Cervical cancer screening in women with HIV: an audit of clinical care

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Objectives: Women with HIV (WHV) have an increased prevalence of cervical cancer and are recommended three yearly cervical cancer screening. This is compared with five yearly screening their counterparts. We aimed to describe cervical cancer screening practices for WHV receiving HIV care at a large tertiary hospital.

Methods: We performed a retrospective audit on all women who were in HIV care up until January 2023 at the Alfred Hospital, a tertiary hospital in Melbourne, Australia, specializing in HIV care. Cervical cancer screening results for Medicare eligible people are recorded in The National Cervical Cancer Screening Register (NCCSR) and these were extracted for women in care. Screening was categorized as up-to-date and consistent with national screening guidelines or overdue.

Results: We identified 156 WHV in care of which 115 were included in the analysis. Of these, 57 (49.6%) had cervical screening on time and consistent with national guidelines, including 49 (86%) who had a normal last result and 8 (14%) with an abnormal last result. Half the women, 58 (50.4%) were overdue screening. Of those overdue, 52 (89.7%) were more than 6 months and 45 (76.3%) were more than 12 months overdue. Among the women overdue, 47 (81%) had a normal last result and 7 (12.1%) an abnormal last result.

Conclusion: We found that over half of the women included were overdue for their cervical screening test, with the vast majority being overdue by more than twelve months. Improved access to cervical cancer screening is needed in this population to achieve national guidelines targets.

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Introduction

Cervical cancer is the 14th most common cancer among women in Australia with 942 new cases diagnosed in 2022 [1]. Squamous cell carcinoma constitutes the predominant form, representing 70% of cases. In contrast, adenocarcinoma is less prevalent, comprising 25%. The average age of diagnosis in Australia is 50 years of age, with highest incidence of cervical cancer being in those aged 60–69 years [2,3].

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Table 1. Australian management recommendations based on cervical screening result in the general population.

HPV/Liquid-based cytology testing report	Recommended management
HPV not detected	5 yearly routine HPV screening
HPV 16/18 detected	Refer colposcopy Reflex LBC performed automatically (clinical collected specimens) or LBC at colposcopy (self-collected specimens)
Oncogenic HPV (not 16 or 18) detected	Reflex LBC performed automatically If HSIL, Possible HSIL or any glandular abnormality; refer colposcopy. If LSIL or negative LBC, repeat HPV test 12 months *Grade C Evidence*
Oncogenic HPV detected at repeat test in 12 months	Refer colposcopy if HSIL, possible HSIL or any glandular abnormality > 50 years Women who identify as ATSI Women overdue for screening by at least 2 years All women with self-collected samples If LSIL or negative LBC repeat CST in 12
Oncogenic HPV positive at repeat test at 24 months Unsatisfactory HPV test	If any HPV refer colposcopy A repeat test should be taken in 6–12 weeks

CST, cervical self-test; LBC, liquid-based cytology.

High-risk types of human papillomavirus (HPV), a sexually transmitted infection, are responsible for over 90% of cervical cancer cases [2]. HPV infection in the general population is acquired in 60% of sexually active adults within three years of sexual debut [4]. The lifetime risk of infection is estimated to be 85% in adults, however most people self-clear the infection within 12–24 months [5,6]. HPV infection may manifest in low or high-grade intraepithelial neoplasia (LSIL, HSIL), the latter being associated with the greatest risk of cancer progression. Although certain oncogenic subtypes, including 16 and 18 are responsible for the majority of HPV-related cancer, there appears to be a shift in the prevalence of other HPV oncogenic types (not 16/18) among women with HIV with high-grade cervical lesions [7]. Cervical cancer is the most frequently detected cancer in women with HIV (WHV) globally and is an AIDS-defining illness [8]. Compared to their counterparts, WHV are six times more likely to develop cervical cancer in Australia [1], and have a higher prevalence of oncogenic HPV among women without cytological abnormalities [7,8]. Shared behavioral risk factors for HIV and HPV infections may explain these observed differences. It is recommended that WHV in Australia are screened three-yearly between the ages of 25–74 years, in keeping with the Australian National Cervical Cancer Screening program guidelines' recommendation for immunocompromised women [9,10]. This is in contrast to five-yearly screening recommended in the Australian general population [11]. The Cervical Screening Test detects HPV DNA, and has been used for screening since 2017, and can delineate if HPV types 16/18 are present. In the circumstance of a positive HPV DNA result, liquid-based cytology should then be performed, either reflexively on clinician-collected, or at colposcopy for self-collected specimens. Follow-up with colposcopy is recommended if oncogenic HPV (type 16/18) is detected or high grade squamous intraepithelial lesion is identified on cytology even if nontype 16/18 HPV DNA was detected (Table 1) [10,11]. It is important to note that worldwide and within some jurisdictions, practice differs for cervical screening. For example, the US guidelines published by the IDSA recommend liquid base cytology as the preferred screening method for women aged 21–29 years, with yearly screening for three consecutive years and three yearly thereafter [12]. Given the increased prevalence of cervical cancer in WHV, the effectiveness of screening to prevent cervical cancer, we sought to describe results of cervical cancer screening in WHV and see if they are consistent with screening guidelines at the state-wide HIV service of a large tertiary hospital in Melbourne, Australia.

Materials and methods

Patient cohort

We performed a retrospective analysis of all adult WHV in care up until January 2023 at the Alfred Hospital, which is the state-wide HIV service for Victoria. Until self-collection testing became available at this facility in mid-2023, this service was unable to perform cervical cancer screening on site with clinic patients required to seek screening with their general practitioner. For this study, we accessed a HIV database which includes all patients with HIV linked into care, to identify a population of women eligible for cervical cancer screening. We included female patients (sex-assigned at birth), aged 25–74 years by the end of the calendar years 2018–2022, who were actively linked into care at the Alfred Hospital. Patients were determined "active" if they attended a minimum of two clinic appointments at the Alfred between January 2018 and December 2022, with at least

one appointment in the most recent 12 months. We excluded transgender women, women who had undergone total hysterectomies, and those who had died. We then confirmed the list of patients under the care of each treating clinician and excluded any patients who had transferred care elsewhere or been lost to follow-up.

Cervical cancer screening results

Results from screening tests were extracted from The National Cervical Cancer Screening Register (NCCSR), either by the treating clinicians or one of the researchers after permission from the clinician. The register is a national electronic register which collates cervical cancer screening data for Australian residents who are Medicare-eligible and have a Medicare card [13]. Results were not able to be obtained from women who were Medicare ineligible, or patients who could not be found in the NCCSR. The NCCSR provides recommendations for the screening interval based on the collecting clinician's clinical notes provided. If medical conditions including HIV or immunocompromise are not provided, the recommendation will default to the routine screening interval for nonimmunocompromised populations.

Data collected

For the included patients, the following data were collected up until October 2023: demographics, including age and sex, cervical cancer screening, including last screening test and result, and recommended date of next screen. The results of cervical cancer screening were obtained in a summary format from the NCCSR. These cervical screening results data were added to the patient's electronic medical record and reviewed at the patient's next clinic appointment. The range of possible results that can be obtained are HPV not detected, oncogenic HPV detected (not 16/18), and oncogenic HPV detected (16/18).

In some circumstances, women also completed a cytological assessment with liquid-based cytology (LBC), including samples taken during colposcopy. Reporting occurred according to the Australian modified Bethesda System [14], the range of results included normal, possible low-grade squamous intraepithelial lesion (pLSIL), low-grade intraepithelial lesion (LSIL), possible high-grade squamous lesion (pHSIL), high-grade intraepithelial lesion (HSIL), and squamous cell carcinoma.

Finally, some cervical histopathology results may have been available if tissue biopsies were performed. LSIL or HSIL identified lesions may be further categorized into intraepithelial neoplasia subcategories (CIN 1–3), referring to preinvasive mucosal lesions (CIN 1) and early invasive lesions (CIN 3). Each individual had a single outcome, and any follow-up colposcopy or histopathology results were treated as confirmatory data.

Results were described as consistent or inconsistent with recommendations for cervical cancer screening in WHV [10]. Inconsistent screening could relate to screening that was not performed on time, or not performed at all and the proportion of those with normal screening in the on-time versus overdue groups were compared by chi-square test (Stata, College Station, USA). The study was approved by Alfred Hospital Ethics Committee, Melbourne, Australia (Project 356/23).

Results

Demographics

We identified 156 women were in care between January 2018 and January 2023 at the Alfred Hospital (Fig. 1). Of these 156 patients, 30 were excluded from the study analysis as they were: receiving care elsewhere ($n = 20$), prior hysterectomy ($n = 5$), transgender women ($n = 4$), and or deceased patients ($n = 1$). Of the remaining 126 women, 11 did not have access to Medicare, resulting in 115 WHV included in the study analysis.

Screening outcomes

Of the 115 women, 57 (49.6%) had cervical screening on time and consistent with national guidelines. Among the 57 women with on-time screening, eight (14%) had an abnormal last result: four women with oncogenic HPV (non 16/18), two with oncogenic HPV (16/18) detected, and two with LSIL and HPV detected. The final two women had LSIL or a low-risk lesion where HPV was not detected. The remaining 49 (86%) had on-time screening and a normal last result.

Of the 115 women, 58 (50.4%) were overdue for cervical screening test and 16 (27.1%) were in the age group of highest cervical cancer incidence (60–69 years). Of the 58 women overdue, the majority 52 (89.7%) were more than 6 months overdue and 45 (77.6%) were more than 12 months overdue. Of the 58 women overdue, 47 (81.0%) had a normal result on their most recent screen, four (6.9%) had no prior screening result on the registry, and seven (12.1%) had an abnormal result on their most recent screen ($P = 0.9$ comparing abnormal results in on-time versus overdue groups). Of the seven abnormal results: one woman had HSIL with CIN 3 lesion on biopsy, two had oncogenic HPV (non 16/18), one had oncogenic HPV (16/18), and three had LSIL or had an abnormal colposcopy, but normal cytology/histopathology and negative HPV.

In addition, 68 (59.1%) women were not identified as immunosuppressed or high risk in the register and therefore were recommended repeat screening in 5 years. Only two (1.7%) results were from self-collected samples consistent with this method of screening not being widely available over the time of the study.

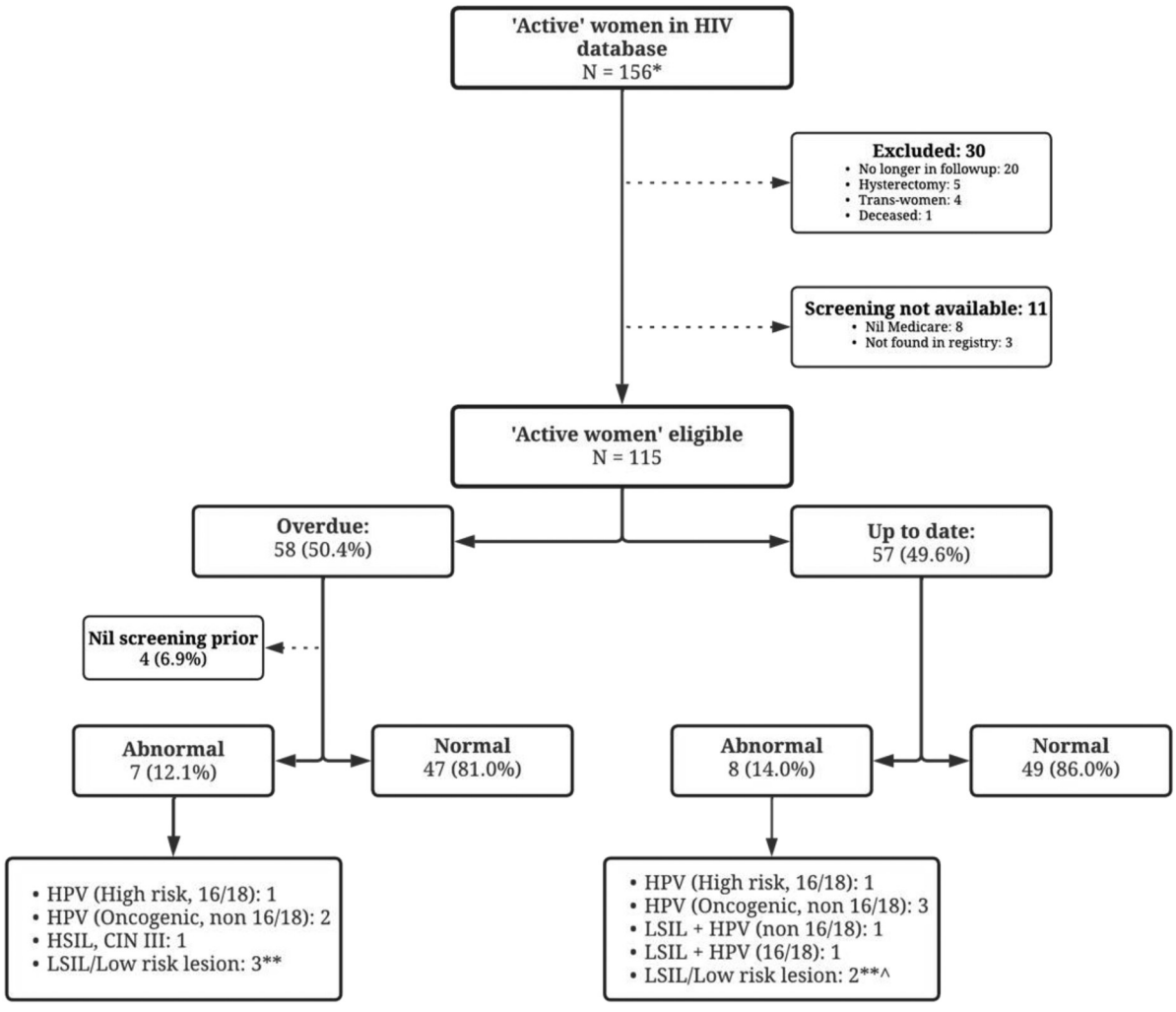

Fig. 1. Women with HIV who are actively managed at Alfred Hospital, as of October 2023. CIN, cervical intraepithelial neoplasia; HPV, human papillomavirus; HSIL, high-grade squamous intraepithelial lesions; LSIL, low-grade squamous intraepithelial neoplasia. [a]As of 16/10/23. [b]LSIL cytology where HPV is negative or not reported. Low-risk lesion: colposcopy abnormal (Impression LSIL/metaplasia/HSIL) but cytology and/or histology negative and HPV negative. [c]Including one patient with LSIL but colposcopy/histology report unavailable.

Discussion

We found that over half of the women receiving HIV care were overdue for their cervical screening test, with the majority being overdue by more than twelve months. The audit revealed most screening tests were requested by general practitioners rather than HIV or other specialist physicians in hospital or sexual health clinic models of care. Importantly, cervical cancer screening was not routinely available at the Alfred Hospital in the audit period until self-collection was introduced more recently, hence screening was largely performed in primary care settings. This emphasizes the importance of improving communication between primary and specialist care services and highlights the need for cancer-screening training across both sectors, particularly for patients with shared care arrangements. The NCCSR recommends rescreening in 5 years for women with normal results, which is consistent with guidelines for women who are not immunocompromised or WHV. In these cases, the provider may be unaware of the HIV diagnosis, or of the need to provide this information. Although decreasing, there is still considerable stigma regarding HIV and this may prevent women disclosing their diagnosis with their general practitioners, especially women from culturally diverse communities. Alternatively, there may also be lack of knowledge amongst some providers about the recommended frequency of screening for WHV.

The findings of this study can be compared to the global context. A comparable study in South Africa [15] found suboptimal screening uptake at 32.9% for WLHIV, where screening is recommended every 3 years from diagnosis. While older women were over three times more likely to

have been screened, this study only investigated a history of screening rather than the screening interval. High demand for primary care, competing staff duties, and limited expertise and policies were listed as potential barriers. Conversely, a Canadian study [16] showed that 68.5% of WLHIV had received cervical cancer screening within the past year and 86.2% had been screened in the past three years; in a setting where annual screening is recommended. However, one-quarter of patients had never discussed cervical cancer screening recommendations with a healthcare provider, suggesting increased need to promote awareness amongst healthcare professions. In other high-income countries, such as in France, one study demonstrated screening uptake among WLHIV was 76.5% and not lower than the general population; however, poor education and lack of health insurance was associated with reduced screening uptake [17].

Self-collected CST samples were available in Australia from July 2022 and as a screening tool in the Alfred Hospital HIV clinic from mid-2023. Our findings show that the use of self-collected specimens was underutilized. Globally, self-collected specimens may offer a potential solution to barriers in screening uptake. A survey of WLHIV revealed self-collection was well accepted, with 90% of participants reporting high levels of convenience and comfort [18].

Although patients presenting to a specialist HIV center are routinely asked about screening during consultations, recall of the last screening date may be inaccurate. Accessing the online NCCSR requires administrative setup and may be laborious during a busy clinic. Furthermore, we anticipated finding a significant proportion of those overdue screening were a result of the COVID-19 pandemic with a reliance on telehealth appointments during multiple lockdowns in Melbourne. We found that 23.7% (14/59) of those overdue ought to have had their screening performed during the COVID period (March 2020–December 2021).

Our study had limitations; we did not ascertain individual reasons for why some women were overdue for screening. Importantly, we were unable to view the results of 8 women who did not have access to Medicare which may have underestimated the true rate of overdue screening. This is a population of interest, as these women are considered to be at a higher risk; they may never have had any screening, migrated from countries without a robust screening program or migrated from places where the prevalence of HPV is higher. Furthermore, our results are from a single center in Australia, and do not account for those who have had a history of screening performed overseas. However, due to the lack of data from Australia and the importance of cervical cancer screening, this represents an important analysis for improvement of outcomes.

In conclusion, this audit revealed that cervical cancer screening for WHV under hospital-based care can be improved to meet recommended guidelines in Melbourne, Australia. Barriers that should be addressed to improve outcomes include improving education for patients, primary care and HIV specialists on screening guidelines and collection methods, improved communication across all sectors, and streamlining the process. Finally, addressing practical or emotional barriers including stigma and discomfort is paramount, and may be overcome by newer screening methods such as self-collected samples.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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