMi ARC was –0.95g/m²/year (n=113; 95%CI –2.36, 0.23). Two patients (1.3%) had any treatment-related treatment-emergent serious adverse event; neither discontinued migalastat.

Conclusions: In this real-world observational study, migalastat preserved cardiac size and renal function over median 5.7 years with no new safety findings reported.

Epidemiology of Inherited Metabolic Disorders in a Specialist Paediatric Metabolic Clinic in India: A Single-Centre Registry Analysis of 349 Cases

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Background:A national registry infrastructure for these disorders in India remains underdeveloped. This analysis draws on a practice-level clinical registry established at a specialist paediatric metabolic centre in Karnataka, built to track all centre referrals. We aimed to characterise the epidemiology, molecular landscape, and clinical burden of this cohort.

Methods: Retrospective cross-sectional analysis of a de-identified clinical genetics registry (n = 606). Cases classified as 'Metabolic Disorder' were extracted (n = 349). Variables included diagnosis, disease sub-category, sex, age at presentation, inheritance pattern, zygosity, variant classification, phenotype terms,dietary/pharmacological management. Molecular data present for 270 genotyped cases. Disease sub-categorisation used systematic keyword mapping. Descriptive statistics were performed in Python.

Results: Metabolic disorders constituted 57.6% of the total registry (349/606). The cohort was 56.6% male (107M:82F), 91.4% paediatric (age <18 years); median age at last review was 24 months (range 1–948). Dominant sub-groups included organic acidaemias (6.6%), mitochondrial disorders (3.4%), lysosomal storage disorders (2.9%),urea cycle disorders (2.6%). Autosomal recessive inheritance predominated (73.7%); consanguinity was present in 54.8% of cases with parental data. Pathogenic variants were identified in 79.6% of molecularly characterised cases; variants of uncertain significance in 19.3%. The five most common phenotype terms were seizures (52.7%), global developmental delay (24.6%), developmental regression (22.9%), vomiting (21.8%), and encephalopathy (19.5%). Whole exome sequencing was the primary diagnostic modality (50.0%).

Conclusion: This registry documents a diagnostically diverse inherited metabolic disease cohort in which organic acidaemias, lysosomal storage disorders, and urea cycle disorders predominate. High consanguinity, autosomal recessive inheritance,neurological burden characterise this south Indian paediatric population. Whole exome sequencing is now the primary diagnostic tool. This registry originated as a practice-level tracking tool and cannot substitute for coordinated national surveillance. These findings highlight the need for national inherited metabolic disease registry infrastructure in India to support population-based epidemiology, newborn screening policy, equitable access to care.

Hereditary Fructose Intolerance presenting with hepatic dysfunction and hypoglycaemia and prior to exposure to dietary fructose: Diagnostic Pitfalls

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Background:Hereditary fructose intolerance (HFI) is a rare treatable inborn error of fructose metabolism that can present with vomiting, feeding aversion, hepatomegaly, liver dysfunction and hypoglycaemia after exposure to fructose. Diagnosis can be delayed because the phenotype overlaps with glycogen storage disease and congenital disorders of glycosylation. We describe the diagnostic journey of three children in whom recognition of HFI was delayed by atypical and evolving presentations and inadequate test strategies.

Methods & Results: We retrospectively reviewed the clinical, biochemical, radiological and genetic findings in three children referred to our metabolic service.

Case 1: A female child with recurrent vomiting, food selectivity, hepatomegaly and persistently raised alanine aminotransferase from 12 months of age. After negative metabolic screening, a homozygous ALDOB variant was identified, and she was diagnosed with HFI; liver size and transaminases improved after fructose restriction.

Case 2: A male child with developmental delay, poor visual fixation, microcephaly, fasting hypoglycaemia in infancy, hepatomegaly and abnormal transferrin isoelectric focusing suggestive of congenital disorder of glycosylation. Extensive genetic testing was initially negative. Marked self-restriction in dietary fructose later prompted targeted testing at 6 years of age and a novel homozygous ALDOB variant was found, confirming HFI.

Case 3: A female infant exclusively fed with formula feeds presented with vomiting, poor weight gain, recurrent fasting hypoglycaemia, and hepatomegaly and was suspected of glycogen storage disease. A homozygous ALDOB frameshift variant was identified. Symptoms slowly improved and fructose restriction was initiated upon weaning.

Conclusions:Hereditary fructose intolerance should be considered in children presenting with vomiting, food selectivity, hypoglycaemia and raised transaminases, particularly when the presentation mimics glycogen storage disease or with a type 1 deficient transferrin glycosylation pattern, and even without prior exposure to dietary fructose. Early recognition is important because dietary fructose restriction is effective and may prevent subsequent liver injury.

Cardiac involvement in adults with Glycogen Storage Disease Type IIIa: an observational cohort study

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Background: Glycogen Storage Disease type IIIa (GSD IIIa) is associated with development of left ventricular hypertrophy (LVH). The adult cardiac phenotype remains incompletely characterised.

Methods: Retrospective observational study of adults with GSD IIIa at two tertiary centres. Clinical, biochemical and dietary data were analysed alongside ECG, echocardiography and cardiac magnetic resonance imaging (CMR). LVH was defined using British Society of Echocardiography criteria. Data are presented as median (range).

Results: Eighteen adults were included (56% male), age 34 years (18–56) with follow-up 9 years (2–18). Echocardiography was available in 17/18 (94%). LVH was present in 10/17 (59%) using combined IVSd/LVMI criteria, predominantly mild–moderate, with severe LVH in 2/17 (12%). IVSd identified more patients than LVMI (53% vs 31%). Among 16 with both measures, 5 (31%) had both elevated IVSd and LVMI, 3 (19%) had isolated IVSd elevation, and none had isolated LVMI elevation. All patients with available data had preserved systolic function.

LVH was first documented at a median of 19 years (n=9). ECG (14/18) demonstrated LVH in 10/14 (71%) with no arrhythmias. CMR was performed in 6 patients: LVH was present in 5/6 (83%), with preserved systolic function in all, and myocardial fibrosis in 2/6 (33%). One patient demonstrated focal inferoseptal fibrosis; another had diffuse fibrosis with progressive hypertrophy despite liver transplantation and required primary prevention ICD implantation (1/18, 6%).

Creatine kinase, lactate, triglycerides, uric acid, BMI and hypertension showed no association with LVH. Three patients died (ages 34–52), with no cardiovascular deaths.

Conclusion: LVH is common in adults with GSD IIIa, emerging in the second decade and typically mild–moderate. Hypertrophy is characterised by regional wall thickening rather than global increases in LV mass on echocardiography. In this cohort, the overall cardiac phenotype appears benign. Echocardiography remains appropriate for assessment; however, these findings support consideration of CMR in higher-risk patients.

From Guidance to Practice: An Audit of PKU Management in Northern Ireland

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Background: Phenylketonuria (PKU) is a rare, autosomal recessive condition affecting amino acid metabolism, in which patients are unable to break down phenylalanine (Phe). If left untreated, phenylalanine accumulates in the blood and brain, leading to neurocognitive and neuropsychiatric problems as well as developmental delay. With careful low-protein dietary

management, patients can avoid complications. Those who are co-factor responsive may also benefit from pharmacological therapy.

Northern Ireland has one of the highest incidences of PKU in Europe, with approximately 1 in 5,000 babies diagnosed compared with 1 in 12,000 in the rest of the UK. In 2025, a revised European guideline on the diagnosis and management of PKU was published. This audit aims to assess the standard of care offered to patients with PKU under the care of the Royal Belfast Hospital for Sick Children (RBHSC) and benchmark it against these recommendations.

Methods: This retrospective audit will include all paediatric patients with PKU treated at RBHSC. All patients diagnosed with PKU who require treatment will be included. Patient electronic records will be audited over the 12-month period prior to 10/04/2026.

The audit will assess current practice across the following domains: access to specialist services (metabolic specialist, dietitian, neuropsychology, and social services); transition and educational support; clinical discussions around PKU-associated symptoms (gastrointestinal, mental health, and neurodevelopmental); monitoring of PKU-related risks (bone mineral density, nutritional deficits, disordered eating, and pregnancy precautions); and lifestyle advice. Phe level monitoring and sapropterin responsiveness are excluded, as these are being audited separately. Findings will be compared against current guideline recommendations and presented graphically.

Results: Data collection and analysis are ongoing.

Conclusion: This audit will help to identify areas of good practice and opportunities for improvement. Outcomes will inform the development of a clinical template which will ensure any current shortfalls in adherence to the guidelines are addressed.

Impact on biochemical markers following reduced dose olipudase alfa in adults with acid sphingomyelinase deficiency

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Background: In 2025, due to manufacturing issues and the possibility of a shortage of drug for compassionate use, we reduced the dose of olipudase alfa enzyme replacement therapy for adults with acid sphingomyelinase deficiency (ASMD).

Methods: We report on disease markers, clinical events and patient reported symptoms in 4 adults whose dose of olipudase alfa was reduced by at least 60% from September 2025. All patients (age 28-54 years) had been treated for at least 6 years prior to the reduction of dose and were clinically stable. Data were extracted from standard clinical records.

Results: Treatment doses (given every 2 weeks) were reduced as follows: Patient 1: 160 → 60 mg for 184 days; Patient 2: 260 mg → 100 mg for 140 days; Patient 3: 260 mg → 100 mg for 175 days, and Patient 4: 220 → 80 mg for 157 days. There was no change in haemoglobin, platelet count, alanine transaminase, HDL-cholesterol or LDL-cholesterol concentrations during the period of dose reduction. There were no new clinical events and no significant symptoms reported by the patients. N-palmitoyl-O-phosphocholineserine (PPCS) concentration was unchanged in 1 patient, unavailable in 1 patient, and increased in 2 patients (though remained within the normal reference interval i.e. < 200 ng/mL).

Conclusion: In the short term, a significant reduction in olipudase alfa dose was not associated with any deterioration in biochemical markers, or clinical symptoms, in adults with ASMD. In

patients, who are stable, with good disease clearance already achieved by treatment, this opens the possibility of maintaining disease control with lower treatment doses. Further studies should be done to investigate this.

Understanding the experiences and support needs of families living with Ketotic Hypoglycaemia to inform service delivery

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Background: Ketotic Hypoglycaemia (KH) is a diagnosis of exclusion where a child can drop their blood glucose significantly, after a longer than normal fast and/or during intercurrent illness. At present, there a lack of literature exploring the psychological impact on families living with KH. However, the limited literature highlights several important themes reported by this patient group which echo our own clinical experiences. This project explored the challenges and support needs of families living with KH to address this current gap in understanding to inform service delivery.

Method: All 153 patients with a diagnosis of KH under the Southwest Paediatric Metabolic service were sent an online questionnaire between November 2023 and January 2024 exploring challenges and support needs. Participants were also invited to complete a semi-structured interview. Interview domains include children's wellbeing in relation to KH, emotional impact of KH on families and support needs for parents of children with KH.

Results: Twenty-five families completed the questionnaire. 56% of respondents reported experiencing anxiety associated with KH, 68% reported experiencing challenges associated with illness management and 60% identified challenges associated with explaining the condition to others. Respondents identified that they would find additional support helpful (48% would like to attend an online webinar, 52% a parent group and 52% an information leaflet). Two participants completed a semi-structured interview and themes of the emotional and psychological impact of the diagnosis were identified. Additional themes included uncertainty and lack of clear prognosis, gaps in support and information and coping mechanisms and resilience.

Conclusion: The findings reveal meaningful challenges experienced by families affected by KH and underscore the importance of accessible information and psychosocial support. By identifying key support needs, this work lays a foundation for service enhancements aimed at improving the overall experience and wellbeing of children and families affected by KH.

7.5-year efficacy outcomes with cipaglucosidase alfa plus miglustat in adults with Pompe disease in ATB200-02, an open-label Phase I/II study

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Background: ATB200-02 (NCT02675465) evaluated cipaglucosidase alfa plus miglustat (cipa+mig) in adults with Pompe disease.

Methods: ATB200-02 included four cohorts: three ambulatory (two enzyme replacement therapy [ERT] experienced [prior ERT duration: 2–6 years and ≥7 years]; one ERT naïve) and one ERT-experienced, non-ambulatory cohort. Participants received cipa+mig (20 mg/kg intravenous plus 260 mg oral) biweekly. Assessments included: % predicted 6-minute walk distance (pp6MWD), % predicted sitting forced vital capacity (ppFVC), Rasch-built Pompe-specific Activity (R-PAct) and safety.

Results: Twenty-nine participants enrolled: 17 ERT experienced, ambulatory; six ERT naïve, ambulatory; and six ERT experienced, non-ambulatory. Twenty-four participants completed the study, and five discontinued. Baseline mean (standard deviation [SD]) pp6MWD was 60.2 (16.20) % and 67.8 (12.61) % for ERT-experienced and ERT-naïve ambulatory groups, respectively. Mean (SD) change from baseline (CFBL) at 5 years was +4.8 (9.08) % and –1.5 (19.71) %, and at 7.5 years was +2.7 (9.20) % and +0.9 (15.00) %. Baseline mean (SD) ppFVC was 57.4 (17.42) % and 57.2 (20.84) % for ERT-experienced and ERT-naïve ambulatory groups, respectively. Mean (SD) CFBL at 5 years was –0.2 (9.18) % and +5.0 (8.07) %, and at 7.5 years was –4.2 (5.95) % and +0.7 (5.77) %. pp6MWD and ppFVC data were unavailable for non-ambulatory patients. Across ambulatory participants, R-PAct total scores at 5 years were relatively stable versus baseline, with a mean (SD) % CFBL of 0.8 (17.04) %. Cipa+mig was generally well tolerated up to 7.5 years.

Conclusions: Long-term cipa+mig treatment demonstrated durable stability or improvements in muscle function, pulmonary function and patient-reported outcomes across Pompe disease populations over 7.5 years, with consistent trends despite the inherent variability of small cohorts, especially at later time points. This abstract was presented at the 2026 ACMG Annual Meeting in Baltimore, MD, USA. Supported by Amicus Therapeutics, Inc.

Long-term complications in methylmalonic acidaemia in adults

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Background: Methylmalonic acidaemia (MMA) is a rare autosomal recessive disorder associated with significant morbidity and mortality. The mut^0 genotype is linked to a severe phenotype, but adult outcome data remain limited. This study aimed to characterise long-term complications and genotype–phenotype correlations in adults with MMA.

Methods: We conducted a retrospective analysis of 14 patients (7 female, 7 male) with vitamin B12-unresponsive MMA, aged 22–42 years. All were followed from age 18 years in a multidisciplinary metabolic clinic. Data included age at diagnosis, onset of complications, clinical and neurocognitive outcomes, organ involvement, biochemical markers, and transplant history.

Results: Seven patients (50%) had the mut^0 genotype. All mut^0 patients developed complications in early life, with universal learning disability and PEG feeding. Plasma MMA levels exceeded 500 µmol/L in all mut^0 patients.

Chronic kidney disease occurred in all mut^0 patients; 5 (36%) required renal replacement therapy and transplantation. Rejection occurred in 4 (29%); 2 underwent re-transplantation and 2 were awaiting transplantation. Two patients died while awaiting combined liver–kidney transplantation (ages 31 and 34 years).

In contrast, only one mut$^-$ patient developed renal failure requiring dialysis. Additional complications, observed exclusively in mut^0 patients (MMA >800 µmol/L), included optic atrophy (n=3), cardiomyopathy (n=2), metabolic myopathy (n=3), renal osteodystrophy (n=3), and epilepsy (n=1).

Overall, mut^0 patients had worse outcomes, including higher rates of renal disease, mortality, metabolic decompensation, and neurological impairment.

Conclusions: Adults with mut^0 MMA experience severe, progressive multisystem disease. Early genotype-stratified management and timely consideration of combined liver–kidney transplantation may improve outcomes.

Multifactorial Progressive Osteoporosis in Adults with PMM2-CDG: A Five-Patient Case Series

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Background: Reduced bone mineral density (BMD) is a recognised feature of PMM2-CDG, attributed to factors including hypogonadism, reduced mobility, and nutritional deficiency. However, data in adults and the extent of longitudinal progression remain limited.

Methods: We retrospectively reviewed five adults with genetically confirmed PMM2-CDG (3 males, 2 females; median age 28 years) attending a single tertiary metabolic centre. Clinical, endocrine, and serial DXA data were analysed.

Results: Endocrine abnormalities were identified in 4/5 patients, including hypogonadotropic hypogonadism in males and hypergonadotropic hypogonadism in females. Reduced BMD was present in all patients (5/5), ranging from osteopenia to severe osteoporosis.

Longitudinal assessment demonstrated progressive bone loss, with lumbar spine Z-scores ≤ -3.0 in two patients and interval reductions in hip BMD of up to 6% over 2–3 years. Notably, deterioration occurred across a spectrum of BMI and mobility, including individuals with normal BMI and those receiving hormone replacement therapy.

Despite previous reports of skeletal involvement in PMM2-CDG, this series highlights persistence and clinically significant progression of bone disease into adulthood.

Conclusion: Osteoporosis in PMM2-CDG is common, progressive, and multifactorial. Shared genetic and individual factors—particularly endocrine dysfunction, impaired mobility, and low BMI—contribute to skeletal fragility. Standard hormone replacement alone may be insufficient to prevent bone loss. Early baseline DXA, regular surveillance, and proactive multidisciplinary management are essential. Consideration of earlier pharmacological intervention, including anti-resorptive or anabolic therapies, may be warranted, although further evidence is needed.

Intrafamilial phenotypic variability in m.3243A>G mitochondrial disease: Implications for cascade testing and multisystem surveillance

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Introduction: Mitochondrial disorders, particularly those associated with the m.3243A>G variant, demonstrate marked phenotypic heterogeneity. Clinical manifestations range from severe neurological disease to later-onset cardiometabolic and auditory phenotypes. Recognition of affected individuals outside neurology remains challenging, and cascade testing offers an opportunity to identify previously unrecognised cases within families.

Methods: Following identification of a mitochondrial disorder in an index case presenting with status epilepticus, cascade testing was undertaken in maternal relatives. Clinical evaluation included review of medical history, multisystem assessment, and targeted genetic testing. Heteroplasmy levels were assessed using urinary sediment samples, given their higher diagnostic yield in adults.

Results: Cascade testing identified a maternal relative in the sixth decade with no prior unifying diagnosis. Clinical assessment revealed a multisystem phenotype comprising cardiomyopathy, diabetes mellitus, and sensorineural deafness. These features had previously been managed across separate specialties. Urinary heteroplasmy was identified at 44%, supporting the diagnosis of mitochondrial disease. In contrast, the index case demonstrated a predominantly neurological phenotype, highlighting significant intrafamilial variability. The findings illustrate that clinically relevant mitochondrial disease may remain unrecognised in individuals presenting with non-neurological features, particularly in later adulthood.

Conclusion: This case highlights the value of cascade testing in mitochondrial disease for identifying affected relatives with atypical or non-neurological presentations. Marked

intrafamilial phenotypic variability can obscure diagnosis, particularly when patients present with cardiometabolic and auditory features rather than classical neurological manifestations. Mitochondrial disease should be considered in adults with the combination of diabetes, deafness, and cardiomyopathy, especially in the context of a suggestive family history. Early recognition enables appropriate multisystem surveillance, targeted management, and informed genetic counselling.

Factors affecting long-term outcomes in a cohort of adults with LC-FAODs

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Background: Long-chain fatty acid oxidation disorders (LCFAODs) are heterogenous metabolic conditions presenting at any age. There is limited long-term outcome data in adults. We aimed to characterise clinical progression and severe disease determinants.

Methods: We conducted a retrospective review of 45 adults with LCFAOD (VLCAD, CPTII, LCHAD, CPTI) at a single metabolic centre, assessing clinical data and outcomes. Majority had biochemical +/- genetic confirmation.

Results: The cohort included patients with VLCAD(n=18), CPTII(n=18), LCHAD(n=5), and CPTI(n=4). Median age was 35 (range 18−79). Mean age of symptom onset was 12, with an 11-year mean diagnostic delay; 58% were diagnosed in adulthood. Myalgia (20/45) and rhabdomyolysis (16/45) were common presentations.

Rhabdomyolysis was most frequent in CPTII and VLCAD with a median of 2 episodes (range 0-28). Baseline CK was 57−24,608IU/L, >100,000IU/L during crises. 12 experienced hypoglycaemia, mainly in LCHAD and CPTI. 14/31 were homozygous; two had dual CPTII/VLCAD variants. Fibroblast studies supported diagnosis. Initial acylcarnitine profiles were abnormal (21/37) and remained so in two thirds.

Cardiac involvement was seen(n=12). Pregnancies(n=29, CPTII,VLCAD) were uncomplicated barring 5 miscarriages and 4 metabolic decompensations. Mood disorders were common(n=15). One patient required renal transplant.

Functional impact varied: 39/45 were independently mobile, 23/45 reported reduced walking distance; 14 required mobility aids. LCHAD patients had markedly reduced fasting tolerance. Admissions averaged 2.4/patient. Six used carbohydrate-polymer; 27/45 used MCT oil. Four LCHAD patients required cornstarch/glycosade, and 4/45 used carnitine.

Risk factors for recurrent metabolic decompensation and mobility impairment included childhood onset symptoms (12/15), homozygous variants (7/11), dietary or follow up non adherence (7/15), chronic pain, mood disorders or gynaecological conditions (7/15).

Conclusion: This cohort highlights risk factors for metabolic decompensation and long-term outcomes in adult LCFAOD. Diagnostic delay remains substantial, with frequent adulthood presentations. Standardised lifelong follow-up, disease awareness, cardiac surveillance, and dietary and physiotherapy support are essential to improve outcomes.

When a Simple Test Saves a Life: Neonatal Galactosemia Diagnosed by Benedict Test in a Resource Limited Setting

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Intrroduction: Galactosemia is caused by deficiency of enzymes in carbohydrate metabolism that converts galactose to glucose. The enzyme deficiencies associated are galactose-1-phosphate uridyltransferase (GALT 1) , galactokinase, UDP galactose-4-epimerase. Defect in converting galactose to glucose causes accumulation of galactose in tissues leading to cataract, renal and liver dysfunction and cognitive impairment and even may lead to lethal consequences.

Case Presentation: A 16 - day - old baby with an uncomplicated antenatal and birth history, presented with jaundice and progressive darkening of urine with a 20% of weight loss and one episode of hypoglycaemia. Examination revealed icterus, hepatosplenomegaly and bilateral cataract. Biochemical investigation showed direct hyperbilirubinemia with very elevated alpha-fetoproteins in serum. Positive urine Benedict test and negative glucose by strip method favoured galactosemia. High galactose levels in a dried blood specimen confirmed the diagnosis. There was a gradual reduction of bilirubin and undetectable reducing substances on second day after starting soya- based formula.

Discussion: In low resource healthcare settings, revisiting basic biochemical tests such as the Benedict test can be lifesaving when evaluating neonates with cholestasis, cataracts, and failure to thrive.

Key words: Galactosemia, direct hyperbilirubinemia, cataract

Diagnostic Delay and Divergent Phenotypes in Metachromatic Leukodystrophy: Real-World Evidence Supporting Newborn Screening in the Era of Gene Therapy

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Metachromatic leukodystrophy (MLD) is a rare lysosomal storage disorder causing progressive motor and cognitive decline with premature mortality. With disease-modifying therapies emerging, early diagnosis is critical to enable timely intervention and preserve treatment eligibility. We report real-world data from a retrospective cohort of 17 patients with confirmed MLD across two UK tertiary centres (GOSH n=12; Evelina n=5), assessing diagnostic delay, phenotype-specific trajectories, referral pathways, and treatment outcomes.

Patients were stratified by age at symptom onset into late-infantile (LI; ≤2.5 years), early-juvenile (EJ; 2.6–<6 years), and late-juvenile (LJ; 6–<16 years). The cohort included five LI, five EJ, four LJ, and three presymptomatic individuals identified through family screening. All presymptomatic patients were diagnosed at 1 month and received gene therapy (GT) at 10–12 months.

Among symptomatic patients (n=14), median diagnostic delay was 18.5 months. LI patients showed prolonged delay (range 12–38 months; median 23 months). EJ patients showed heterogeneity, with delays ranging from 1–44 months (median 6 months). LJ patients had shorter delays (range 1–6 months; median 6 months).

Diagnosing clinicians included paediatric inherited metabolic disease specialists (47%), paediatric neurologists (24%), general paediatricians (12%), and clinical geneticists (6%). Regression was the main trigger for investigation. Once assessed by specialists, diagnostic turnaround was rapid (<2 months), indicating mainly pre-specialist delay.

In LI patients, supportive care only (5/5) was provided. EJ treatments included supportive care (2/5), GT (2/5), and haematopoietic stem cell transplantation (1/5). LJ treatments included supportive care (2/4), GT (1/4), and investigational intrathecal enzyme replacement therapy (ERT) (1/4). Three deaths occurred, all in EJ patients; none followed GT or ERT.

Comparison before and after GT commissioning showed no reduction in diagnostic delay.

These data demonstrate heterogeneity in diagnostic trajectories, with delays mainly before specialist assessment, particularly in EJ disease, highlighting a diagnostic gap and supporting newborn screening.

Rare Disease Awareness in Young People in the UK: Insights from a Survey

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Rare diseases affect approximately 300 million people worldwide, and many are caused by inherited metabolic disorders. Despite this, public awareness remains limited. Improving awareness among young people may strengthen health literacy, promote advocacy, and support earlier recognition of rare conditions. This youth-led study aimed to evaluate awareness, perceptions, and educational needs related to rare diseases in young people.

An anonymous cross-sectional online survey was conducted between May 2025 and March 2026 among individuals aged 13–24 years in the UK (UK). The questionnaire, developed with input from young people and pilot-tested before distribution, assessed knowledge of rare diseases, understanding of how they differ from common conditions, sources of information, perceived barriers to awareness, and preferred educational resources. The survey was distributed through youth networks, educational institutions, and social media. Responses were analysed using descriptive statistics.

A total of 150 participants completed the survey. Respondents were aged 13–16 years (27.9%), 17–20 years (39.3%), and 21–24 years (32.9%). Awareness of rare diseases was limited: 44.7% reported knowing only "a little," 30.5% had heard of rare diseases but reported minimal knowledge, and 5% had never heard of them. Only 25.5% correctly identified that rare diseases collectively affect around 1 in 17 people in the UK.

Participants recognised key characteristics of rare diseases. Most agreed that rare diseases affect smaller populations (72.3%), often have limited treatment options (73%), and are less widely

understood than common conditions (78%). Information sources included school or university education (56%), social media (47.5%), and family or friends (42.6%).

Perceived barriers included poor communication (56%), limited visibility (41.1%), and complex resources (33.3%). Despite limited knowledge, 84.4% expressed interest in learning more. Integrating education on rare and inherited metabolic diseases into school curricula and digital platforms may improve awareness and support earlier recognition and referral to specialist metabolic services.

Review of prescribing practice in Urea Cycle Disorders- one adult centre experience

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Background: Urea Cycle Disorders (UCDs) are a heterogenous group of chronic, progressive and disabling conditions, which may result in early death. Whilst they are generally incurable, access to therapeutic products is essential to prevent the progression of the disease, metabolic decompensation and maintain the patients' quality of life. The aim of the project was to review the therapy prescribing practice for patients with UCDs.

Methods: Reasons for prescribing and switching of ammonia scavengers in a large cohort of adults with UCDs was evaluated as a service review. Data extracted included: clinical demographics, age of diagnosis, weight change over time, admissions to hospitals and biochemical parameters.

Results: Seventy-one adults with UCDs were included (OTCD n=33, ASS n=14, ASL n=9, ARGD1 n=8, HHH n=1, CPSD n=2). 3/33 OTCD patients, 2/9 ASL, 12/14 ASS, 5/8 ARGD1, 1/1 HHH and 1/2 CPSD were early-onset cases, while all remaining patients had late-onset diagnosis. 14/71 patients were gastrostomy-fed. 33/71 patients had intellectual disability. 29/71 patients are on 2 ammonia scavengers (sodium benzoate with sodium phenylbutyrate (15/29) or glycerol phenylbutyrate (14/29)). Patients who started their therapies in childhood, continued their treatment while under the adult service. Hypernatraemia and recurrent rise in plasma ammonia and/or plasma glutamine leading to acute admission were the main reasons for the medication switches. Body weight increase and subsequent increase in the medication dosage led to partial compliance in 3 adult-onset OTCD patients. The highest non-adherence due to side effects was reported in adult-onset OTCD patients, which led to multiple medication switches in 2 cases.

Conclusions: Prescribing for UCD patients occurs within specialized, multi-disciplinary team to ensure proper dosage adjustment and monitoring for adverse effects. Treatment plans are often tailored to the individual, focusing on maintenance therapy and symptom management to avoid organ damage. Patients' preference regarding the medication formula is always considered.

Pancreatitis in Two Adolescents with Argininosuccinic Aciduria: Expanding the Phenotypic Spectrum

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Background: Argininosuccinic aciduria (ASA), caused by argininosuccinate lyase deficiency, is characterised by hyperammonaemia, neurocognitive impairment, hepatic dysfunction, and systemic nitric oxide deficiency. Pancreatitis is not widely recognised as a complication of urea cycle disorders and has rarely been reported in ASA. Its occurrence remains poorly characterised.

Methods / Case Series: We report two adolescents with biochemically stable ASA, maintained on safe minimum protein intake, who developed acute pancreatitis.

Case 1: A 12-year-old boy (glutamine ~533 µmol/L; argininosuccinate 230–300 µmol/L) presented with pancreatitis (lipase 667 U/L; peak 2607 U/L) without hyperammonaemia. Initial imaging was unremarkable. He required short-term total parenteral nutrition (TPN). Persistent symptoms and modestly elevated lipase (~400 U/L) prompted repeat imaging, showing inflammatory changes and a probable reactive peripancreatic lymph node. He re-presented two months later with recurrent pancreatitis (lipase 578 U/L) and is undergoing further evaluation including MRCP and genetic testing.

Case 2: A 14-year-old girl (glutamine ~800 µmol/L; argininosuccinate 200–300 µmol/L) presented with necrotising pancreatitis complicated by hyperammonaemia (peak 315 µmol/L). Imaging revealed extensive peripancreatic collections progressing to a walled-off pseudocyst. Management included intravenous scavengers, TPN, and antibiotics. Despite radiological progression, she improved clinically, and collections resolved on follow-up imaging.

Results: Pancreatitis occurred despite metabolic stability and absence of common risk factors. Severity ranged from recurrent mild disease to necrotising pancreatitis with secondary hyperammonaemia.

Conclusion: Pancreatitis is not recognised in the ASA phenotypic spectrum. These cases suggest a potential association independent of metabolic decompensation. Proposed mechanisms include nitric oxide deficiency, mitochondrial dysfunction, and chronic metabolic stress. Awareness is important, as pancreatitis may precipitate hyperammonaemia and complicate management. Further data are needed to determine whether this represents an under-recognised complication warranting inclusion in future guidelines.

Natural History and Comorbidities of Childhood Ketotic Hypoglycaemia: Experience from a Regional Specialist Centre

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Background: Idiopathic ketotic hypoglycaemia (IKH) is the most common cause of hypoglycaemia in early childhood, yet its natural history remains incompletely defined. Although often considered benign and self-limiting, increasing recognition of atypical and persistent cases challenges this assumption. We aimed to characterise presentation, comorbidities, and outcomes of children with ketotic hypoglycaemia (KH) referred to a large regional centre.

Methods: We conducted a retrospective cohort study of children with KH reviewed by paediatric metabolic and/or endocrine services in Manchester, UK, between 2019 and 2024. Clinical, biochemical, genetic, and outcome data were analysed.

Results: A total of 157 children (53% female) were included; 76% were managed by metabolic services and 24% by endocrinology. Median age at symptom onset was 2.36 years (earlier in the metabolic cohort: 1.99 vs 2.73 years), with median age at first review of 3.15 years. Mean height SDS was significantly below zero (−0.75, $p \leq 0.0001$), while weight SDS was not significantly different. Median age at discharge was 6.53 years, with no inter-specialty difference.

Neurodevelopmental comorbidities were present in over a quarter (7.6% ADHD/ASD; 17.8% developmental or speech delay). A precipitating illness was identified in 84.7%, most commonly gastrointestinal; family history was uncommon (3.8%). Among 41 children with recurrent KH who underwent genetic testing, no causative diagnosis was identified; one unrelated metabolic disorder and several variants of uncertain significance were detected. Overall, 11.6% had persistent symptoms beyond 7 years.

Discussion: These findings challenge the view of KH as uniformly benign. The high prevalence of neurodevelopmental comorbidities and persistence in a subset suggest clinical heterogeneity and potential unrecognised mechanisms.

Conclusion: While most children with KH remit by mid-childhood, a significant minority have persistent symptoms beyond 7 years, warranting closer follow-up and consideration of extended metabolic and genetic evaluation.

Timeliness in PKU Care: A National Audit into Turnaround Time of Dried Blood Spots and Frequency of appointments for Adults with PKU in the UK

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Introduction: A Care consensus document for The Dietetic Management of Adults with Phenylketonuria in the UK was published in 2022. This recommended auditing two outcomes:

1. Aim to report the blood phenylalanine result back within 3 working days (WD) of receipt of the blood result from the laboratory.

2. Agree to follow up with patient 6–12 month appointment if on treatment. 12 month appointment if not on treatment. Less frequent follow-up arrangements may be agreed upon if appropriate (e.g., male patients with hyperphenylalaninaemia).

Methods: An audit data collection tool was designed and distributed to each UK Adult IMD Centre. This inclusively counted days from date of Dried Blood Spot (DBS) sample, to result receipt by dietitians and provision to patient. Centres audited the first 20 DBS received in October 2025. Data was collected on offered clinic appointment intervals. Appointments unattended/cancelled by patients were counted. Ad-hoc contact was excluded. The tool identified if offered appointments were within agreed review periods. Centres were asked to audit 20 patients, randomised depending on their booking systems.

Results: Eight Centres completed the audit. Mean time from result receipt to patient provision was 1.4WD (1.5 calendar days) (n=160); end to end from collection to provision averaged 4.3WD (5.7 calendar days); 99% of DBS results were provided within the standard of 3WD.

Appointment follow-up target was met 64% of the time (n=135), Mean interval between offered appointments was 39 weeks.

Discussion: Results suggest improvement is required to consistently meet the care consensus standard for review periods.

Reasons for missing targets were not explored but questions are raised around resource and caseloads.

A mean turnaround of 5.7 days from sample collection to patient provision appears too long. Delays, evidently unrelated to dietitian processing, may stem from postal and home logistic factors. Home monitoring systems could expedite results.

Short-term use of a slow-release Phenylalanine-free microtablet protein substitute in children and adolescents with Phenylketonuria

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Background: In phenylketonuria (PKU), adherence to protein substitutes (PS) is often suboptimal due to poor palatability and the burden of high volumes. A novel Phe-free L-amino acid microtablet, incorporating a cellulose-based taste-masking coating and a sodium-alginate slow-release matrix with added micronutrients addresses these barriers. This study evaluated its short-term tolerability, acceptability, and adherence in children with PKU, with extended follow-up in a subgroup.

Methods: A 7-day observational study was conducted in a single centre in children aged ≥3 years following a low-Phe diet. The microtablet provided 54 g protein equivalent (PE)/100 g. Participants replaced at least one daily PS dose with 10 g or 20 g PE of the test product. Daily gastrointestinal (GI) symptoms, intake, and adherence were recorded. Acceptability was assessed using structured ratings of palatability, ease of use, and overall preference. Three adolescents continued the product for 28 days to assess longer-term tolerability and adherence.

Results: Ten participants (5 males, 5 females; median age 13.5 years, range 5.1−17.6) completed the 7-day study. Adherence to the microtablet was high (80%), exceeding adherence to usual PS (70%). At baseline, eight children reported none/mild GI symptoms, mainly flatulence; one child experienced moderate to severe symptoms including constipation, diarrhoea, bloating, and burping. By day 7, all reported none/mild symptoms, with complete resolution in the child with severe symptoms. Acceptability ratings were comparable to usual PS (mean 3.2 vs 3.3/5), and nine children (90%) reported no difficulty taking the product. During the 28-day extension, adherence remained high, GI tolerance was maintained and increased preference was noted, particularly due to reduced aftertaste.

Conclusions: This novel slow-release microtablet PS was well tolerated, acceptable, and associated with high adherence in children with PKU. Its taste-masked, low-volume format offered practical advantages that may support sustained dietary adherence. Longer-term controlled studies are needed.

Defining the inherited metabolic disorder landscape in numbers using structured databases: proportion and mortality across EU-5

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Background: Inherited metabolic disorders (IMDs) are individually rare, which can make it challenging to get the IMD voice heard across care pathways and policy. However, collectively they represent a substantial and under-characterised group of conditions.

Despite their number, the overall scale and impact of IMDs within the rare disease landscape, and their burden on healthcare systems, remain poorly understood.

This study aimed to quantify IMDs as a whole: specifically, the proportion of rare diseases that are IMDs and the mortality attributable to IMDs across EU-5 countries.

Methods: IEMbase (accessed 11/12/2025) identified 2,026 IMDs, which were incorporated into a curated IMD database.

Each condition was mapped to Orphanet's disorder-level ORPHAcodes, to estimate the proportion of rare diseases represented by IMDs.

Mortality data were obtained from the WHO Detailed Mortality Database, using the most recent year available. IMD relevant ICD-10 codes were identified, and deaths attributable to IMDs were calculated across age groups (1−4, 0−14, all ages) in EU-5 countries (UK, France, Germany, Italy, Spain).

Results: Of the 2,026 IMDs identified in IEMbase, 1,340 unique disorder-level ORPHAcodes were mapped, representing 20.5% of all rare diseases.

Analysis of the 2019 WHO Detailed Mortality Database showed that IMDs accounted for an average of 0.08% of all deaths across EU-5 countries (UK: 0.05%). In contrast, IMDs accounted fora substantially higher proportion of paediatric mortality, accounting for 2.5% of all deaths in children under 14 years (UK: 2.06%). This burden was greatest in early childhood, where IMDs accounted for 6.1% of deaths in children aged 1−4 years (UK: 7.75%).

Discussion and conclusions: These findings highlight that IMDs constitute a substantial proportion of the rare disease landscape and account for a disproportionate share of IMD deaths in childhood. This underscores the need for improved recognition, data capture, and prioritisation within healthcare policy and rare disease strategies.

Two-Year Sapropterin Outcomes in Phenylketonuria: Longitudinal Study of Metabolic, Dietary, Psychosocial Effects

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Background: Evidence on the long-term impact of sapropterin in phenylketonuria (PKU) is limited. Understanding its effects on dietary restrictions, growth in children, and caregiver burden is essential to optimize PKU management.

Methods: This prospective, two-year longitudinal study with a comparison group followed 33 children with PKU after sapropterin responsiveness assessment (21 responsive, 12 non-responsive). Outcomes included metabolic control, prescribed protein intake, dietary patterns, growth, psychological measures, and caregiver burden.

Results: Sapropterin-responsive children increased natural protein intake from 10 g to 28 g/day at 2 years ($p < 0.001$), with reduced protein substitute intake (60 g [56−63] to 45 g [40−60], $p < 0.05$); no changes occurred in non-responsive children ($p > 0.05$). Animal-based foods (cheese, eggs, meat, fish) were introduced in 52% (11/21) of responsive children once tolerance exceeded approximately 25 g/day. The caregivers of responsive children reported reduced financial, familial-social, and personal burden (all $p \leq 0.05$), alongside decreased food neophobia ($p < 0.005$) and caregiver depression ($p = 0.013$). In sapropterin-responsive children, weight and BMI z-scores remained stable, while height z-score increased over 24 months ($p = 0.03$); non-responsive children had higher weight and BMI z-scores than responsive children at 24 months ($p = 0.037$ and $p = 0.026$). Blood phenylalanine concentrations remained within recommended target ranges overall, with lower median values in responsive children at several time points. Caregivers of sapropterin-responsive children reported reduced dietary burden and greater flexibility in daily food choices, whereas families of non-responsive children continued to experience high levels of care-related strain.

Conclusions: Sapropterin enabled more flexible, sustainable dietary management in responsive children with PKU, supporting metabolic control, growth, and improved family well-being and reduced burden of care; however, the extent of dietary liberalization varied between individuals according to their PKU severity. Equitable access to therapies and long-term dietetic support are essential.

Use of skin testing to advise therapy options in Pompe patients following suspected IgE mediated infusion associated reactions (IAR)

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Background: Enzyme replacement therapy with Myozyme® has been available for the treatment of Pompe disease since 2006. In recent years 2 other second generations ERTs have also become available (Pombility® & Nexviadyme®) widening the therapy options for this patient cohort.

Methods: Four patients who developed suspected IgE mediated infusion associated reactions (2 switched patients and 2 treatment-naïve), were referred to the UCLH Allergy Service to evaluate their hypersensitivity response to all three ERT compounds to advise on individualized treatment options with possible desensitation protocols. Patients 1 and 3 were switched from Myozyme® (>6 and 3 years on treatment respectively) to Nexviadyme® and patients 2 and 4 were initiated on Nexviadyme® (naïve).

Results:

- Skin testing (skin prick testing (SPT and intradermal testing ID)) was performed on all 4 patients at different concentrations (Nexviadyme®: SPT 10mg/mL and ID 0.1mg/mL; Pombility®: SPT 15 mg/mL and ID 0.105 mg/mL; Myozyme® SPT 5mg/mL and ID 0.5 mg/ml).
- Patient 1 and 2 showed positive skin prick testing to both second generations ERTs, patient 3 showed positive results to Myozyme® and Pombility® with an equivocal reaction to Nexviadyme® and patient 4 tested positive to all 3 ERTs.
- Patient 1, who tested negative to Myozyme®, tolerated subsequent challenge with the drug. Patient 2 has opted for treatment discontinuation. Patient 3 is currently on a desensitization programme with Nexviadyme® and patient 4 will start a desensitization protocol with Myozyme®.

Conclusions: Referral to the allergy service can assist clinical teams to better individualize ERT therapy options for patients with suspected IgE mediated IAR and to safely deliver treatment in ERT allergic patients.

Review of genotype-phenotype correlation regarding sapropterin responsiveness in adult patients living with PKU

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Introduction: International databases, such as BIOPKU, have compiled phenylalanine hydroxylase (PAH) variants with their predicted responsiveness to sapropterin. However, patient numbers reported are small and hence applicability limited. We aimed to compare predicted responsiveness to sapropterin (determined by genotype) with clinical responsiveness in adult patients living with PKU.

Methods: Genotypes (pathogenic PAH variant(s), with associated BIOPKU responsiveness information from the genetics report) were compared with the real-world responsiveness to sapropterin (defined as a 30% reduction in bloodspot phenylalanine levels) for 23 adult patients within the Bristol cohort.

Results: 17/23 (74%) patients were clinically responsive to sapropterin. Of these, 11/17 (65%) had at least one allelic variant predicting either no responsive and/or an ambiguous response to sapropterin. 2/17 (12%) patients had biallelic variants considered to be non-responsive (c.912+1G>A/c.1315+1G>A (classical/classical) and c.745C>T/c.1222C>T (mild to classical/classical)) but responded clinically – albeit with delayed/prolonged responsiveness, indicating nuance lost with binary responsiveness labels. Further review of identified alleles revealed 51% residual enzyme activity reported in the c.745C>T nucleotide aberration which may explain clinical responsiveness in this patient.

Conclusion: Binary responsiveness labels can cause patients to be differentially excluded from potential responsiveness testing. Metabolic centres should be encouraged to add real-world patient data to databases such as BIOPKU to add power to conclusions that inform real-time patient decisions/guidelines.

A single-centre patient experience survey of parents and carers of children on low protein diets

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Background: The paediatric metabolic dietitians at the Willink Unit support over 100 patients with inherited disorders of amino acid metabolism, dietetically managing them as inpatients and outpatients. This survey was distributed to gather families' opinions of the service, to highlight strengths and identify areas of improvement.

Methods: The survey was split into 4 sections: Patient Experience; Communication and blood results; Prescriptions and supplies; Clinic appointments and care. Multiple choice and free-text questions were used to obtain quantitative and qualitative data. Free-text responses were examined using thematic analysis to identify key themes.

Results: 24 families completed the survey. 88% reported their experience of the service to be 'very good' with positive themes around support, explanations and care. 54% stated no improvements. 2 suggested organising more family events, and 2 related to different specialisms. All reported receiving blood results and preferred methods were phone (46%) and email (26%). All were satisfied, and 88% very satisfied with how they receive results, praising proactive contact.

All participants felt clinic appointment frequency was 'about right' and were satisfied with their appointment duration. Participants felt they saw who they needed 'always' or 'most of the time'. Half of respondents (n=12) added comments: 58% reported that no changes were required and 42% shared positive experiences. One suggestion was more information about research, and entertainment for children. Most stated 'always' receiving prescription products (71%), yet 67% of comments were around the unreliability of accessing them either due to the GP or delivery company; 'too many links in the chain.'

Conclusion: Communication and support were highly valued by families. Negative experiences relating to the current prescribing system were consistent with previous audit findings, highlighting the need to simplify this process. Additionally, concerns regarding different specialties indicated a need to communicate the dietitians' role and influence across multidisciplinary care.

Variability in dietary management in Isovaleric Acidaemia (IVA): A retrospective longitudinal cohort study

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Background: Management practices of classic (c) and attenuated (a) IVA vary. This study addresses uncertainties of dietary management, 1) protein restriction 2) leucine free amino acid (LFAA), 3) age-related need for emergency regimen (ER).

Methods: Longitudinal data, including protein intake, ER use and decompensation episodes were abstracted from medical records (1990-2025).

Results: The cohort comprised, 21cIVA (16 pre-NBS screen, 2 NBS, 2 prospectively managed, 1 mover-in) and 13 aIVA patients (age median/range: 21yr2m/ 5yr5m-36yr1m and 8yr/ 3m-41yr9m respectively). Five cIVA patients were excluded (2 neonatal deaths, 3 missing data).

In neonates (n=7) protein restriction median 2.0g/kg/d [1.8-2.1], n=2 unrestricted human-milk-feeding. Thereafter, safe level of protein intake (SI) for age in 14/16 cIVA contrary to 2/12 aIVA. Restriction was relaxed (parental choice) in 4/14 by age 8yrs, after as adults (n=6/8) by age 20. None received LFAA supplements. All cIVA patients received glycine and/or L-carnitine supplementation. ER use was documented 191 times in 15/16 cIVA (median/range per patient: 10/0-38 times). Related hospitalisations occurred 68 and 16 times before and after the age of 9yrs respectively. Metabolic decompensations occurred 15 times in patients <6yrs and another 3 later in life (6-9yrs).

Five aIVA patients used ER 20 times (median/range times per patient: 3/1-10) with no decompensations or ER use after the age of 6yrs. One had 5/10 illness related hospitalisations. cIVA adults (n=9), had 4 hospitalisation occurrences (pancreatitis n=1, pregnancy=1, vomiting n=2) and no metabolic decompensations.

In cIVA, body mass index (BMI) z-scores at age 16yrs (n=10) (median/range: -0.17/-1.9-1.49), with corresponding height z-scores (median/range: +0.17/-1.43-1.23], were relative to population norms.

Discussion/Conclusion: In cIVA metabolic stability and good growth was achieved on protein restriction (SI), glycine and L-carnitine even on relaxed diet. No metabolic decompensations occurred beyond age 9yrs. Protein relaxation seems possible in some, but continued use of ER appears prudent.

Cholestatic Jaundice with Hypocalcaemia: One Pathway and a Unifying Diagnosis

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Background: An 8-month-old boy presented to his GP with 'yellow sclera ?Gilbert's'. LFTs were requested and showed conjugated hyperbilirubinaemia (35 µmol/L), significantly elevated transaminases and ALP, with comparatively mildly raised GGT. Patient was admitted for further assessment and was additionally found to be hypocalcaemic (cCa 1.54mmol/L) with evidence of rickets.

PTH was appropriately raised (306 ng/L) and 25-hydroxyvitamin D was undetectable. A urine metabolic screen found nothing specifically diagnostic, as did plasma amino acids and acylcarnitines. Beutler testing excluded classical galactosaemia.

A prolonged PT time responded well to i.v. vitamin K. Despite high-dose oral cholecalciferol(D3), serum 25-hydroxyvitamin D remained undetectable. Other fat-soluble vitamins (A&E) were also very low.

Methods and Results: Plasma bile acids (analysed by FIA-MS/MS) did not show any diagnostic findings. However, subsequent urine analysis revealed an abnormal profile with significant increases in sulpho-/glyco- conjugates of dihydroxy- and tri-hydroxy-cholenoate. These strongly suggested a diagnosis of 3-beta-hydroxy-C27-oxidoreductase deficiency (HSD3B7), a primary bile acid synthesis disorder. Results were communicated, with advice to commence bile acid replacement (cholic acid), rather than ursodeoxycholic acid (ineffective in this disorder) and confirm by genetics.

Despite convincing biochemical evidence of HSD3B7 deficiency, cholic acid replacement could not commence without genetic confirmation due to high treatment costs. However, as liver function was rapidly declining, the biochemical evidence was subsequently deemed sufficient to commence treatment. Genetic confirmation was received a week later, with homozygous pathogenic truncating variants in HSD3B7 detected.

Conclusion: This case highlights the importance of sending both plasma and urine for bile acids, given the abnormal intermediates were not detected in plasma. This case also serves as a reminder to consider bile acid synthesis disorders as a unifying explanation in patients with cholestatic jaundice, together with deficiencies in fat-soluble vitamins (here presenting as hypocalcaemia due to Vitamin D deficiency), particularly when refractory to supplementation.

The holistic management of Late Onset Pompe Disease through nurse and physio led clinics- the Birmingham experience

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Background: Holistic management of late-onset pompe disease (LOPD) is vital as patients progress along their disease trajectory.

A nurse and physiotherapy led clinic for patients with late-onset pompe disease (LOPD) was introduced into the Lysosomal Storage Disorders service at University Hospitals Birmingham in March 2023 to provide holistic care to patients on and off Enzyme Replacement Therapy (ERT)

to support them through their life journey. This service was developed in response to local case experience which demonstrated that life events, mental well-being, and social circumstances can significantly influence symptom burden beyond the natural progression of the disease.

Methods: A monthly clinic was introduced offering patients one-hour appointments, delivered face-to-face or remotely, enabling discussion of physical, psychological, and social needs. A structured proforma guides consultations. Outcome measures used include R-PAct, North Star, and the 6-minute walk test. The Neuromuscular Disease Quality of Life Goal (NMD QOLG) was trialled to support personalised goal setting and capture patient-reported outcomes. A virtual exercise class was also delivered alongside the clinic.

Results: To date, 45 clinic appointments have been provided, and 16 patients have participated in the virtual exercise programme. Clinic interventions have included, onward referrals to community therapy teams, speech and language therapist, continence services, Occupational therapy, orthotics, wheelchair services, respiratory physiotherapy, signposting to patient support groups and exercise advise.
A patient satisfaction survey was conducted to gather feedback on both the clinic and the virtual exercise group, with the aim of continuously improving the service and ensuring it meets patient needs.

Conclusion: Preliminary findings indicate improved patient engagement, identification of unmet psychosocial needs, and positive feedback regarding the dedicated time and holistic approach. Patients particularly valued the opportunity to discuss non-physical aspects of their condition and access tailored exercise support. Ongoing evaluation will further inform service development and long-term impact.

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Sleep Disturbance in Mucopolysaccharidosis Type III (Sanfilippo Syndrome): A Service Review of Pharmacological Management Efficacy and Safety

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Background: Mucopolysaccharidosis type III (MPS III, Sanfilippo syndrome) is a lysosomal storage disorder characterized by relatively mild somatic involvement and severe, progressive central nervous system manifestations. Sleep disturbance is one of the most burdensome symptoms reported by caregivers, significantly affecting patient and family quality of life. Sleep management in MPS III remains challenging, with limited consistency in outcomes and sparse real world data on efficacy and safety.

Methods: A retrospective service review was conducted at a highly specialized lysosomal storage disorder center. Clinical records from 28 patients with MPS III were reviewed, focusing on the prevalence and characteristics of sleep disturbance, pharmacological treatment, perceived efficacy, treatment duration, and reported adverse effects.

Results: The cohort included 20 patients with MPS IIIA, 6 with MPS IIIB, and 2 with MPS IIIC. Sleep disturbance was documented in 82.1% (23/28) of patients; occurring in 95% of those with MPS IIIA and 50% of those with MPS IIIB and IIIC. Among 22 patients reporting primary sleep disturbance, difficulties with both sleep onset and maintenance predominated (86%), 9% reported maintenance problems and 4.5% with sleep onset. Pharmacological treatment was prescribed in 95.6% of cases, with melatonin used universally (median 6 mg/day), followed by chloral hydrate (36.3%; median 825 mg/day) and promethazine (18.1%; median 10 mg/day). Notably, 45.3% of treated patients required poly-medication (two medications in 36.3% and three

in 9%).Treatment efficacy was highly variable. While some achieved full-night sleep (16.6%) or good sleep most nights (33.3%), many others reported only inconsistent improvement (27.7%) or short-term benefits (16.6%), Median treatment duration was 3 years. Adverse effects were reported in 27.7% of cases, most commonly daytime somnolence.

Conclusions: Sleep disturbances are highly prevalent in MPS III and constitute a significant therapeutic challenge. In this real world cohort, pharmacological management demonstrated variable efficacy with a relatively favorable safety profile.

Peri-operative Management Guide for Inherited Metabolic Diseases

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Background: Inherited metabolic diseases (IMDs) are a heterogeneous group of conditions with shared risks of metabolic decompensation during peri-operative stress, alongside important condition-specific management differences. This complexity creates uncertainty for anaesthetists, leading to frequent specialist input, even in low-risk cases, and potential safety risks when guidance is unclear or not followed. At our tertiary centre, variability in practice and a safety incident (IR1) highlighted the need for clearer, accessible guidance. This project aimed to develop a pragmatic tool to support both autonomous and specialist-supported peri-operative management of children with IMDs, while maintaining safety.

Methods: We conducted a quality improvement project to design a concise peri-operative management guide, synthesising BIMDG recommendations into a concise practical format. IMDs were grouped by metabolic subtype, with clear escalation criteria for metabolic team involvement. Core peri-operative principles (fasting, fluids, bloods, and drugs) were standardised, while highlighting key condition-specific differences. Stakeholder engagement included anaesthetic team feedback, which identified a need for clearer guidance despite uncertainty around preferred format.

Results: A 3-page infographic guide was developed and shared as a PDF. Feedback from metabolic medical and nursing staff informed revisions, including clarifying terminology, addressing practical challenges, and reinforcing condition-specific management. For example, while some emergency regimens are considered safe as fasting fluids, substrate composition varies and requires caution. The guide was presented at a consultant-led anaesthetic meeting, with further feedback pending.

Conclusion: The guide supports differentiation between low- and high-risk cases, promoting appropriate escalation and reducing adverse events. It has potential to standardise care, improve safety, and bridge the gap between specialist knowledge and frontline peri-operative practice, while supporting decision-making, reducing unnecessary workload, and enhancing multidisciplinary communication.

Development of an erythrocyte debrancher enzyme assay to biochemically confirm a diagnosis of GSD IIIb

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Background: Glycogen storage disease type III (GSD III) is caused by a lack of debrancher enzyme activity. The biochemical diagnosis is typically carried out by measuring the enzyme activity in leucocytes, but this cannot distinguish between GSD IIIa (muscle and liver pathology) and GSD IIIb (liver pathology only). A biopsy of each tissue is required to confirm a diagnosis of GSD IIIb. We have previously received samples from patients genetically confirmed to have GSD IIIb. In each case, erythrocyte glycogen content was grossly elevated, whilst leucocyte debrancher activities were within the reference range. This is in contrast to GSD IIIa where the leucocyte enzyme activity is deficient. We therefore considered that a deficiency of the debrancher enzyme in erythrocytes might elevate glycogen in patients with GSD IIIb.

Methods: We adapted the current leucocyte assay for measuring debrancher activity and modified it to use erythrocytes as the sample type. Residual erythrocytes were used from patients with GSD IIIa, GSD IIIb and unaffected patients.

Results: Within a set of 8 patient samples, two of whom are confirmed to have GSD IIIa and a single GSD IIIb patient, we show that this novel erythrocyte debrancher assay can distinguish between affected and unaffected individuals, with GSD IIIa and IIIb patients having lower debrancher activities.

Conclusion: There is potential for this erythrocyte assay, in combination with the leucocyte test, to be used to biochemically confirm a diagnosis of glycogen storage disease type IIIb without the need for invasive tissue biopsies.

Complications of Central Venous Access in Metabolic Patients Undergoing Hemofiltration

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Background: Acute metabolic decompensation in children with inherited metabolic disorders often necessitates intensive care management, including continuous veno-venous hemofiltration (CVVH). This requires central venous catheter (CVC) insertion (including vascath, double/triple lumen lines), a procedure associated with significant risks in this vulnerable population.

Objectives: To evaluate the complications associated with CVC insertion in metabolic patients undergoing hemofiltration, and to identify modifiable factors to improve patient safety and clinical outcomes.

Methods: A single-centre retrospective audit was conducted over the period 2009–2024, including 87 paediatric patients with confirmed or suspected metabolic disorders requiring acute CVVH. Data collected included patient demographics, indication for hemofiltration, number of insertion attempts, and immediate and late complications. Mechanical, procedural, infectious, and thrombotic complications were analysed alongside mortality outcomes.

Results: Median age at CVVH was 7 days, median weight 3.2 kg. CVVH indication was hyperammonaemia (47/87,54%) hyperleucinaemia (12/87,13.7%) and lactic/metabolic acidosis/other (28/87,32%). Immediate complications were noted in 18/87 (20%) patients, no immediate complication in 42/87, incomplete data in 27/87. Complications included cardiac arrest(5), hemopneumothorax (1), haematoma or other bleeding(5), difficulty accessing device(2), catheter malposition (1) dislodgement(1), and suboptimal flow for dialysis(3).

Late complications (including line-associated thrombosis, device dysfunction and infection) were noted in 9/87 (10.3%), no late complication in 51/87, incomplete data in 27/87.

Number of insertion attempts was correlated with higher complication rates. Low body weight (<2 kg) and severe metabolic instability further increased procedural risk. The overall mortality rate was 37%, reflecting the severity of underlying disease, although procedural complications contributed to morbidity.

Conclusions: Central venous access is essential for CVVH in metabolic patients but carries a high risk of complications. Minimising insertion attempts, using ultrasound guidance, 49tandardizing insertion and maintenance protocols are key strategies to reduce risk. Multidisciplinary collaboration and ongoing audit are essential to improve outcomes in this high-risk population.

Development of a selective HPPD inhibitor without an off-target liability

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Background: Hereditary tyrosinaemia type 1 (HT-1) and alkaptonuria (AKU) are inborn errors of tyrosine catabolism caused by deficiency of fumarylacetoacetate hydrolase (FAH) or homogentisate dioxygenase (HGD) respectively, leading to accumulation of toxic metabolites. The current standard of care treatment is nitisinone, a small molecule inhibitor of the first committed step in tyrosine degradation, 4-hydroxyphenylpyruvate dioxygenase (HPPD). While nitisinone has transformed HT-1 management, some patients develop neurocognitive impairments, the cause of which remains unclear.

Methods and results: Here, we demonstrate that nitisinone potently inhibits sepiapterin reductase (SPR), a key enzyme in tetrahydrobiopterin (BH4) biosynthesis, which may contribute to adverse effects. Addressing this, we developed FTX-249, a novel HPPD inhibitor with minimal SPR inhibition. FTX-249 effectively rescues a mouse model of HT-1 without inducing behavioural phenotypes associated with nitisinone in mice.

Conclusion: These findings support further development of selective HPPD inhibitors that mitigate off-target toxicity and provide improved treatments for HT-1 and AKU.

Sleep study severity as a predictor of intraoperative airway difficulty in **M**ucopolysaccharidosis patients: a single-centre experience

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Background: Mucopolysaccharidoses (MPS) have historically been associated with varying degrees of respiratory dysfunction, most typically with progressive upper airway obstruction resulting in increased anaesthetic risk. Identifying reliable pre-operative predictors of airway difficulty is essential. Sleep studies are routinely performed in MPS patients, but their predictive value for intraoperative airway challenges remains unclear.

Methods: A retrospective single-centre review was conducted including patients with MPS types I, II, IV, and VI who underwent anaesthetic procedures. A total of 109 patients were identified, of whom 77 had both sleep study and intraoperative airway data available for correlation. Intraoperative airway difficulty was graded by the anaesthetic team (scale 1–4: easy to failed airway) and compared with sleep study severity (scale 0–3: none to severe obstruction). Statistical analysis was performed using GraphPad Prism (version 11.0.0). Comparisons were performed using the Mann–Whitney U test.

Results: In the overall MPS cohort (n=77), a significant correlation was identified between sleep study severity and intraoperative airway difficulty (p=0.0001). Subgroup analysis demonstrated significant correlations in MPS I post bone marrow transplant (n=30, p=0.006) and MPS IV (n=13, p=0.002). No statistically significant correlation was observed in MPS I patients receiving enzyme replacement therapy (n=8, p=0.137), MPS II (n=19, p=0.140), or MPS VI (n=7, p=0.196).

Conclusions: Sleep study severity appears to correlate with intraoperative airway difficulty in the overall MPS cohort, supporting its potential role as a pre-operative risk stratification tool. However, this association is not consistent across all MPS subtypes, likely reflecting small subgroup sizes and disease heterogeneity. The retrospective design represents an additional limitation. Larger prospective studies are required to validate these findings and to determine how sleep study parameters can be incorporated into clinical decision-making and perioperative planning.

Continuous glucose monitoring in assessment of susceptibility to ketotic hypoglycaemia in children diagnosed with spinal muscular atrophy in infancy on disease-modifying therapies

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Background: Children with spinal muscular atrophy (SMA) are at risk of severe ketotic hypoglycaemia due to reduced muscle mass and limited glycogen stores, particularly during fasting or intercurrent illness. They appear to have additional susceptibility to metabolic acidosis, postulated to be secondary to altered fatty acid mitochondrial beta-oxidation in skeletal muscle. Disease-modifying therapies for SMA have improved survival but may introduce additional risk factors including low body mass index and progressive bulbar impairment for children diagnosed after symptom onset. We aimed to evaluate baseline glucose profiles in children with SMA diagnosed in infancy receiving disease-modifying therapies.

Methods: A prospective study was conducted in 10 children with SMA. Continuous glucose monitoring (FreeStyle Libre 2) was applied for 7 days. Participants completed diet diaries, and baseline anthropometric and biochemical data were collected. Urine metabolic screening was performed to exclude alternative causes of hypoglycaemia. Previous fasting tolerance and

hypoglycaemic episodes were reviewed. Data was analysed descriptively and through individual time-series curve analyses.

Results: Ten patients were enrolled. Eight had two SMN2 copies and two had three copies. Therapies included nusinersen (n=3), risdiplam (n=2), and prior gene therapy (n=6). One participant had no usable glucose data, and two had shortened monitoring periods. Low body mass index was observed in nearly all (9) patients. Review of clinical history identified prior hypoglycaemic episodes with severe metabolic acidosis during intercurrent illness for multiple patients. Full results of baseline glucose monitoring will be available by the time of the conference.

Conclusion: Children with SMA diagnosed in infancy and treated with disease-modifying therapies appear to be susceptible to severe ketotic hypoglycaemia with metabolic acidosis when unwell. Proactive nutritional strategies, definitive feeding options and monitoring during illness may reduce risk. These results may be 51eneralizable to children with other congenital neuromuscular diseases. The study was limited by small sample size.

Glutathione Synthetase Deficiency: a rare differential diagnosis of neonatal metabolic acidosis

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Introduction: Glutathione Synthetase deficiency is an ultrarare autosomal recessive metabolic disorder of the gamma-glutamyl cycle. Moderately severely affected patients can present with unspecific signs including haemolytic anaemia and high-anion gap metabolic acidosis. We encountered a newborn with an atypical presentation, who was diagnosed with Glutathione Synthetase deficiency.

Case Presentation: A now 6-month-old child was born at term by an emergency C-section due to poor CTG. Though in good condition, the newborn had a cord gas of ph. 7.1 and BE -13 mmol/l and was admitted to critical care for CPAP support. The metabolic acidosis persisted with a normal to mildly increased anion gap (maximum 19 mmol/l) and normal blood ketones, glucose and ammonia, and no signs of haemolysis. Boluses and continued bicarbonate supplementation of 5mmol/kg was required for correction. Blood lactate was transiently elevated (maximum 4.1 mmol/l). Urine pH was 5.5. Urine showed generalised moderate amino aciduria, increased lactate and a gross increase of pyroglutamate. Pyroglutamic aciduria and metabolic acidosis in the absence of evidence of intoxication pointed to a diagnosis of glutathione synthetase deficiency and supplementation with ascorbic acid and alpha tocopherol was started. Prior to diagnostic confirmation, a urine dip stick test showed ketonuria of 4+, which was not in keeping with the suspected diagnosis, however this could be attributed to the high dose of ascorbic acid. Genetic testing confirmed the presence of a homozygous pathogenic missense variant in GSS. The child has been thriving and remained well on current treatment.

Conclusion: Moderately severe Glutathione Synthetase deficiency can present with unspecific symptoms and requires targeted biochemical or genetic testing for diagnosis.

False positive ketone stick results upon ascorbic acid supplementation can cause additional confusion.

Determinants of Bone Density Change in Gaucher Disease: A Multisite Mixed-Effects Analysis

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Introduction: Skeletal involvement is a major complication in Gaucher disease, with variable response to treatment. While the underlying pathophysiology remains incompletely understood, bone marrow infiltration, osteonecrosis, and osteoporosis all contribute to disease burden. We aimed to identify clinical and treatment-related factors associated with changes in bone density (ΔZ-score) across different skeletal sites.

Methods: GAUCHERITE includes clinical, radiological, and therapeutic data from patients followed at all UK national specialist centres from diagnosis to September 2019.

BMD Z-scores from the lumbar spine, total hip, and total radius (RUTOT) were extracted for patients on Gaucher Disease specific treatment. Cleaned DXA data were aligned to annual treatment anniversaries using linear interpolation, and annualized changes in Z-scores (ΔZ-score) were calculated. Demographic data, smoking status, body mass index (BMI), alongside disease specific variable were collected (splenectomy status, genotype, treatment delay, Zimran score).

Mixed linear models were used to evaluate predictors of ΔZ-score over time, accounting for both between-subject and within-subject variability.

Results: Bisphosphonate use was a consistent positive predictor of bone density response at the spine ($\beta=0.034$, $p=0.009$), hip ($\beta=0.029$, $p=0.020$) and RUTOT ($\beta=0.048$, $p<0.001$). Higher Zimran scores were associated with slower improvement (RUTOT: $\beta=-0.004$, $p=0.021$), while lower baseline Z-scores predicted rapid improvement at the hip ($\beta=-0.013$, $p=0.003$). No significant associations were observed for gender, splenectomy status, genotype, BMI, or symptom-to-treatment interval.

Conclusion: Bisphosphonate use is a key determinant of improvement in bone density, while higher disease severity is associated with slower response. Demographic, genetic, and most clinical factors did not independently influence skeletal response, highlighting the primary role of bisphosphonate and baseline disease burden.

Future proofing The Metabolic Service: MCADD Clinic – a nurse led approach

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Background: Medium chain acyl CoA dehydrogenase deficiency (MCADD) requires regular follow up including nutritional guidance, growth monitoring, and ongoing family education to ensure confident use of an emergency regimen during illness. Families frequently contact specialist nurses and dietitians when their child is unwell, yet routine follow up remained largely Consultant led. This created a mismatch between who families relied on during illness and who they routinely saw in clinic. We aimed to develop a nurse led MCADD clinic to improve continuity, accessibility, and family centred care,

Methods: A structured nurse led clinic pathway was developed. From age one, families were offered biannual nurse led reviews, with consultants continuing routine appointments until the first birthday. Consultations focused on a health review, proactive education, and detailed discussion of emergency regimen use. Families could request medical review at any point. Informal feedback was collected from families attending the new clinic model.

Results: Families reported reassurance in seeing clinicians they routinely contact during illness, describing the experience as familiar and supportive. One parent noted, "The nurses and dietitians are the people I speak to if my child is unwell, so seeing them in clinic feels familiar." Others valued the option of medical review when needed. The model strengthened relationships, improved continuity, and enabled earlier identification of emerging issues due to increased familiarity and trust.

Conclusion: Early experience indicates that a nurse led MCADD clinic supports a more responsive and family centred approach to long term management, enhancing confidence, continuity, and flexible access to medical review. Further evaluation will examine its impact on engagement, education across childhood and transition, and unplanned contact with the team. Service benefits include increased Consultant availability for complex patients, reduced waiting times, and enhanced professional development for metabolic nurse specialists, supporting retention and strengthening service resilience.

A homozygous intronic variant in NDUFAF8 causes optic atrophy and learning difficulties

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Background: NDUFAF8 is a mitochondrial respiratory chain complex I assembly factor that stabilises NDUFAF5. Bi-allelic variants in NDUFAF8 have previously been described in patients with Leigh syndrome in infancy (PMID: 31866046). We describe a series of patients homozygous for a deep intronic pathogenic variant in NDUFAF8 who present predominantly with optic atrophy, without radiological features of Leigh disease, and with a milder clinical phenotype.

Methods: A retrospective review of medical records including radiological and laboratory records was conducted.

Results: Five patients, age range 4 months – 21 years old are homozygous for the c.195+271C>T pathogenic variant in NDUFAF8 (NM_001086521.2). All are of Irish heritage. One patient presented antenatally with bilateral mild ventriculomegaly and intrauterine growth restriction. The other patients presented with visual impairment during early childhood, with bilateral optic nerve atrophy. One child has periventricular leukomalacia on MRI brain, one has partial agenesis of the corpus callosum, and two have a normal MRI brain.

Three patients had mild delays in their gross motor development in infancy and have required learning supports in school, and one is in third level education with no learning supports. To date

there has been no evidence of cardiac involvement, hearing impairment, myopathy, seizures or endocrinopathy.

Biochemistry including serum lactate, ammonia, plasma amino acids and urinary organic acids was normal in all. However, mild intermittent neutropenia is present in this cohort, with no apparent increased rate of infection. Functional studies in cultured fibroblasts in two patients demonstrate an isolated deficiency of mitochondrial complex I activity.

Conclusion: Individuals who are homozygous for the c.195+271C>T NDUFAF8 pathogenic variant have a clinical course 54haracterized by optic atrophy, mild learning difficulties, and mild neutropenia. This expands the known phenotype of NDUFAF8-related mitochondrial disease. NDUFAF8-related mitochondrial disease is likely to be an underdiagnosed cause of optic atrophy in otherwise healthy individuals.

Enhancing Enzyme Replacement Therapy in Lysosomal Storage Disorders: Faster Infusion Rates Across the UK

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Background: Lysosomal Storage Disorders (LSDs) are rare, multisystemic inherited metabolic conditions. Enzyme replacement therapy (ERT) is part of standard treatment for some LSDs. ERT is administered through regular weekly or alternate-week intravenous infusions, initially under supervision in specialised NHS centres and then continued usually lifelong at patients' homes via homecare services. Prolonged infusion duration increases treatment burden for patients and use of nursing resource in both hospital and homecare services. Infusion protocols and strategies for reducing infusion duration outside the manufacturer's recommendations vary across the UK.

Methods: A Microsoft Forms® survey was distributed to adult and paediatric pharmacists and nurses at UK LSD centres to assess current use of faster-than-SmPC (Summary of Product Characteristics) infusion rates. Data collected include eligibility criteria, treatments involved, implementation settings, monitoring, and safety outcomes.

Results: All centres responded (6 adult, 6 paediatric). Half (6/12) reported using infusion rates faster than SmPC recommendations. Use varied by centre: accelerated rates were offered only on patient request (4/12), to selected patient groups (2/12), or routinely to all eligible patients (2/12). Accelerated treatments included agalsidase beta, alglucosidase alfa, avalglucosidase alfa, cipaglucosidase alfa with miglustat, laronidase, elosulfase, idursulfase, and galsulfase.

Infusion time reduction strategies included eliminating early slow-rate steps (5/12) and increasing maximum infusion rates (3/12). Accelerated rates were implemented either in hospital (1/12) or at patients' homes (3/12), depending on centre policy.

No centre reported an increase in infusion-associated reactions following adoption of faster rates.

Conclusions:Accelerated ERT infusion rates outside SmPC recommendations are already in use across LSD centres without evidence of elevated infusion-related reactions. While practice varies, centres successfully shorten treatment duration by modifying infusion protocols. Sharing of local protocols and outcomes may improve equity of access, reduce treatment burden, shorter nursing visits and lower overall NHS cost.

Metabolic Pharmacist Roles Across the UK: Current Practice and Service Provision

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Background: Pharmacists are medicine experts, playing a critical role within multidisciplinary teams (MDTs) caring for patients with inherited metabolic disorders (IMDs) in the UK. This study characterises UK pharmacists' scope of practice and their integration within MDTs.

Case Study / Methods: A Microsoft Form® survey captured pharmacists' work patterns, prescribing activities, MDT involvement, and perceived barriers within IMD services. Responses were analysed descriptively.

Results: Fourteen of sixteen UK IMD pharmacists responded to the survey. All were senior clinical pharmacists working in paediatric (n=8), adult (n=5), and mixed (n=1) services, with a median IMD-commitment of 50% (range 10 −100%). Centre size ranged from fewer than 500 patients to over 2000 patients, with <500 patients the most reported category (n=6).

Independent prescribing capability was reported by 13 pharmacists, although only six currently prescribe for IMD patients. Barriers to prescribing included newness to the role, funding limitations and governance constraints. Prescribing activities include repeat prescribing, dose adjustments and initiation of new medicines across inpatients, outpatients and homecare settings. Pharmacists supported therapies including enzyme replacement, oral chaperones, substrate-reduction therapies, ammonia scavenging, compassionate-access and off-label treatments.

Ten pharmacists participated in IMD clinics, seven attend transition clinics, and five see patients independently. Thirteen pharmacists attend IMD MDT clinical and governance meetings. One pharmacist reported referring to other specialities.

Barriers to development included a lack of protected IMD time, insufficient funding and limited local support or mentorship.

Discussion/Conclusion: UK IMD pharmacists reported advanced expertise and broad MDT engagement, contributing to patient care, clinical governance and professional representation. However, independent prescribing and clinic involvement remain constrained by structural barriers. Addressing funding, protected time, and access to professional development may enable pharmacists to deliver greater clinical impact and service efficiency, mirroring benefits observed in primary care settings where pharmacist integration improves workflow, clinical outcomes, and patient experience.

Service improvement: Clinical Nurse Specialist (CNS) led clerking of Neuronal Ceroid Lipofuscinosis (CLN2) Batten disease patients

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Background: CLN2 Batten disease, neuronal ceroid lipofuscinosis type 2, is a rare genetic disease caused by deficiency of the enzyme tripeptidyl peptidase 1 (TPP1). A deficiency of TPP1 results in abnormal storage of proteins and lipids (lipofuscin) primarily in neurons and other cells.

Cerliponase alfa (Brineura®) is a enzyme replacement therapy (ERT) consisting of a recombinant form of TPP1. It is administered into the cerebrospinal fluid (CSF) by infusion every fortnight via a surgically implanted ventricular access device.

Patients are admitted to the day unit for a whole day procedure. Patients are required to be medically examined and assessed prior to their infusion to confirm the procedure can proceed, mitigating risks of infusion related reactions or waste of high-cost medication. As there are no designated metabolic resident doctors or trainees, clerking was often delayed causing patient dissatisfaction and prolonged admissions.

Method: The team identified a need for a clearer pathway for the admission of CLN2 patients utilising the expertise of the CNS team. An application was submitted for funding in 2024 for the Paediatric Physical assessment and Clinical Reasoning module. The module was successfully completed by the Lead CLN2 CNS in June 2025.

Supervision and support were provided by the Metabolic Consultant to ensure CNS competence in the clerking and clinical examination of patients.

Results: CNS led clerking has been successfully implemented since December 2025 supporting a smoother pathway for CLN2 patients receiving Cerliponase alfa, Brinuera ® infusions.
Patients' admission times have reduced, improving patient satisfaction and service delivery.
Positive feedback has been received by professionals and parents.

Discussion: Professional development as a CNS will support career progression, staff satisfaction and staff retention in services.

CNS led clerking could be 57tilized for other patient investigations and procedures to reduce workload on resident doctors.

Galactosaemia and cheese: cheese analysis for lactose and galactose content in the UK, 2022-2026

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Background: The international clinical guidelines for galactosaemia recommend if cheese has a galactose content of <25mg/100g then it is allowed in the diet for galactosaemia. In the past 20 years the Galactosaemia Support Group have analysed over 190 different samples of cheese for lactose and galactose. The UK currently allow extra mature cheddar, vintage cheddar, Italian parmesan, Grana Padano, Emmental, Gruyere, Comte, Jarlsberg. The aim is to analyse more cheese types to see if anymore can be included in the diet.

Methods: 46 cheese samples were analysed for lactose and galactose in 2022 (n17), 2024 (n23) and 2026 (n6). Analysis was carried out by Campden BRI (Chipping Campden) limited, UK.

Results: Pecorino (n5, mean <10.5mg/100g) and low fat extra mature cheddar (n2, mean <10.5mg/100g) were found to be low enough.

Mozzarella (n5, mean 653mg/100g), Blue Stilton (n5, mean 72.5mg/100g), Red Leicester (n5, mean 138.64mg/100g) and Feta (n3, 38.6mg/100g) were found to be too high or too variable in galactose.

Brie and Camembert were found to be borderline as 5/5 Brie samples were found to be low enough in 2022 analysis (mean <10.5mg/100g), but only 2/5 low enough in 2024 analysis (mean 32.5mg/100g). Similarly, only 2/5 Camembert samples were low enough, while 3 were just over 25mg/100g (mean of 26.4mg/100g).

2026 analysis of one brand; Le Brie President (n3, all samples <6.25mg/100g) and President Camembert (n3, all samples <6.25mg/100g) were all below the < 25mg/100g threshold.

Conclusion: Pecorino and low fat extra mature cheddar are low enough in galactose to be included in the diet. Mozzarella, Blue Stilton, Red Leicester were too high in galactose, and Feta was too variable (due to being a young cheese). Brie and Camembert are variable but with certain brands being low enough to include in the diet for people with galactosaemia.

An Exercise and Dietary Induced Fat-Free Mass Increase in Two Patients with Phenylketonuria (PKU)

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The evidence in Phenylketonuria (PKU) and exercise is limited, including the nutrition advice provided and long-term effects on blood phenylalanine levels and body composition.

This abstract reports on two case studies; a male and female with PKU and their progress.

Patient 1 is a 25-year-old male who boxed 5 times a week. He was reviewed over 3 years and his training changed to Hybrid training (weight-lifting and cardiovascular training). He started on 120g protein (100g protein substitute and 20g natural protein) (1.4g/kg). It is likely natural protein intake was higher. This was increased to 140g (120g protein from protein substitute and 20g natural protein) (1.5g/kg). Adequate carbohydrate-intake advice was also provided, including pre, post and during exercise. Weight increased from 84.8kg to 93.5kg, body fat from 20-21.4% and fat free mass increased from 67.8kg to 73.5kg, a 5.7kg rise. Phenylalanine levels varied from 650-1050umol/l. There was minimal blood phenylalanine levels and contact between annual reviews.

Patient 2 is a 26-year-old female on Sapropterin. She was running long distance several times a week and wanted to strength train twice weekly. She started on 85-90g protein (60g protein substitute and 25-30g natural protein) (1.9g/kg). This increased to 125g (100g from protein substitute and 25g from natural protein) (2.5g/kg). Adequate carbohydrate-intake advice was also provided for pre, post and during activity. In a year weight increased from 47.9kg to 51.1kg, body fat, from 18.9-20.2% and fat-free mass from 39.4kg to 41.6kg, a 2.2kg rise. Phenylalanine

levels varied from 200-600umol/l. There was very regular contact and frequent blood phenylalanine levels between clinic reviews.

These cases show the differences in exercise undertook, dietary advice provided and resulting increases in fat-free mass for both athletes. It illustrates how muscle gain is possible in PKU with adequate training, nutrition and support.

Characterization of Maple Syrup Urine Disease in a Chilean Cohort: Genotypic Variations and Metabolic Control

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Background: Maple syrup urine disease (MSUD) is a deficiency in the branched-chain α-ketoacid dehydrogenase complex (BCKDH), leading to branched-chain amino acid (BCAA) accumulation. Diagnosis relies on elevated BCAA and alloisoleucine. Treatment includes a leucine-restricted diet, BCAA-free formulas, and precise supplementation.

Objective: To characterize a Chilean MSUD cohort regarding diagnostic BCAA levels, genotype, and metabolic control.

METHODS: A retrospective analysis of clinical records was performed. Variants in four MSUD-related genes were identified. Diagnostic and follow-up BCAA levels (2024–2025) were measured by LC-MS/MS. Data are presented as median (IQR).

Results: Forty-nine patients were included (57% female), median age of 14.4 (IQR:10.5–23.1) years. In the absence of neonatal screening, the median age at diagnosis was 18 (IQR:10-49) days. Baseline diagnostic levels were: leucine 1406 (IQR: 981–1679) µmol/L, isoleucine 401 (IQR:178–512) µmol/L, valine 321 (IQR:243–723) µmol/L and alloisoleucine 111 (IQR: 69–183) µmol/L. Variants in BCKDHB were found in 24 patients, including four novel variants: c.196+5G>A, c.577dup (p.Ala193Glyfs*), c.362dup (p.Asn121Lysfs6), and c.397G>T (p.Gly133). The most frequent variant (n=12) was c.641T>A (p.Ile214Lys). Variants in BCKDHA (n=3), DBT (n=2), and DLD (n=1) included three additional novel variants: c.937G>C (p.Ala313Pro), c.51G>A (p.Leu17=), and c.1517C>T (p.Ser506Leu), respectively. During follow-up, leucine levels were 232 (IQR: 200–255) µmol/L in patients ≤5 years (n=9) and 277 (IQR: 234–346) µmol/L in those >5 years (n=39, excluding the DLD patient), with 60% of measurements within the recommended range. Median isoleucine and valine levels were 257 (IQR: 183–306) µmol/L and 396 (IQR: 332–489) µmol/L, respectively.

Conclusion: The diagnostic delay highlights the urgent implementation of universal neonatal screening to ensure early intervention and prevent the severe metabolic crisis associated with late diagnosis. This cohort exhibits a predominance of BCKDHB variants, specifically the potential population-specific p.Ile214Lys variant. While long-term metabolic control was adequate for most patients.

Estimating prevalance of long chain fatty acid oxidation disorders in the UK

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Long chain fatty acid oxidation disorders (LC FAOD) are inherited metabolic conditions not currently included in the NHS newborn blood spot screening (NBS) programme. Consequently, UK epidemiology primarily reflects clinically identified symptomatic cases and may underestimate milder or presymptomatic disease. A previous global epidemiology model estimated LC-FAOD prevalence. This study applied that model using the most updated epidemiological information to estimate overall and diagnosed LC-FAOD prevalence in the UK without NBS.

An LC-FAOD birth incidence of 0.0022% was applied, derived from 2005-2023 German and US NBS reports. UK birth rates were estimated using median United Nations Population Division data. Severity distribution at birth was assumed to be 8% asymptomatic, 18% mild, 30% moderate, and 44% severe.

The current study estimated 534 individuals living with LC-FAOD in the UK in 2026 and 542 in 2030. In 2030, 225 patients were projected to be paediatric (53% diagnosed; 119 patients) and 317 adult (49% diagnosed; 156 patients). New diagnoses at birth were estimated at 9-10 annually and all-age deaths at 15 annually. The all-population prevalence (all ages) was estimated at 7.6 per million population while diagnosed prevalence was 3.9 per million. By application of a published epidemiology model to estimate total and diagnosed LC-FAOD prevalence in the UK without NBS, this study found that 51% of patients will be underdiagnosed.

Estimates are primarily informed by German and US data and may have limited applicability to the UK due to differences in ethnic composition and consanguinity, which may influence both incidence and severity distributions. Severity may be overestimated, as undiagnosed UK cases are more likely to be attenuated or asymptomatic than severe paediatric presentations. Despite phenotypic heterogeneity, LC-FAOD are associated with lifelong metabolic vulnerability and an ongoing risk of serious, potentially life-threatening decompensation across all age groups and severity categories.

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Multiple acyl CoA dehydrogenase deficiency (MADD): single-centre review of paediatric clinical, dietetic and biochemical disease severity spectrum

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Background: MADD is a rare disorder of the electron transfer flavoprotein system which impairs fatty acid oxidation and amino acid metabolism, resulting in cellular energy deficiency and toxic metabolite accumulation including acyl-carnitines. A spectrum of clinical severity exists. We report a single-centre paediatric cohort review of biochemical characteristics and associated management strategies.

Method: Retrospective case-note review of clinical and biochemical records of current paediatric cohort of MADD from 2006-2026.

Results: Of nine patients identified, n=7 are alive (aged 3−17y, median 10.9), n=2 died at 4m and 5y from acute cardiorespiratory causes. N=7 were diagnosed in their first week of life, of whom n=3 were identified incidentally via MCADD newborn screening, n=2 were tested as at-risk siblings, and n=2 presented symptomatically with cardiac arrest. N=2 presented later at 12w and 1y 6m with cardiac arrest and hypoglycaemia, respectively. Variants were identified in ETFDH (n=7) and ETFA (n=2) with no clear genotype-phenotype correlation.

Serial acylcarnitine profiles differentiated those with severe and less severe clinical outcomes, and those with riboflavin responsiveness. More severe disease had relatively higher concentrations of long-chain acylcarnitines (C16 and C14:1 compared to C8).

Medication included riboflavin (150-400mg daily) (7/9), ketone bodies (2/9), L-carnitine (7/9) and coenzymeQ10 (4/9).

Those with severe disease (6/9) have a prescribed diet comprising 20-24% energy from long-chain triglyceride, no medium-chain triglyceride, 6-13% from protein and 63-76% from carbohydrate. Of these, 5/6 required enteral tube feeding. 3/9 continued normal diet, of whom one has additional uncooked cornstarch to support fasting times. All avoid extensive fasting and have glucose polymer emergency regimens for illness management.

Discussion / Conclusion: MADD management is challenging, and the disease course can be unpredictable with a spectrum of severity. Despite dietary and pharmacological treatment, routine acylcarnitine profiles remain abnormal and may help inform bespoke management planning in combination with early disease course.

Cognitive and Behavioural Profiles of Children and Young People with Inherited Metabolic Disorders: A Retrospective Clinical Audit

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Background: Inherited metabolic disorders (IMD) are associated with a range of neurological and neurodevelopmental outcomes; however detailed behavioural and psychological profiles remain under-characterised. This audit describes the cognitive and behavioural presentation of children and young people (CYP) attending a specialist neurometabolic clinic and explores co-morbid neurodevelopmental and mental health needs.

Method: A retrospective case-note review was conducted for 104 CYP (mean age = 9.05 years, range 1.3-16.8; 49% female). Demographic and clinical data were extracted, including age, sex, ethnicity, metabolic diagnosis and co-morbid neurodevelopmental conditions. Standardised cognitive and developmental assessments (including Wechsler intelligence and Bayley developmental scales) were analysed alongside questionnaire measures, including the Adaptive Behaviour Assessment System, Strengths and Difficulties Questionnaire, Social Responsiveness Scale and Conners questionnaires.

Results: The sample was ethnically diverse, with majority of families from non-White British backgrounds. Forty-six metabolic conditions were represented with mucopolysaccharidosis, maple syrup urine disease, galactosaemia and phenylketonuria most common. Co-morbid neurodevelopmental needs were frequent, including intellectual disability (34.6%), speech and language difficulties (23.1%), developmental delay (10.6%), autism (9.6%), ADHD (5.8%) and specific learning difficulties (13.4%). Full scale IQ cognitive scores were predominantly in the extremely low or low ranges (73%). Questionnaire data indicated widespread adaptive, social communication and emotional difficulties, with attentional difficulties most commonly reported.

Conclusions: CYP attending the neurometabolic clinic present with highly complex cognitive, developmental, behavioural and emotional profiles. Whilst diagnosed neurodevelopmental comorbidities were present in a minority, questionnaire findings indicated a higher burden of unmet or under-recognised needs, raising the possibility of diagnostic overshadowing. Findings highlight the importance of culturally responsive and accessible assessment pathways. At a service and policy level, assessment tools and referral processes may need adapting to ensure equitable access, improve early identification of needs, and inform research on effective multidisciplinary care for CYP with IMD.

Paediatric Aldolase A deficiency: Case report, treatment & biomarkers of an ultra-rare inherited metabolic disorder

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Background: Aldolase A deficiency (ALDOA/Glycogen Storage Disorder XII) is an ultra-rare disorder of glycolysis with fewer than 20 cases reported worldwide. It is associated with haemolytic anaemia, myopathy, rhabdomyolysis and, more rarely, seizures.

Case Presentation: We report the case of a 7-year-old patient who first presented as a neonate with non-spherocytic haemolytic anaemia (NSHA), before developing myopathy, intermittent rhabdomyolysis and epileptic seizures. There was also a reported history of developmental impairment with a later established ADHD diagnosis. Our patient was referred to the paediatric metabolic service at 5 years of age with a genetic (ALDOA c.643A>g; p.(Lys215Glu), c.899_901delTCT; p.(Phe300del)) and biochemical (Aldolase 0.4 IU/g Hb RR 1.4-4.9) diagnosis of Aldolase A deficiency and have been under follow-up for 2 years.

Intervention/Management: A modified ketogenic diet (KD) with MCT was initiated for management of both the underlying glycolytic disorder and the presumed secondary epilepsy. Compliance was limited and seizure control did not improve, though a subjective improvement in attention was reported. Due to tolerance and lack of significant response, the diet was discontinued and symptomatic management was instituted. A novel and unexpected finding, sustained isolated elevation of propionylcarnitine (C3), was observed throughout follow-up which was comprehensively investigated, including with untargeted metabolomics.

Discussion: This case further establishes and potentially expands the phenotype of Aldolase A deficiency with a developmental phenotype. Additionally, we report a novel ALDOA variant along with untargeted metabolomic results. We also noted an increase in propionylcarnitine, previously reported in other glycolytic disorders but not ALDOA deficiency, and consider this as a marker of haemolytic anaemia (HA).

Conclusion: Aldolase A is an ultra-rare disorder, likely underdiagnosed and with no established management. This may be the first reported case in the UK and we report phenotype, treatment and biomarkers, with consideration of C3 as a marker of glycolytic disorders/HA.

Lived Experience: Insights into Familial Chylomicronaemia Syndrome

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Background: Familial Chylomicronaemia Syndrome (FCS) is an ultra-rare inherited lipid disorder caused by a mutation in one of five genes, affecting approximately 1 or 2 in 1,000,000 people. Using a digital survey, we aimed to gain insight into the lived experience of people with FCS.

Methods: A digital survey was conducted by Action FCS and Metabolic Support, which ran between 20/10/2025 and 30/11/2025. Questions were designed based on the NICE patient organisation submission template and in-house FCS knowledge. The survey was disseminated via social media, newsletters, and targeted outreach. Surveys were available in English. Data were analysed using a mixed methods approach using both descriptive statistics and thematic content analysis.

Results: 40 responses were received and included people living with FCS (n=31) and parents/carers of someone living with FCS (n=9). Respondents were from Estonia (n=1), Germany (n=1), Pakistan (n=1), the UK (n=28), USA (n=8), and the unspecified (n=1) with an average patient age of 40 years (range: 4−73).

Dietary management remains the principal strategy for controlling FCS, achieved primarily through the reduction of fat intake, which can be challenging and expensive to follow. People living with FCS had significant worries about the consequences of consuming too much fat.

Responses revealed significant impact of FCS on the daily lives of people living with it from a social and health perspective, with significant impact reported on their career, relationships, education and finances. EQ-5D-3L data confirmed significantly reduced quality of life (average 0.68, n=38) compared with general UK population norms (0.89).

Conclusion: These findings provide valuable insight into the lived experience of individuals with FCS across multiple countries, highlighting the substantial and multifaceted impact of FCS on daily life.

There is a clear need for improved clinical support, greater awareness, and access to effective treatments to reduce the impact of this condition.

Single-centre experience of parenteral nutrition when acutely managing methylmalonic acidaemia and propionic acidaemia

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Background: Promoting anabolism and avoiding catabolism are essential in managing organic acidaemia (OA). When enteral nutrition (EN) is not possible, parenteral nutrition (PN) is often required. At our centre, bespoke PN must be prescribed 31 hours in advance, whereas standard PN is available same day. This creates challenges in delivering timely, appropriate nutrition. Evidence on PN in OAs remains limited, prompting this service evaluation, reviewing PN use when acutely managing patients with OAs.

Method: A retrospective review of admissions requiring PN between 09/2022-12/2025. Data was collected from electronic records. Data displayed as mean (range).

Results: 14 patients (propionic acidaemia n=6, 33% tube-fed; methylmalonic acidaemia n=8, 100% tube-fed), aged 7y 8m (11m-16y 10m), accounted for 35 PN admissions, equating to 181 PN days (d). Mean protein restriction: 0.93g/kg (0.79-1.17g/kg).

98% were unplanned admissions. PN indications included vomiting, pancreatitis and metabolic acidosis. On average, patients were prescribed PN within 1d of admission (0−4d) and without usual protein intake for 4.5d (1-28d).

All unplanned admissions started on a portion of a standard PN bag with intravenous fluids (0-20% dextrose) +/- intralipid to meet requirements. In 26% of admissions, patients received incorrect or delayed intravenous nutrition. Progression to bespoke PN to address electrolyte and fluid challenges was required in 26% of admissions and undertaken after 4d (2-9d). Mean PN duration was 5d (1-14.5d).

All patients titrated from PN to EN, maintaining consistent energy and protein provision, over 2.5d on average (1-9.5d). Titration errors occurred in 12% of admissions. Mean time from stopping PN to discharge was 4d (2 hours-20.5d) and total length of stay was 12d (3-42d).

Conclusion: A portion of standard PN with intravenous supplementation is initiated promptly. However, the requirement for bespoke PN, delivery and titration errors, highlight the need for improved protocols to ensure timely, safe, and metabolically appropriate care.

BIMDG

British Inherited Metabolic Disease Group