

Front-to-back wiping and dabbing behaviours post-toilet are significantly associated with anal neoplasia & HR-HPV carriage in women with a previous HPV-mediated gynaecological neoplasia

Steve Simpson, Jr.¹, Penny Blomfield², Alyssa Cornall^{3,4}, Sepehr Tabrizi^{3,4,5}, Leigh Blizzard¹, Richard Turner^{1,6}

¹ Menzies Institute for Medical Research, University of Tasmania, Hobart, Australia; ² Gynaecologic Oncology, Royal Hobart Hospital, Hobart, Australia; ³ Regional HPV Labnet Reference Laboratory, Department of Microbiology and Infectious Diseases, The Royal Women's Hospital, Parkville, Australia; ⁴ Murdoch Childrens Research Institute, Parkville, Australia; ⁵ Department of Obstetrics and Gynaecology, University of Melbourne, Parkville, Australia; ⁶ School of Medicine, University of Tasmania, Hobart, Australia

Introduction

- Anal cancer is a human papillomavirus (HPV)-mediated neoplasia of the squamous epithelium of the anal canal and anal margin(1), aetiologically and histologically quite similar to the more common cervical cancer.
- One of the peculiarities of anal cancer epidemiology, however, is its much higher frequency among women, who comprise nearly two-thirds of cases(2, 3).
- Within women, a key risk group for anal cancer is women with a previous HPV-mediated gynaecological neoplasia, though the mode by which HR-HPV transfers to the anus has been unclear.

Aims

Following our previous case-series study(4), we sought to evaluate the prevalence and determinants of HPV-mediated anal neoplasia by cytology and post-high-resolution anoscopy histology, and anal carriage of HR-HPV, in a cohort of women with a history of an HPV-mediated gynaecological neoplasia under follow-up care in Tasmania, Australia.

Methods

Cohort recruitment & data collection

- Women prospectively recruited between May 2012 and December 2014 from two public tertiary referral centres within Tasmania for follow-up care for gynaecological neoplasia, namely the Royal Hobart Hospital servicing southern Tasmania, and the Launceston General Hospital, servicing northern Tasmania.
- Participants asked to complete a questionnaire querying relevant covariates previously identified as being related to anal cancer and HPV carriage
 - In addition, participants were queried about their wiping practices after urination and/or defecation, specifically whether they wiped in a front-to-back direction, a back-to-front direction, or if they dabbed.
- Medical records were reviewed by study nurses for relevant clinical information regarding the participant's gynaecological primary event, as well as participants' utilisation of barrier contraception.

Biological measures

- At colposcopy examination, a sample from the anus was taken by a Dacron swab, inserted into the anus and withdrawn with rotation, and swabbed up to 5cm from the anal verge. Swab then immersed in Hologic ThinPrep solution and sent to RHH Pathology. There, a 2mL aliquot was removed and stored at -80°C until HPV typing, the remainder used for liquid cytology.
- Women with abnormal anal cytology invited for high-resolution anoscopy (HRA), with biopsies taken as appropriate. Biopsy histology evaluated at RHH Pathology
- HPV typing was done at the Royal Women's Hospital after the conclusion of recruitment using Roche Cobas and Linear Array assays.

Statistical analysis

- Covariates of abnormal anal cytology, abnormal post-HRA histology, and carriage of HR-HPV types assessed by log-binomial regression; covariates of grade assessed by log-multinomial regression(5).

Results

Cohort characteristics

- 163 women (126 in Hobart, 37 in Launceston) evaluated for anal cytological, histological & HPV outcomes.
 - Majority of cervical primary (89.7%), and mostly high-grade/SCC primary (97.0%)
- Majority (60.1%) of women sampled had normal anal cytology, while 12% had possible or definite low-grade neoplasia, 17% had possible high-grade and 12% had definite high-grade neoplasia by cytology (Table 1).
- Of the 50 women with anoscopies and biopsies, 18 had normal anoscopy, 19 had low-grade histology and 13 had high-grade histology.
- HR-HPV testing of anal samples found 49.1% to have no anal HR-HPV carriage, while of those with HR-HPV detected, a surprisingly large proportion were non-16 or 18 types (19.6%), particularly type 51, found in 11.7% of samples tested.

Table 1. Distribution of anal cytology, histology and HR-HPV carriage

	n/N (%)		n/N (%)
Anal cytology result		Anal HPV typing result (LA)	
Normal	98/163 (60.1)	HPV negative	80/120 (66.7)
Possible/definite LSIL	19/163 (11.7)	16 only	4/120 (3.3)
Possible/definite HSIL	46/163 (28.2)	16 & other HR	3/120 (2.5)
Anal histology result		18 & other HR	3/120 (2.5)
Normal on cytology, no anoscopy	98/163 (60.1)	16, 18 & other HR	1/120 (0.8)
Normal histology	18/163 (11.0)	51 only	2/120 (1.7)
LGAIN	19/163 (11.7)	51 & other HR	9/120 (7.5)
HGAIN	13/163 (8.0)	16, 51 & other HR	2/120 (1.7)
Anoscopy not done or insufficient	15/163 (9.2)	16, 18, 51 & other HR	1/120 (0.8)
Anal HPV typing result (Cobas)		Other HR	15/120 (12.5)
HPV negative	75/123 (61.0)		
16/18 only	8/123 (6.5)		
Other HR types only	32/123 (26.0)		
16/18 and other HR	8/123 (6.5)		

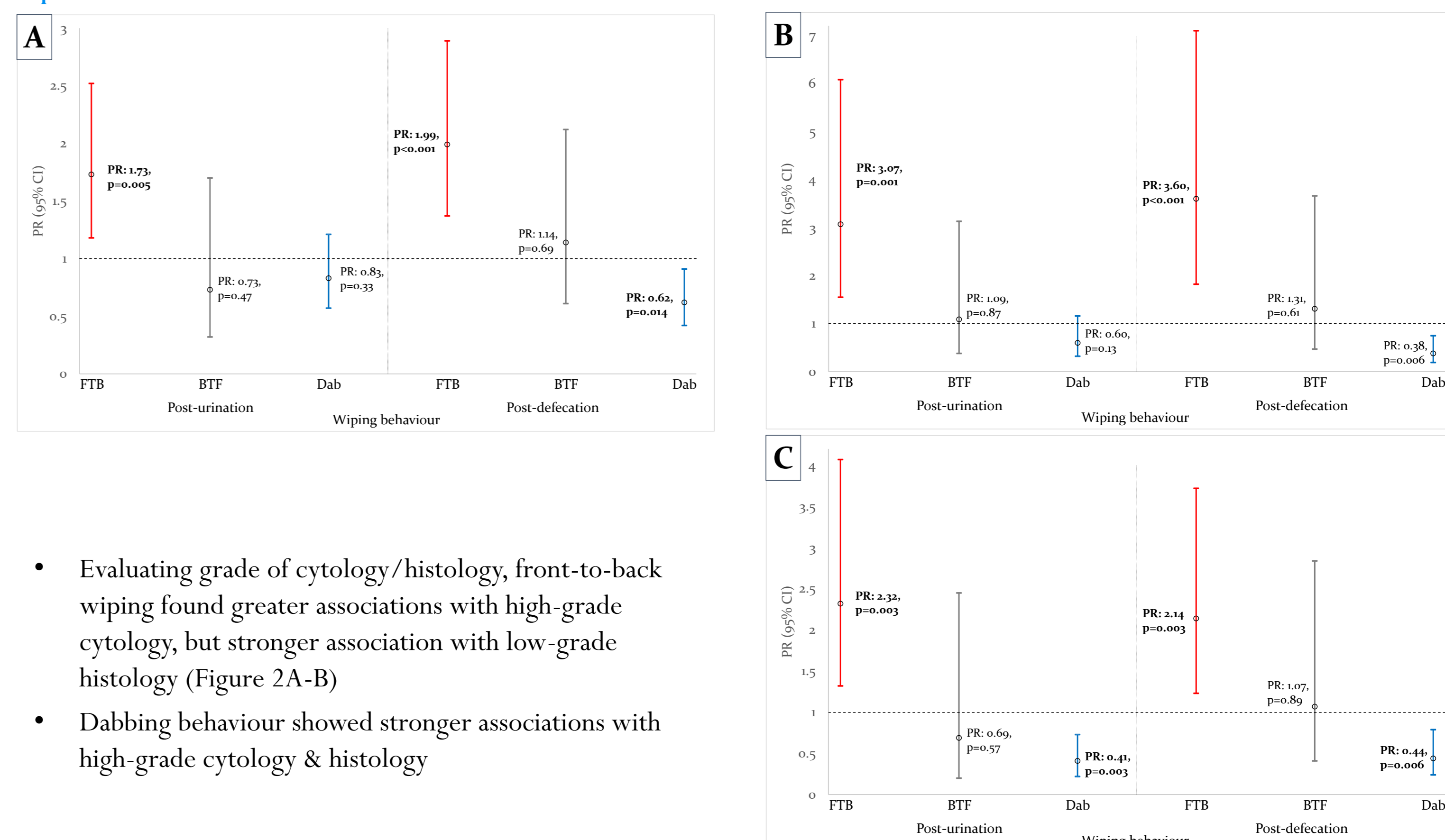
Previously demonstrated anal neoplasia/HR HPV covariates

- A number of previously demonstrated factors were also found here to be associated with anal outcomes, including older age (>42) and having ever been pregnant, as well as GI/anal conditions like haemorrhoids, anal fissure, inflammatory bowel disease and anogenital skin condition.
- Tobacco smoke exposure, active and passive, were also positively associated.
- Some evidence of an overall exposure to wood-burning smoke with all anal outcomes, as found previously(6), but restriction to smoke exposure in the home showed an attenuation in magnitude and significance.

Post-toilet wiping & anal outcomes

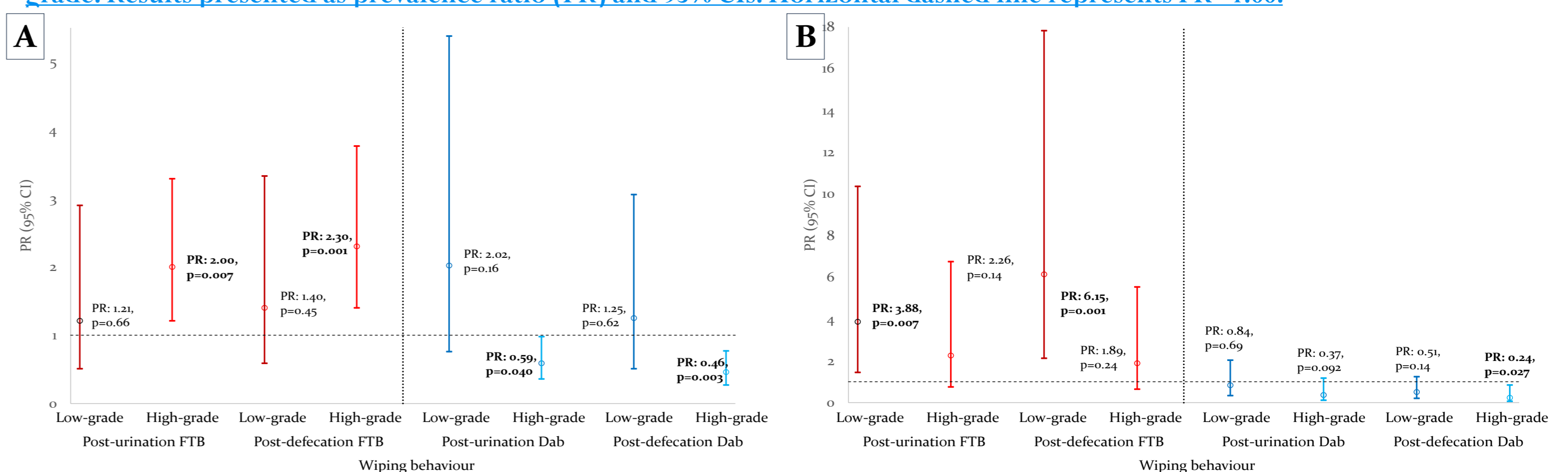
- Front-to-back wiping associated with significantly increased prevalence of all anal outcomes, while dabbing associated with decreased prevalence (Figure 1A-C), particularly post-defecation.
- Back-to-front wiping showed no association with any outcome.

Figure 1. Front-to-back (FTB), back-to-front (BTF), and dabbing (Dab) behaviours associations with A) anal cytology, B) anal histology & C) anal HR HPV carriage. Results presented as prevalence ratio (PR) and 95% CIs. Horizontal dashed line represents PR=1.00.



- Evaluating grade of cytology/histology, front-to-back wiping found greater associations with high-grade cytology, but stronger association with low-grade histology (Figure 2A-B)
- Dabbing behaviour showed stronger associations with high-grade cytology & histology

Figure 2. Front-to-back (FTB) and dabbing (Dab) behaviours associations with A) anal cytology grade and B) anal histology grade. Results presented as prevalence ratio (PR) and 95% CIs. Horizontal dashed line represents PR=1.00.



Conclusions

- Prevalence of anal cytological/histological abnormality and HR-HPV carriage similar to that found in similar populations^{2,3}
- We have demonstrated for the first time a potent association of post-toilet wiping with the prevalence of anal cytological and histological abnormality, and HR-HPV carriage, front-to-back wiping being associated with significantly increased prevalence, while dabbing post-toilet was associated with decreased prevalence, while back-to-front wiping was not associated with any outcome.
- There is appreciable biological plausibility to this pathway of HR-HPV autoinoculation to the anus, given the well-recognised potential for autoinoculation of faecal flora by BTF wiping resulting in urinary tract infections in women(7).
- Internal consistency of the associations found here, including consistency between separate, albeit related, measures like cytological and histological abnormality and HR-HPV carriage, as well as the previously discussed biological plausibility, give some confidence to the observed associations.
- HPV vaccine makes application of these findings somewhat limited in the long-term, but the large cohort of women who were sexually active prior to vaccine are yet at risk for anal cancer and other HR-HPV-associated neoplasia.

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