Lack of association of anal symptoms with anal high-grade squamous intraepithelial lesions, among gay and bisexual men in the Study of the Prevention of Anal Cancer (SPANC)

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Sexual Health Conference, November 9th 2017

Lack of association of self-reported anal symptoms with anal HSIL

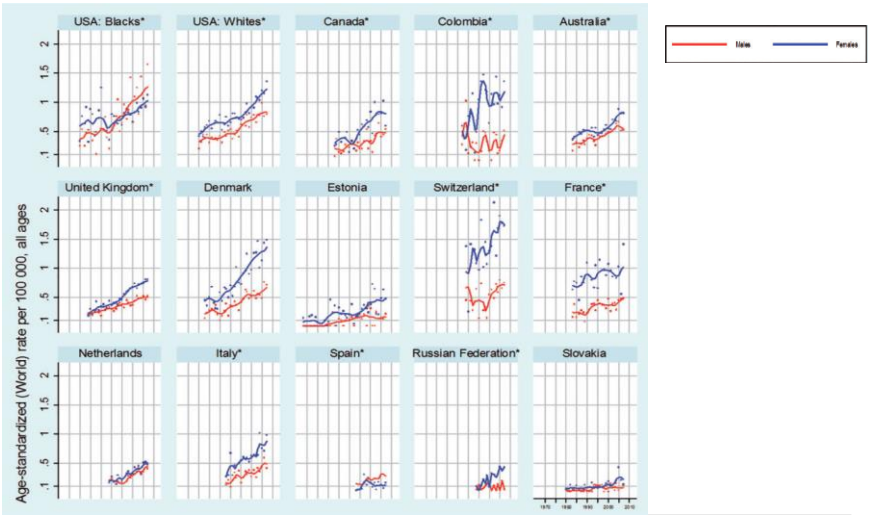
Disclosure of Interest

I have no conflict of interest to declare

Overview

- Why study high grade squamous intra-epithelial lesion (HSIL) and anal symptoms
- Methods of SPANC study
- Methods of this analysis
- Results
  - Prevalence of anal symptoms
  - Anal symptoms as predictors of HSIL
- Conclusions

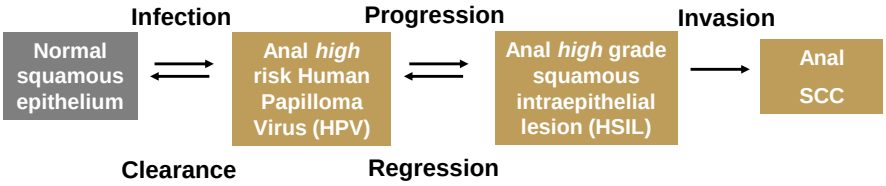
Increasing incidence of anal squamous cell carcinoma (SCC)



[4] Islami et al. International Journal of Epidemiology. 46 (2017) 2322-2327

Human Papilloma Virus, HSIL and anal SCC

- 90% of anal cancer is caused by Human Papilloma Virus (HPV)



5 Brickman C, Palefsky JM. Himan papillomavirus in the HIV-infected host:epidemiology and pathogenesis in the antiretroviral era. Curr HIV/AIDS Rep 2015; 12: 6-15

Lack of association of self-reported anal symptoms with anal HSIL

Anal cancer is concentrated in certain populations

Population	Relative risk	Annual Incidence (per 100,000)
General population	1 (referent)	1-2
Women with previous anogenital HPV disease	5-20	5-20
Organ transplant recipients	5-10	5-20
HIV negative Gay and Bisexual men (GBM)	5-20	5-20
HIV positive people (excluding GBM)	10+	10-30
HIV positive GBM	50	70-130

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Anal Symptoms

- Anal SCC may present with anal lump and/or bleeding, but often presents late
- Unknown whether anal HSIL is associated with anal symptoms
- Cervical HSIL can be associated with abnormal vaginal bleeding, which is an indication for cervical colposcopy referral
- If anal symptoms are associated with anal HSIL – could be clinically useful to indicate need for further investigation

Aim

- To assess if any anal symptom is independently associated with the presence of intra-anal HSIL

Machalek *et al. BMC Public Health* 2013, 13:946
http://www.biomedcentral.com/1471-2458/13/946

BMC Public Health

STUDY PROTOCOL Open Access

The Study of the Prevention of Anal Cancer (SPANC): design and methods of a three-year prospective cohort study

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- Overall aim: to inform the development of an anal cancer screening program
- 617 participants
- GBM aged ≥ 35 years (HIV pos & neg)
- Cytology, HPV testing, high-resolution anoscopy (HRA) and biopsies at each of 5 visits over 3 years

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Baseline cohort characteristics

		n=617
Median age, years (IQR)		49 (43-56)
Lifetime no. of male partners	≥ 200	318 (51.7%)
Lifetime condomless receptive anal sex	≥ 50	226 (37.5%)
Condomless receptive anal sex past 6 mo	≥ 2	193 (31.3%)
HIV positive		220 (35.7%)

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Anal symptoms and HSIL
Methods: Composite cytology-histology

Anal squamous intraepithelial lesion category	n	% (95% CI)
Composite negative	**183**	**28.0 (24.4-31.7)**
Composite HSIL (*Excluding SCC)*	**231**	**34.5 (34.5–42.5)**

- n=414
- Other composite diagnoses excluded

Anal symptoms and HSIL
Methods: Questionnaire

- History of the following symptoms collected via baseline questionnaire.
    - Anal itch
    - Anal discharge
    - Anal bleeding
    - Pain with defecation
    - Lump in the anus
    - Tearing of the anus
    - Anal ‘sores’
    - “Feeling that something was left after a bowel movement”

Statistical analyses

- Logistic regression for association of each anal symptom (last month and last 6 months separately) with composite HSIL (versus composite negative)
- Any symptom with p<0.1 included in multivariate model including factors previously shown to be independent predictors of HSIL[1]

1. Machalek et al. Papillomavirus Research 2016;2:97-105

Lack of association of self-reported anal symptoms with anal HSIL

Symptom prevalence at baseline visit: n=414

Self-reported anal symptom	Last month prior to HRA			Last 6 months prior to HRA		
	n	%	(95% CI)	n	%	(95% CI)
Any anal symptom	231	55.8	(50.9-60.6)	297	74.4	(69.9-78.6)
Anal discharge	16	3.9	(2.2-6.2)	22	5.3	(3.4-7.9)
Anal Itch	88	21.3	(17.4-25.5)	137	33.1	(28.6-37.9)
Anal sores	19	4.6	(2.8-7.1)	43	10.5	(7.7-13.8)
Anal lump	25	6.0	(3.9-8.8)	58	14.0	(10.8-17.7)
Pain defecating	53	12.8	(9.7-16.4)	88	21.3	(17.4-25.5)
Anal bleeding	77	18.6	(15.0-22.7)	147	35.5	(30.9-40.3)
Anal tearing	22	5.3	(3.4-7.9)	59	14.3	(11.1-18.0)
Feeling “something left after a bowel movement”	133	32.1	(27.6-36.9)	167	40.3	(35.6-45.2)

Lack of association of self-reported anal symptoms with anal HSIL

Anal symptoms within last 6 months

Self-reported anal symptom	Composite negative n (%)	Composite HSIL n (%)	OR (95% CI)	P-value
Any anal symptom	135 (73.8)	171 (74.0)	1.01 (0.65-1.58)	0.953
Anal discharge	7 (3.8)	15 (6.5)	1.75 (0.70-4.38)	0.235
Anal Itch	56 (31.7)	79 (34.2)	1.12 (0.74-1.69)	0.591
Anal sores	17 (9.3)	26 (11.4)	1.26 (0.66-2.40)	0.487
Anal lump	22 (12.0)	36 (15.6)	1.35 (0.76-2.39)	0.301
Pain defecating	37 (20.2)	51 (22.1)	1.12 (0.69-1.82)	0.646
Anal bleeding	62 (33.9)	85 (36.8)	1.08 (0.71-1.63)	0.538
Anal tearing	23 (12.6)	36 (15.6)	1.28 (0.72-2.29)	0.399
Feeling "something left after bowel movement"	75 (41.0)	92 (39.8)	0.95 (0.64-1.42)	0.812

Lack of association of self-reported anal symptoms with anal HSIL

Anal symptoms within last month

Self-reported anal symptom	Composite negative n (%)	Composite HSIL n (%)	OR (95% CI)	P-value
Any anal symptom	105 (57.4)	126 (54.6)	0.89 (0.60-1.32)	0.565
Anal discharge	6 (3.3)	10 (4.3)	1.33 (0.48-3.74)	0.583
Anal Itch	39 (21.3)	49 (21.2)	0.99 (0.62-1.60)	0.980
Anal sores	7 (3.8)	12 (5.2)	1.39 (0.54-3.61)	0.498
Anal lump	7 (3.8)	18 (7.8)	2.12 (0.87-5.20)	0.099
Pain defecating	24 (13.1)	29 (12.6)	0.95 (0.53-1.69)	0.865
Anal bleeding	35 (19.1)	42 (18.2)	0.94 (0.57-1.55)	0.806
Anal tearing	10 (5.5)	12 (5.2)	0.95 (0.40-2.25)	0.903
Feeling "something left after bowel movement"	64 (35.0)	69 (29.9)	0.79 (0.52-1.20)	0.270

Adjusted analysis

Papillomavirus Research 2 (2016) 97–105

Contents lists available at ScienceDirect

Papillomavirus Research

journal homepage: www.elsevier.com/locate/pvr

Prevalence and risk factors associated with high-grade anal squamous intraepithelial lesions (HSIL)-AIN2 and HSIL-AIN3 in homosexual men

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Variable		Composite-HSIL versus composite-negative[a] (n=415) n (%)	Adjusted OR (95% CI)	p-Value
HIV status	HIV-negative	128/263 (48.7)	1.00	0.035[1]
	HIV-positive	104/152 (68.4)	1.69(1.03–2.76)	
Lifetime receptive partners with a condom	0–1	5/24 (20.8)	1.00	0.032
	2–5	19/52 (36.5)	1.79 (0.66–4.87)	
	6–10	25/42 (59.5)	2.24 (0.82–6.11)	
	>10	176/286 (61.5)	2.51 (1.03–6.08)	
Lifetime receptive partners without a condom	0–1	18/63 (28.6)	1.00	0.001
	2–5	52/105 (49.5)	2.24 (1.13–4.42)	
	6–10	56/85 (65.9)	3.92 (1.90–8.12)	
	>10	106/162 (65.4)	3.26 (1.62–6.56)	

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Adjusted analysis: HSIL and Lump

Self-reported anal symptom	OR (95% CI)	P-value
Anal lump last month	2.05 (0.81-5.14)	0.128
Number of receptive intercourse partners with condom	1.39 (1.07-1.80)	0.015
Number of receptive intercourse partners without condom	1.26 (0.99-1.59)	0.057
HIV status	1.62 (1.00-2.61)	0.050

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HSIL and lump

- HSIL lesions reported as more likely to be flat

Self-reported history of anal warts in the last 12 months	Composite Negative	Composite HSIL
No	180	197
Yes	1	28

HSIL and warts

- History of anal warts associated with anal lump in the month prior to HRA (OR 3.68, p=0.02)

and

- History of warts associated with composite HSIL (OR 25.6, p<0.001)
- Warts and HSIL share same causal pathway: HPV
- 70% of men had more than one HPV type detected

Conclusion

- Anal symptoms commonly reported by SPANC participants at baseline – including bleeding in over 1/3
- Intra-anal HSIL was not significantly associated with any symptom on univariate analysis
- Trend towards association of anal lump in last month with HSIL at baseline likely explained by history of anal warts
- Findings suggest anal symptoms are not a clinically useful marker of the presence of anal HSIL among GBM

Acknowledgements

Kirby Institute, UNSW
Andrew Grulich
Mary Poynten
Jeff Jin
Brian Acraman
Garrett Prestage
Leonie Crampton
Patrick McGrath
Robert Mellor
Piero Pezzopane
Kathy Petoumenos
Matthew Law

Western Sydney Sexual Health
Richard Hillman

Community representatives
Lance Feeney
Russ Gluyas

St Vincent's Hospital, Sydney
Carmella Law
Daniel Seeds
Marko Garcia
Andrew Carr

RPA Sexual Health
David Templeton

Douglass Hanly Moir Pathology
Annabelle Farnsworth
Jennifer Roberts
Clare Biro
Adele Richards
Julia Thurloe
Deborah Ekman
Ross McDonald
Marjorie Adams

University of Sydney
Kirsten McCaffery
Kirsten Howard
Patrick Kelly

Melbourne Sexual Health Centre
Kit Fairley

Royal Women's Hospital, Melbourne
Suzanne Garland
Sepehr Tabrizi
Alyssa Cornall
Samuel Philips
Dorothy Machalek

The SPANC team thanks the participants. The SPANC study is funded by a NHMRC program grant (# 568971) and a Cancer Council NSW Strategic Research Partnership Program grant (#13-11). Cytological testing materials are provided by Hologic (Australia) Pty Ltd. The Kirby Institute is affiliated with the Faculty of Medicine, University of New South Wales and funded by the Australian Government of Health and Ageing. The views expressed in this publication do not necessarily represent the position of the Australian Government.

Funded as a Cancer Council NSW Strategic Research Partnership