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Recurrent Post Coital Bleeding: Should colposcopy still be mandatory?

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Contribution to Authorship

JT, CDW, YJ conceived and developed the protocol to perform this retrospective analysis.

JT, MO, JB were involved in collecting, retrieving and analysing the data.

All authors were involved in drafting and reviewing of the manuscript, and approving the final 'to be published' version.

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screening reference laboratory.

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Materials and Methods

A retrospective cohort analysis of women with PCB referred to the Royal Women's Hospital (RWH) colposcopy clinic was conducted.

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... follow-up were prospectively recorded until the date of their last visit at the RWH colposcopy clinic ...

Screening record retrieval from the VCCR and review ...

..... has been endorsed by the RWH Human Research Ethics Committee

Table 1. Post Coital Bleeding(PCB) 2000-2016 Cohort(1), n=1846 and Post Coital Bleeding(PCB) 2018-2019 Cohort(2), n=215, Royal Women's Hospital, Victoria.

Table 2 Referral cytology or co-test correlated with repeat cytology at colposcopy, Post Coital Bleeding Cohort(1) 2000-2016 (n=1846) and Cohort(2) 2018-2019, (n=215) Royal Women's Hospital, Victoria.

Table 3 Performance of Colposcopy and Repeat Cytology at Colposcopy for CIN2+ (histological high grade squamous intraepithelial neoplasia (CIN2/3), adenocarcinoma in situ (AIS) and cancers), Post Coital Bleeding 2000-2016 Cohort(1), n=1846, Royal Women's Hospital, Victoria.

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Table ST1 Post Coital Bleeding 2000-2016 Cohort(1). Royal Women's Hospital, Victoria. Cytology at colposcopy correlated with histopathology

Table ST2 Post Coital Bleeding 2000-2016 Cohort(1). Royal Women's Hospital, Victoria. Negative referral cytology group: cytology at colposcopy correlated with histopathology

Table ST3 Post Coital Bleeding 2000-2016 Cohort(1). Royal Women's Hospital, Victoria. Colposcopy predictions correlated with histopathology

Table ST4 Post Coital Bleeding 2000-2016 Cohort(1). Royal Women's Hospital, Victoria. Negative referral cytology group: colposcopy predictions correlated with histopathology

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ABSTRACT

Background: Colposcopy has been recommended for all women with recurrent post coital bleeding (PCB) even if their cervical cytology or co-test (involving oncogenic human papillomavirus [HPV] DNA testing and cytology) are negative.

Aims: To determine the risk of cervical cancer and its precursors amongst women with recurrent PCB with negative cytology or co-test.

Materials and Methods: A retrospective analysis of two cohorts of women with PCB referred to a tertiary colposcopy clinic. Cohort(1) (n=1,846) between 1st Jan 2000 and 31st Dec 2016 (cytology based screening) and Cohort(2) (n=215) from 1st Jan 2018 to 31st Dec 2019 after introduction of primary HPV screening.

Results: In 1,217 (65.9%) of women in Cohort(1) referred with negative cytology, there was 1 cancer (0.08%) and 22 high grade squamous intraepithelial lesions (HSIL(CIN2/3)) on

histopathology. In Cohort(2), there was no cancer nor HSIL in 83 women with negative co-tests (negative for oncogenic HPV and cytology). False negative cytology after a negative referral cytology or co-test was low with two percent of repeat cytology at initial colposcopy showing possible high grade squamous intraepithelial lesions (pHSIL) or worse.

Conclusions: Women presenting with PCB and negative cytology alone have a low risk of cancer and could have HPV testing before being triaged to colposcopy. We showed that with the assurance of a negative co-test and the low likelihood of false negative cytology, these women could avoid colposcopy unless cervical cancer is clinically suspected. There is a need for a larger cohort study to substantiate our findings with more precision.

Introduction

Post coital bleeding (PCB) is bleeding after sexual intercourse. Recurrent or persistent PCB raises concern in women and clinicians alike, as it can be a warning symptom of serious disease including cervical cancer. Reported rates of invasive cervical carcinoma diagnosed in women with PCB with no or normal referral cytology ranged from nil to 3.6%.^{1,2,3} However, PCB is a relatively common symptom, occurring in 0.7 to 9.0% of women⁴ and is mainly caused by benign pathology, such as ectropion, cervicitis and polyps.⁵ It is also the most common presenting symptom of genital Chlamydia Trachomatis infection.⁶ In Australia, there is heightened awareness of the association between PCB and cervical cancer due to the O'Shea versus Sullivan case (1994), in which a young symptomatic woman died after delay in diagnosis of cervical cancer. On retrospective review of that case, it was found that the original cytology was a false negative, with the presence of precancerous cervical intraepithelial neoplasia 3 (CIN 3) and possibly also micro-invasive cancer cells.⁷ Following this case, guidelines were introduced stating that colposcopy should be performed in symptomatic women even if cytology is negative. Guidelines from the Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG), introduced in 1995, recommend that cervical cancer should be excluded in all women with persistent abnormal vaginal bleeding. A single episode of PCB in a woman who had both a normal smear and cervical appearance did not warrant immediate referral, but recurrent or persistent symptoms

mandated colposcopic examination.⁸ In its latest statement in March 2018, RANZCOG recommended gynaecological referral for recurrent or persistent PCB, but colposcopy was no longer mentioned.⁹ The Australian guidelines in the new National Cervical Screening Program (NCSP) recommend that women with PCB should have a co-test involving oncogenic human papillomavirus [HPV] DNA testing and cytology. However, if PCB recurs or persists despite a negative co-test (negative for oncogenic HPV and negative cytology), women should be referred to a gynaecologist for appropriate assessment, including colposcopy, to exclude genital tract malignancy.¹⁰

The aims of our retrospective study are to determine the following outcomes amongst women referred with post coital bleeding:

- i. The incidence of cervical cancer and its precursors on histology
- ii. The incidence of abnormal cytology at colposcopy after negative referral cytology
- iii. The incidence of cervical cancer and its precursors on histology with negative co-tests in the new cervical screening program.

Materials and Methods

A retrospective cohort analysis of women with PCB referred to the Royal Women's Hospital (RWH) colposcopy clinic was conducted. Two cohorts were evaluated: Cohort(1) are women who presented between 1st January 2000 and 31st December 2016 during cytology based screening; and Cohort(2) from 1st January 2018 to 31st December 2019 after commencement of a new cervical screening program in Australia, using primary HPV testing with partial genotyping and reflex liquid based cytology (LBC) triage.¹⁰ At their first visit, all attendees were invited to consent to recording of their medical data in the 'On-Display' database, a colposcopy electronic medical record introduced to the hospital in 2000 for clinical care, and also consent to retrieve screening records from the Victorian Cervical Cytology Registry (VCCR). Demographics, clinical history, examination, treatment, and follow-up were prospectively recorded until the date of their last visit at the RWH colposcopy clinic or the 31st December 2019 for those having ongoing care. We did not have an electronic record of the number of episodes nor the duration of the PCB. Screening record retrieval from the VCCR and review of medical records provided missing referral cytology data. Cytological findings were classified according to the Australian Modified Bethesda System 2004¹⁰ and histopathology according to the LAST Standardization.¹¹ One case of ungradable dysplasia was reclassified as high-grade squamous intra-epithelial lesion (HSIL) for the purpose of this study. CIN2+ is used to define a group of histologically proven high-grade disease (HSIL(CIN2/3), adenocarcinoma in situ [AIS] or cervical cancer). We recorded our

histopathology results as the most abnormal result from colposcopic directed biopsies at initial or follow-up colposcopy, or at excisional treatments.

A descriptive analysis of the data was undertaken. Categorical variables were compared using chi-squared (χ^2) with significant P values set at ≤ 0.05 . Statistical analysis was performed using R version 3.61 (The R Project for Statistical Computing).¹² This study meets the National Health and Medical Research Council requirements for quality assurance/audit projects and has been endorsed by the RWH Human Research Ethics Committee (AQA18/45).

Results

Cohort(1)_Cytology-based Screening

Between January 1, 2000 and December 31, 2016, 1,852 women with PCB were referred for colposcopy. Six women referred with histologically-confirmed cervical intraepithelial neoplasia were excluded, thus leaving 1,846 for analysis. Median age was 30 years (range: 16-75), with 420 (22.7%) <25 years of age, 1,334 (72.3%) 25-50 years of age and 92 (5.0%) >50 years of age. PCB accounted for 20.2% of all referrals to the colposcopy clinic and was more common in women 25-50yo (22.7%) than women >50yo (14.9%), (diff 7.8%, 95% CI, 4.6-10.6%, $p < 0.001$) (Table 1).

Referral cytology was recorded for 1,678 (90.9%) women, of which 1,630 (88.3%) were performed within 1 year prior to colposcopy and 48 (2.6%) between 1 and 2 years previously. One thousand two hundred and seventeen women (65.9%) were referred with negative cytology, 417 (22.6%) were abnormal and no referral cytology recorded for 168 (9.1%) women in the two years prior to colposcopy.

The majority of women, 1,296 (70.2%), were seen only once for colposcopy, 279 (15.1%) had treatments which include loop excision or laser ablation of cervix and 271 (14.7%) had further colposcopy reviews, up to 8.2 years after first referral, with a median duration of one year. Most of the women who returned for colposcopy after a year were repeat referrals.

We do not have data on the macroscopic appearances of the cervix from the referring doctors. At our colposcopy, 7 (0.38%) were recorded as frankly invasive in appearance and 589 (31.9%) had benign features (342 cervical ectropion, 93 inflamed cervix, 69 cervical polyp, 43 atrophy, 32 Nabothian cysts and 10 condylomas).

Abnormal histopathology with CIN2+ was found in 6.9% (128/1846) of women comprising 12 cancers (0.65%), 3 AIS (0.16%) and 113 CIN2/3 (6.1%). Cancers were found in 0.5%

(2/420) of women <25yo, 0.6% (8/1334) of women 25-50yo and 2.2% (2/92) of women >50yo. (Table 1)

Negative Referral Cytology in Cohort(1)

Cytology was repeated at colposcopy for 884 (72.6%) of the 1,217 women with negative referral cytology. Abnormal cytology of possible high-grade squamous intraepithelial lesion (pHSIL) or worse was found in 2.2%. (Table 2) There was only one cancer (0.08%) in a woman whose repeat cytology at colposcopy suggested invasion and 22 (1.8%) HSIL(CIN2/3) on histopathology, of whom 73.7% (14/19) had abnormal repeat cytology at colposcopy.

This compares with 22.3% (93/417) of women referred with abnormal cytology who were found to have CIN2+ comprising 10 (2.4%) cancers, 3 (0.72%) AIS and 80 (19.2%) CIN2/3. The women referred with abnormal cytology were more likely than those with negative cytology to have CIN2+ (93/417 (22.3%) vs. 23/1217 (1.9%), (diff 20.4%, 95%CI, 16.5% to 24.7%, $p<0.001$). This is particularly so with women >50yo with abnormal cytology where 25.0% (2/8) were found to have cancer.

With incidence of CIN2+ on histopathology at only 1.9% (23/1217) when the referral cytology was negative, colposcopy sensitivity for CIN2+ was only 21.7% (95%CI, 7.5% to 43.7%) with colposcopic prediction of HSIL or worse. The sensitivity improved to 65.2% (95%CI, 42.7-83.6%) when we use colposcopic prediction threshold of LSIL or worse. (Table 3, Supplementary Tables ST1-4).

Cohort(2)_HPV Screening

Between January 1, 2018 and 31 December, 2019, 3,717 women referred for colposcopy following HPV screening. HPV was positive in 3,517 women referred and 45.0% of these (1,582) were associated with negative cytology. Of these 3,717 women, 215 (5.8%) were referred with PCB, the majority from the 25-50yo age group (70.7%).

Among the 215 PCB referrals, 103 (47.9%) were HPV negative and 38.6% (83/215) were co-test negative (negative for HPV and cytology). Abnormal repeat cytology of pHSIL or worse was found in 2.0% (1/49) at initial colposcopy in women with negative co-test. There was no CIN2+ found on histopathology in the 83 women with a negative co-test. (Table 1)

This compares with 24.1% (27/112) of CIN2+ in women with PCB and positive HPV with any cytology, comprising 3 (2.7%) cancers, 2 (1.8%) AIS and 22 (19.6%) CIN2/3. When positive HPV tests were associated with negative cytology, there was still 16.3% (8/49) with CIN2+, including 1 cancer and 2 AIS. (Table 4)

Discussion

Recurrent post coital bleeding (PCB) constituted 20.2% of all colposcopy referrals in the period 2000-2016 compared with 5.8% in 2018-2019 (diff 14.4%, 95% CI, 13.3-15.5%, $p < 0.001$). This could be explained by the large number (45.0%) of women in 2018-2019 referred with HPV positive/LBC negative cervical screening test that would not have been seen for colposcopy under the previous cytology-based screening program. The majority (~70%) of PCB referrals from the two cohorts were from the 25-50yo group. More CIN2+ was found in the co-test Cohort(2) (13.0%) than cytology-based Cohort(1) (6.9%) (diff 6.1%, 95% CI, 2.0-11.4%, $p < 0.01$). HPV testing has been shown to lead to earlier detection of CIN2 or worse.¹³ There were 15 cancers in total from the two cohorts, with no significant difference in cancer incidence between those younger or older than 50 years old (≤ 50 yo 0.66% (13/1956), > 50 yo 1.90% (2/105), (diff 1.24%, 95% CI -0.22% to 6.02%, $p = 0.14$). Others have shown cervical cancer is found more often in older women with postcoital bleeding (1 in 2,400 aged 45-54 years).⁴ Our data does support a more cautious approach with older women with PCB who have a positive HPV test and abnormal cytology, as among our small sample size of eight women, 2 (25%) were found to have cancer.

There was only one (0.08%) woman with cancer and 22 (1.8%) with HSIL(CIN2/3) in the 1,217 women with negative referral cytology. These incidence rates are consistent with other studies.^{1,14} The one woman with cancer detected had an invasive smear at her repeat cytology at colposcopy. Similarly, in these women with negative referral cytology and found to have HSIL(CIN2/3), of those who had repeat cytology at colposcopy, 73.7% (14/19) was abnormal with possible low grade (pLSIL) or worse. Reported diagnostic false-negative rates for cervical cytology ranged from 15% to 63% in different study settings.¹⁵ However, false negative cytology for possible high grade squamous intraepithelial lesions (pHSIL) or worse was found in only two percent of repeat cytology at initial colposcopy in both our cohorts with negative referral cytology or co-test.

The validity of the recommendation for colposcopy for all women with recurrent PCB, even with normal cytology, has never been critically evaluated in the Australian population. Colposcopy has always been a tool to assess women with abnormal screening results, whether it be cytology or HPV-based screening. However, it is known that colposcopy performs poorly in populations with low disease prevalence; using a test threshold of LSIL colposcopy had a sensitivity of 0.286 for HSIL disease when prevalence of CIN2+ was just 2.2%.¹⁶ Our PCB Cohort(1) had an overall prevalence of CIN2+ on histopathology of 6.9% but of only 1.9% with negative referral cytology. Using a test threshold of LSIL, our

colposcopic sensitivity for CIN2+ was 65.2% in the negative referral cytology group. Our higher sensitivity could be due to taking cervical punch biopsies even when the colposcopy prediction was LSIL. Repeating cytology at colposcopy in our Cohort(1) with negative referral cytology and using test threshold of pLSIL or worse, returned a sensitivity of 75% in identifying women with CIN2+. Thus in countries where HPV testing has not been introduced and colposcopy services are limited, rather than referring every women with recurrent PCB and negative cytology for colposcopy, an alternative approach could be to repeat the cytology, and only refer those 15% of women whose repeat cytology demonstrates pLSIL or worse for colposcopy. This would have led to identification of the one cancer and seventy-four per cent of HSIL(CIN2/3) in our Cohort(1). However, triage with a HPV test and referring to colposcopy only those with a positive HPV result is a better approach in countries with cytology-based screening which have access to HPV testing. The reported risk of cervical cancer after a negative co-test is 14 per 100,000 women over five years.¹⁷ None of the women in our cohort with recurrent PCB and a negative co-test had CIN2+ diagnosed within the time frame of our study.

Now that Australia has implemented primary HPV screening, the low risk of cancer in women with PCB and negative cervical cytology alone is no longer locally relevant. However this already low risk is a benchmark below which the added protection of a negative HPV DNA test, (ie a doubly negative cotest) is so much more re-assuring that women presenting with PCB do not need to be routinely referred on for colposcopy in the absence of any macroscopic features of invasive cervical malignancy.

What we have shown is that with the assurance of a negative co-test and the low likelihood of false negative cytology when associated with negative HPV, forty percent of our women with PCB could avoid having a colposcopy as their co-tests were negative. However, we will need a larger cohort to substantiate our findings with more precision. This should now be possible through the National Cancer Screening Register which now records national colposcopy data, including the symptom of PCB.

Women presenting with recurrent post coital bleeding and negative cytology alone have a low risk of cervical cancer and should have HPV testing before being triaged to colposcopy. Women with negative co-tests do not require colposcopy. However, even if sexual transmitted infections and common benign cervical pathology have been excluded, they will still need referral to a gynaecologist for further assessment if cervical cancer is suspected.

Limitations

Our outcome status (cervical cancer) is only current as at the last colposcopy clinic visit by

the patient or record in the cervical screening registry. We did not link our cohorts with cancer registry data. Nevertheless, we did not have any woman return with cancer within a year of discharge from the colposcopy clinic.

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Table 1. Post Coital Bleeding(PCB) 2000-2016 Cohort(1), n=1846 and Post Coital Bleeding(PCB) 2018-2019 Cohort(2), n=215, Royal Women's Hospital, Victoria.

AgeGroup	2000-2016				AgeGroup	2018-2019			
	<25yo	25-50yo	>50yo	Total		<25yo	25-50yo	>50yo	Total
All referrals to colposcopy clinic	2641 (28.9%)	5869 (64.3%)	616 (6.7%)	9126	All referrals to colposcopy clinic	353 (9.5%)	2383 (64.1%)	981 (26.4%)	3,717
PCB (% of all referrals)	420 (15.9%)	1334 (22.7%)	92 (14.9%)	1846 (20.2%)	PCB (% of all referrals)	50 (14.2%)	152 (6.4%)	13 (1.3%)	215 (5.8%)
Cohort(1) n=1846				Cohort(2) n=215					
PCB2000-2016 (% of age group)	420 (22.8%)	1334 (72.3%)	92 (5.0%)	1846	PCB2018-2019 (% of age group)	50 (23.3%)	152 (70.7%)	13 (6.0%)	215
Histopathology: Cancer	2 (0.5%)	8 (0.6%)	2 (2.2%)	12 (0.65%)	Histopathology: Cancer	0	3 (2.0%)	0	3 (1.4%)
Adenocarcinoma in situ (AIS)	1 (0.2%)	2 (0.1%)	0	3 (0.16%)	Adenocarcinoma in situ (AIS)	1 (2.0%)	1 (0.7%)	0	2 (0.9%)
HSIL(CIN2/3)	37 (8.8%)	76 (5.7%)	0	113 (6.1%)	HSIL(CIN2/3)	4 (8.0%)	18 (11.8%)	1 (7.7%)	23 (10.7%)
Negative referral cytology n=1217				Negative referral co-test n=83					
% of age group	244 (58.1%)	904 (67.8%)	69 (75.0%)	1217 (65.9%)	% of age group	18 (36.0%)	58 (38.2%)	7 (53.8%)	83 (38.6%)
Histopathology: Cancer	0	1 (0.1%)	0	1 (0.08%)	Histopathology: Cancer	0	0	0	0
HSIL(CIN2/3)	6 (2.5%)	16 (1.8%)	0	22 (1.8%)	HSIL(CIN2/3)	0	0	0	0

HSIL: high-grade squamous intraepithelial lesion

Negative referral co-test : Negative HPV and cytology

Table 2 Referral negative cytology (n=884) or co-test (n=49) correlated with repeat cytology at colposcopy, Royal Women's Hospital, Victoria.

	Repeat Cytology at Colposcopy								
	2000 - 2016 Post Coital Bleeding Cohort(1) with Negative Referral Cytology (n=1217)*								
Referral cytology	Malignancy	Atypical endocervical cells	HSIL	pHSIL	LSIL	pLSIL	Negative	Unsatisfactory	Total
Negative	1 (0.11%)	1 (0.11%)	5 (0.57%)	13 (1.5%)	58 (6.6%)	56 (6.3%)	731 (82.7%)	19 (2.1%)	884
	2018 – 2019 Post Coital Bleeding Cohort(2) with Negative co-test (n=83)±								
Co-test Negative (HPV/LBC Negative)	0	0	0	1 (2.0%)	5 (10.2%)	3 (6.1%)	38 (77.6%)	2 (4.1%)	49

*333 women did not have repeat cytology at colposcopy

± 34 women did not have repeat cytology at colposcopy

HSIL: high-grade squamous intraepithelial lesion

pHSIL: possible HSIL (aka ASC-H)

LSIL: low-grade squamous intraepithelial lesion

pLSIL: possible LSIL (aka ASC-US)

Table 3 Performance of Colposcopy and Repeat Cytology at Colposcopy for CIN2+ (histological HSIL(CIN2/3), adenocarcinoma in situ (AIS) and cancers), Post Coital Bleeding 2000-2016 Cohort(1) with Negative Referral Cytology, Royal Women’s Hospital, Victoria.

PCB2000-2016 Cohort(1) with Negative Referral Cytology n=1217				
	Positive Predictive Value	Negative Predictive Value	Sensitivity	Specificity
Colposcopy HSIL or worse	14.7% (95% CI, 6.8% to 28.8%)	98.5% (95% CI, 98.1% to 98.8%)	21.7% (95% CI, 7.5% to 43.7%)	97.5% (95% CI, 96.5% to 98.4%)
Colposcopy LSIL or worse	6.6% (95% CI, 4.9% to 8.9%)	99.2% (95% CI, 98.6% to 99.5%)	65.2% (95% CI, 42.7% to 83.6%)	82.1% (95% CI, 79.8% to 84.3%)
Repeat Cytology (pLSIL or worse) at Colposcopy	11.2% (95% CI, 8.5% to 14.6%)	99.3% (95% CI, 98.6% to 99.7%)	75.0% (95% CI, 50.9% to 91.3%)	85.9% (95% CI, 83.4% to 88.2%)

HSIL: high-grade squamous intraepithelial lesion

LSIL: low-grade squamous intraepithelial lesion

pLSIL: possible LSIL (aka ASC-US)

Table 4 Histopathology outcomes from Post Coital Bleeding 2000-2016 Cohort(1), (n=1846) and Post Coital Bleeding 2018-2019 Cohort(2), (n=215) at Royal Women's Hospital, Victoria.

Cohort(1)	Post coital Bleeding 2000–2016 (n=1846)								
Referral Cytology	Histopathology								
	Cancer	AIS	HSIL (CIN2/3)	LSIL	Negative	Colp_N	NoEpith	No Bx	Total
Malignancy	3(75.0%)	0	1(25.0%)	0	0	0	0	0	4(0.22%)
Glandular atypia	0	2(50.0%)	0	1(25.0%)	0	0	0	1(25.0%)	4(0.22%)
HSIL	5(8.2%)	1(1.6%)	41(66.1%)	7(11.3%)	7(11.3%)	1(1.6%)	0	0	62(3.4%)
pHSIL	0	0	16(31.4%)	15(29.4%)	15(29.4%)	4(7.8%)	0	1(2.0%)	51(2.8%)
LSIL	1(0.5%)	0	18(9.5%)	57(30.2%)	63(33.3%)	39(20.7%)	1(0.53%)	10(5.3%)	189(10.2%)
pLSIL	1(0.9%)	0	4(3.8%)	20(18.7%)	40(37.4%)	34(31.8%)	1(0.93%)	7(6.5%)	107(5.8%)
Negative	1(0.08%)	0	22(1.8%)	97(8.0%)	440(36.1%)	635(52.2%)	9(0.74%)	13(1.1%)	1217(65.9%)
Unsatisfactory	0	0	1(2.3%)	5(11.4%)	19(43.2%)	17(38.6%)	0	2(4.5%)	44(2.4%)
No Cytology	1(0.6%)	0	10(6.0%)	16(9.5%)	55(32.7%)	84(50.0%)	0	2(1.2%)	168(9.1%)
Total	12(0.65%)	3(0.16%)	113(6.1%)	218(11.8%)	639(34.6%)	814(44.1%)	11(0.60%)	36(2.0%)	1846
Cohort(2)	Post coital Bleeding 2018 – 2019 (n=215)								
Referral co-test (HPV/LBC)	Histopathology								
	Cancer	AIS	HSIL (CIN2/3)	LSIL	Negative	Colp_N	NoEpith	No Bx	Total
16_18/cancer	1(100%)	0	0	0	0	0	0	0	1(0.5%)
16_18/pHSILorHSIL	0	0	5(100%)	0	0	0	0	0	5(2.3%)
16_18/pLSILorLSIL	0	0	1(12.5%)	4(50.0%)	1(12.5%)	2(25.0%)	0	0	8(3.7%)
16_18/Negative	1(6.7%)	2(13.3%)	3(20.0%)	4(26.7%)	5(33.3%)	0	0	0	15(7.0%)
Other/pHSILorHSIL	1(7.1%)	0	8(57.1%)	4(28.6%)	1(7.1%)	0	0	0	14(6.5%)
Other/pLSILorLSIL	0	0	3(8.8%)	12(35.3%)	9(26.5%)	8(23.5%)	1(2.9%)	1(2.9%)	34(15.8%)
Other/Negative	0	0	2(5.9%)	3(8.8%)	11(32.4%)	18(52.9%)	0	0	34(15.8%)
Other/Unsatisfactory	0	0	0	0	0	1(100%)	0	0	1(0.5%)
Neg/pHSILorHSIL	0	0	0	0	1(100%)	0	0	0	1(0.5%)
Neg/pLSILorLSIL	0	0	1(5.6%)	2(11.1%)	6(33.3%)	9(50.0%)	0	0	18(8.4%)
Neg/Negative	0	0	0	12(14.5%)	20(24.1%)	49(59.0%)	0	2(2.4%)	83(38.6%)
Neg/Unsatisfactory	0	0	0	0	0	1(100%)	0	0	1(0.5%)
Total	3(1.4%)	2(0.9%)	23(10.7%)	41(19.1%)	54(25.1%)	88(40.9%)	1(0.5%)	3(1.4%)	215

AIS: adenocarcinoma in situ; Glandular atypia includes AIS, possible high-grade glandular lesion and atypical endocervical cells of undetermined significance; HSIL: high-grade squamous intraepithelial lesion [CIN2/3]; pHSIL: possible HSIL; LSIL: low-grade squamous intraepithelial lesion; pLSIL: possible LSIL; Colp_N: Normal colposcopy; NoEpith: Epithelium insufficient for assessment; No Bx: No biopsy taken with abnormal colposcopy.

HPV16_18: HPV16&/or18 +/- HPVother

HPVother: one or more of 12 non16/18 oncogenic HPV types

HPVnegative: negative HPV