Anal HPV related conditions in women with high grade cervical disease

Gunathilake MPW, Tahir AB, Bellingham FR, Roberts J, Tabrizi SN, Hillman RJ

Disclosures of interest

- Gunathilake MPW
- Tahir AB
- Bellingham FR
- Tabrizi SN

None

- Roberts J - works for DHM
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Background

- Anal cancer is increasing in incidence
- Early diagnosis is strongly associated with improved survival
- Similarities between anal and cervical cancers:
  - high risk Human papillomaviruses (hr HPV) thought to be the causal agents
  - Persistent high grade squamous intraepithelial lesions (HSIL) = recognized precursors of cancers

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Trends in cervical & anal cancers in Australia

Cervical cancer 1991-2012

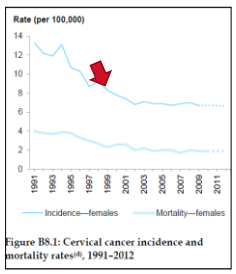
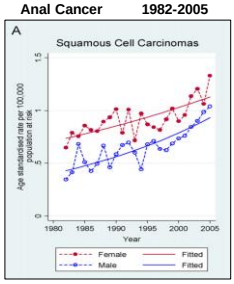


Figure B8.1: Cervical cancer incidence and mortality rates[6], 1991–2012

AIHW Cancer data base

Anal Cancer 1982-2005



Jin F *et al.* Vaccine 2011;29(12):2322-7

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Anal cancer in high risk groups

Key population	Incidence rates per 100 000	Reference
General population	1.0 -2.0	Jin 2011
HIV positive MSM	137	Silverberg 2012
HIV negative MSM	37	Palefsky 2009
Transplant recipients	15	Grulich 2007
†**Women with cervical, vaginal or vulvar CIN2+**	**13.6**	Saleem 2011

† Elevated anal cancer risk continues, despite successful treatment of initial lesion

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Anal HPV related changes women

Population	AIN	Anal HPV DNA	Sample size	Reference
Healthy women		27%	1378	Hernadez et al. 2005
HIV+ women	6%	-	104	Gingelmaier et al. 2010
CIN/VIN/VAIN	12%	-	205	Santoso et al. 2010
Lower genital HPV related disease	-	45%	235	Valari et al. 2011
Cervical dysplasia	17.6%	32.5%	196	Lammi et al. 2014

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Objectives of the study

Objectives: To identify anal cytological changes and HPV genotypes

Study population: women with a history of high grade cervical Pap abnormalities

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Study design

Prospective study
Start date: 16/10/2013

Site: Colposcopy clinic, Westmead Hospital, Sydney
Study participants: Women with a history of high grade cervical Pap abnormalities

Anal and cervical smears obtained and tested for cytology + HPV genotypes

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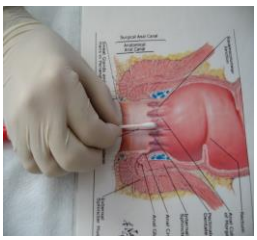
Anal cytology sampling



- blind sampling of anal canal
- moistened Dacron swabs

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Testing methods

Anal & cervical specimens

- Liquid based cytology (Thinprep™)

HPV testing

- MagNA pure 96 system used for HPV DNA extraction (Roche Molecular system)
- HPV Linear Array test for HPV genotyping (Roche Diagnostics)

Ong et al. PLOS one July 2014

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Results

Total number of eligible women

102

Total number consented:

72 (70.5%)

HSIL – CERVIX
72 (100%)
Additional VAIN
02 (2.77%)

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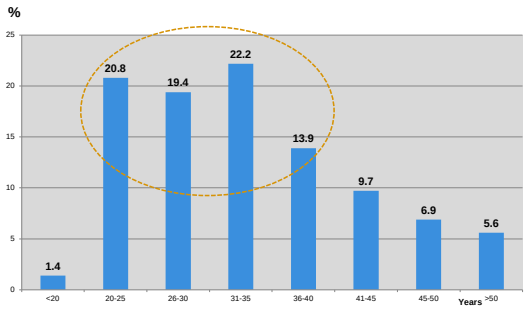
Demography

Age	**Mean 34.1 years** **Median 33.5 years (SD 10.3 years)** **Range 18 - 76 years**

Age distribution of women



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Behavioural characteristics

Age at first sex	**< 16 years** 18 (25%)	**16-20 years** 38(52.8%)	**21-25 years** 11(15.2%)
Lifetime partners	**One** 9 (12.5%)	**2-5** 31(52.1%)	**6-10** 16(22.2%)
History of penetrative anal sex	**Yes** 28 (38.9%)	**No** 42 (58.3%)	**Not answered** 02(2.8%)
History of digital stimulation of anus	**Yes** 17 (23.6%)	**No** 52(72.2%)	**Not answered** 03(4.2%)

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Other characteristics

Smoking	**Current** 27(37.5%)	**Ex smoker** 15(20.8%)	**Never** 30(41.7%)
HIV status	**Positive** 02(2.8%)	**Negative** 59(81.9%)	**Not known** 11(15.3%)
History of STIs	**Yes** 18(25%)	**No** 53(73.6%)	**Not answered** 1(1.3%)

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Concurrent **cervical** cytology

Cervical cytology	Number (%)
Technically unsatisfactory	5 (6.9%)
Negative	44 (61.1%)
LSIL/PLSIL	**10 (13.9%)**
HSIL/PHSIL	**13 (18.1)**

All women previously had cervical HSIL

Anal cytology

Anal cytology	Number (%)	
Technically unsatisfactory	25 (34.7%)	
Negative	43 (58.3%)	
PLSIL	03 (4.2%)	← 5.6% non-negative anal Paps
LSIL	01 (1.4%)	←

All women previously had cervical HSIL

HPV genotypes in anal/cervical samples

Genotypes	Anal	Cervical
Any HR HPV	12 (18.7%)	25 (43.8%)
16	03 (4.68%)	07 (10.9%)
18	0	02(3.1%)
31	02 (3.12%)	02 (3.1%)
Other	51,56,58,59,73	33,35,39,45,52,59,73
≥ 2 genotypes	11(91%)	12 (48%)

- Concurrent HPV infections in 10 (15.6%) sample pairs
- High risk HPV in 02 technically unsatisfactory anal samples

Characteristics of ♀ with abnormal anal Paps

Age	Anal cytology	Anal HPV	Cervical cytology	Cervical HPV
33	Possible LSIL	N/A	HSIL	N/A
59	Possible LSIL	56, 62	LSIL	62
32	Possible LSIL	16,51,58	Normal	16
30	LSIL	6,61	Normal	16

50% of patients with anal PLSIL had contemporary normal cervical smears

Limitations

- Small sample size
- Selected population/ no control samples
- High unsatisfactory rate of anal Pap smears
- Difficulty in obtaining anal Pap smears
  - tight anal sphincters - painful
  - anxiety related to abnormal cervical & anal Paps

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Summary

- Women with HPV related high grade cervical (+ vulval & vaginal disease) are at increased risk of anal cancer
- Increased risk continues, despite successful Rx of cervical lesions
- Unexpected behavioural characteristics - never previously studied population
- Anal Paps = new procedure, with training needed to reduce unsatisfactory rates

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Summary

- 4/72 (5.6%) of all women had non-negative anal Paps
- 4/47 (8.5%) with technically satisfactory anal Paps had non negative results
- 18.7% of all women had anal HR HPV DNA

⇒ potential role for HR HPV DNA testing in anal cancer risk stratification protocols

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Summary

Further work needed to establish:

- refine sampling techniques
- investigate behavioural characteristics further
- determine whether women have persisting infection
- optimum future management protocols

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Thank you