Cervical Cancer Screening Rates in Females Living with HIV at Three Healthcare Settings in the United States, 2010-2019

Leigh Sheridan

A thesis

submitted in partial fulfillment of the

requirements for the degree of

Master of Public Health

University of Washington

2023

Committee:

Aruna Kamineni

Christopher I. Li

Program Authorized to Offer Degree:

Department of Epidemiology

University of Washington

Abstract

Cervical Cancer Screening Rates in Females Living with HIV at Three Healthcare Settings in the United States, 2010-2019

Leigh Sheridan

Chair of the Supervisory Committee:

Aruna Kamineni

Department of Epidemiology

Females living with HIV (FLWHIV) are at greater risk of developing cervical cancer compared to females without HIV. National cervical cancer screening guidelines recommend more frequent screening for FLWHIV to address their increased risk. We sought to examine screening rates among FLWHIV during the most recent decade. This retrospective cohort study was conducted at Kaiser Permanente Washington, Parkland Health, and Mass General Brigham. The study cohort included 18-89-year-old screening-eligible FLWHIV during 2010-2019. Data on sociodemographics, comorbidities, and cervical cancer risk factors and screening tests were extracted from administrative and clinical databases. We reported crude and adjusted screening rates, overall and by test modality. Generalized estimating equation models with Poisson regression were used to estimate screening rate ratios (SRR) and 95% confidence intervals (CI) for the associations between total screening rates and healthcare setting, calendar year, age, race and ethnicity, and comorbidity score. Among 3,556 FLWHIV across the three settings, later calendar years relative to 2010-2013 were associated with lower total screening rates (2014-2016: SRR=0.80, 95% CI= 0.77-0.83; 2017-2019: SRR=0.71, 95% CI=0.68-0.75). Compared to non-Hispanic Black females, non-Hispanic white females had lower total screening rates

(SRR=0.89, 95% CI= 0.81-0.98). Older age (SRR=0.82, 95% CI=0.74-0.89 for 50–65-year-olds vs. 18–29-year-olds) and higher comorbidity burden (SRR=0.89, 95% CI=0.82-0.98 for 9+ vs. 0-6 comorbidity score) were also associated with lower screening rates. The screening rate decrease we observed in this large cohort of FLWHIV during 2010-2019 aligns with guideline changes recommending longer screening intervals and implementation of co-testing. Our finding that white FLWHIV and those with greater comorbidity burden have lower screening rates should be confirmed in other US settings, and the age disparity we report warrants further investigation. Given the higher risk of cervical cancer in FLWHIV, it is especially important to address potential screening disparities.

INTRODUCTION

Females living with human immunodeficiency virus (FLWHIV) are approximately six times more likely to develop cervical cancer compared to females without HIV.[1] FLWHIV are also more likely than their HIV-negative counterparts to develop cervical pre-cancers.[2] HIV-related immunosuppression is considered the most likely mechanism by which HIV infection increases the risk of cervical pre-cancers and cancers, as human papillomavirus (HPV) infection is more likely to persist.[3] Cervical cancer is preventable through screening by means of a cytology test, an HPV test, or a cytology and HPV test together (i.e., co-test).[4]

In recent years, the Centers for Disease Control (CDC), National Institutes of Health (NIH), and HIV Medical Association (HIV-MA) have released multiple iterations of cervical cancer screening guidelines tailored to address the increased risk of cervical cancer among FLWHIV *(Appendix 1).* While cervical cancer screening guidelines specific to FLWHIV have been in place since 2009, there are few studies examining patterns of screening in this population.

Existing literature tends to examine older data prior to the availability of co-testing as a cervical cancer screening modality, and prior to changes in screening guidelines that allowed for co-testing among FLWHIV.[5,6] We sought to address these gaps by examining cervical cancer screening rates overall and by test modality among FLWHIV at three US healthcare settings during the most recent decade.

METHODS

Study Design and Setting

We conducted a retrospective cohort study within the National Cancer Institute-funded Population-based Research to Optimize the Screening PRocess (PROSPR II) consortium [7], and specifically within its cervical PROSPR II Research Center, MultilEvel optimization of The ceRvIcal Cancer Screening process in diverse settings & populations (METRICS). METRICS includes data from three healthcare settings: Kaiser Permanente Washington (KPWA), Mass General Brigham (MGB), and Parkland Health (PH). KPWA is a mixed-model healthcare system providing coverage and care in Washington State. MGB, in the greater Boston area, includes two academic medical centers – Brigham and Women's Hospital and Massachusetts General Hospital – and their affiliated primary care networks. PH is an integrated safety-net healthcare system serving uninsured and underinsured Dallas County, Texas residents with academic oversight from the University of Texas Southwestern. Institutional review boards at each site approved all study activities.

Data Collection and Study Population

The METRICS study cohort included females aged 18-89 years during 2010-2020 with eligibility varying slightly across sites. KPWA included females enrolled in the health plan with a KPWA primary care provider. MGB and PH included females with one or more primary care or women's health visit within those healthcare settings. Information on sociodemographic characteristics (e.g., age, race and ethnicity), comorbidities, cervical cancer risk factors (e.g., absent cervix), and cervical cancer screening tests (i.e., cytology and HPV tests) for the

METRICS cohort was extracted from administrative and clinical databases, including the electronic health record. These data sources and collection methods at KPWA and PH have been previously described[8], and were similar at MGB.

We identified females in the METRICS cohort with a prevalent or incident HIV diagnosis during 2010-2019. At KPWA, HIV status was ascertained using ICD-9 and ICD-10 diagnosis codes (ICD-9-CM codes 042.x-044.x, 079.53, 795.71, and V08; ICD-10 codes B20.x-B22.x, B23.x, B97.35, O98.7x, and Z21) followed by medical record review to confirm HIV diagnoses. MGB ascertained HIV status using ICD-9-CM codes 0.42.x-0.44x and V08, and ICD-10 codes B20.x-B22.x, B24.x, and Z21 with diagnoses confirmed by the presence of at least three diagnosis codes, and with the first occurring code serving as the date of HIV diagnosis. PH ascertained HIV status using a combination of the diagnosis codes, lab results, and HIV clinic visits. HIV diagnosis was confirmed when two of the following occurred: an HIV clinic visit; completion of an HIV RNA or CD4 lab test; and/or an HIV diagnosis code (ICD-9-CM codes 042.x-044.x and V08, and ICD-10 codes B20.x-B22.x, B24.x, and Z21), with the first event serving as the HIV diagnosis date. Females with a history of cervical cancer or cervix removal on or prior to their HIV diagnosis date were excluded.

Comorbidity scores were calculated using comorbidities recorded at each healthcare encounter in a calendar year (KPWA), or a calendar year and preceding calendar years (PH and MGB). For KPWA, comorbidity scores were set to missing for individuals not enrolled in the health plan for the full calendar year.

Analysis

We reported sociodemographic and clinical characteristics of the study population overall and by healthcare setting.

Females accrued person-time beginning on date of METRICS cohort entry for those with prevalent HIV diagnoses or on date of first evidence of HIV diagnosis after METRICS cohort entry, and were censored by the earliest date of cervix removal, cervical cancer diagnosis, disengagement with health care based on lack of primary care utilization for 37 months at MGB and PH, disenrollment from the health plan or re-location outside of the Seattle-Puget Sound SEER registry catchment area at KPWA, re-location out of Dallas County at PH, or end of study on December 31, 2019.

Screening was defined as receipt of a cervical cytology test, co-test, or cervical cancer screening test of unknown modality. We excluded cytology tests received on the same day as a biopsy, colposcopy, or excision as they were considered diagnostic tests. Repeat cytology tests (i.e., those that occurred within four months of an unsatisfactory cytology test) were included only if the repeat test was the first cervical cancer screening test received during follow up. We calculated age as of date of screening and used comorbidity score from the calendar year of screening.

The number of screening tests FLWHIV received during the study period was summed overall and by healthcare setting, calendar year of testing (2010-2013, 2014-2016, 2017-2019), age at testing (18-29, 30-39, 40-49, 50-65, 66-89 years), race and ethnicity (Non-Hispanic Black, Hispanic, Non-Hispanic White, Non-Hispanic Asian/Pacific Islander, and Non-Hispanic Multiracial/Other), and comorbidity score (0-6, 7-8, and 9+). Person-years were summed across the same categories for each characteristic. We calculated crude rates of receipt of cytology

tests, co-tests, and total tests (including tests of unknown modality) per 100 person-years within each category. Rates were adjusted for age group, calendar year group, and healthcare setting.

Generalized estimating equation (GEE) models with Poisson regression were used to estimate screening rate ratios and 95% confidence intervals for the associations between total screening rates and healthcare setting, calendar year, age, race and ethnicity, and comorbidity score. GEE was used to account for within-person correlation due to females receiving more than one cervical cancer screening test during follow-up. Screening rate ratios were adjusted for age, calendar year, and healthcare setting. We repeated these analyses stratified by healthcare setting.

To better understand test modality-specific screening patterns, we calculated rates of receipt of cytology tests, co-tests, and total tests per 100 person-years, overall and stratified by healthcare setting by finer categories of calendar year (2010-2011, 2012-2013, 2014-2015, 2016-2017, and 2018-2019). Rates were adjusted for age using direct standardization with the total study population as the standard population. All analyses were conducted using R.

RESULTS

We identified 3,935 females between the ages of 18-89 living with HIV in the METRICS study cohort (*Figure 1*). After excluding those diagnosed with HIV in 2020 and those diagnosed with cervical cancer or with evidence of cervix removal prior to analytic cohort entry (i.e., date of first evidence of HIV diagnosis during 2010-2019), we identified 3,556 screening-eligible females for analysis.

Females at KPWA, PH, and MGB comprised 6.3%, 83.2%, and 10.5% of the study population, respectively (*Table 1*). Most females across settings entered the analytic cohort during 2010-2013 (64.8%) and were non-Hispanic Black (67.6%). Half of the females across settings had five or more years of follow-up and a comorbidity score of 0-6. Median age at analytic cohort entry was 40 years. The distributions of characteristics varied by healthcare setting.

We enumerated a total of 7,704 cervical cancer screening tests over 18,605 person-years (*Table 2*). The rates of cytology alone, co-testing, and total screening were 32.7 per 100 person-years, 8.6 per 100 person-years, and 41.4 per 100 person-years, respectively. Cytology rates were higher than co-testing rates across calendar year, age, race and ethnicity, and comorbidity score categories with a similar pattern observed for Parkland. However, modality-specific screening rates were similar at KPWA and nearly similar at MGB. We reported age-adjusted rates of cytology alone and total screening rates grouped by two-year categories. After adjusting for age, these results showed consistent decrease in rates of cytology alone and total screening 2010-2019, and a consistent increase in co-testing during the same period (*Supplemental Figure 2*).

Compared to KPWA, total screening rates were lower at MGB and PH (adjusted Screening Rate Ratio (SRR): 0.88 [95% Confidence Interval (CI): 0.79, 0.99] and SRR: 0.69 [95% CI: 0.63, 0.76], respectively) (*Table 2*). Relative to 2010-2013, later calendar years were associated with lower total screening rates (for years 2014-2016 adjusted SRR: 0.80 [95% CI: 0.77, 0.83] and for years 2017-2019 adjusted SRR: 0.71 [95% CI: 0.68, 0.75]). Older age relative to younger age (18-29 years) was also associated with lower screening rates (for ages 50-65 adjusted

SRR: 0.82 [95% CI: 0.74, 0.89] and for ages 66-89 adjusted SRR: 0.43 [95% CI: 0.34, 0.54]. Screening rates were similar for middle-aged females (30-39 and 40-49 years) compared to younger females. Compared to non-Hispanic Black females, non-Hispanic white females had lower total screening rates (adjusted SRR: 0.89 [95% CI: 0.81, 0.98], but Hispanic females and non-Hispanic Asian or Pacific Islander females had higher total screening rates (adjusted SRR: 1.19 [95% CI: 1.11, 1.28] and adjusted SRR: 1.33 [95% CI: 1.08, 1.65], respectively). Screening rates were similar for females with 0-6 or 7-9 comorbidity scores, but females with comorbidity score of 9 or greater had lower screening rates compared to those with 0-6 comorbidity scores (adjusted SRR: 0.89 [95% CI: 0.82, 0.98]).

We observed that site-specific screening rate across calendar year, age, race and ethnicity, and comorbidity score (*Supplemental Tables 2a-2c*) were mostly consistent with total rates, but limited by lack of precision.

DISCUSSION

In this large cohort of FLWHIV, we observed that total cervical cancer screening rates varied by healthcare setting, calendar year, age, race and ethnicity, and comorbidity burden. Our study had a few limitations. Ascertainment of HIV diagnosis differed across sites, with only KPWA chart-confirming diagnoses. We lacked information on immunosuppression levels, and it is possible that screening rates may have differed between those with and without immunosuppression. However, we were able to examine screening rates by comorbidity burden. As the study cohort included females with both incident and prevalent HIV diagnoses, we could not examine whether rates differed among those newly diagnosed (i.e., those with a shorter recommended screening interval) versus those with prevalent diagnoses (i.e., those who may have extended to longer screening intervals after the requisite number of normal screening results). In this study, we examined screening rates over time and by various patient-level characteristics, but our results do not address whether FLWHIV were up to date with cervical cancer screening. Our study had several strengths including a large cohort with longitudinal cervical cancer screening EHR data over a recent 10-year period. These detailed EHR data also allowed us to examine modality of cervical cancer screening received and screening by race and ethnicity and comorbidity burden.

In 2009, the first CDC, NIH, and HIV-MA cervical cancer screening guidelines recommended cytology screening for FLWHIV twice during the first year after diagnosis, with the first screening as close to time of diagnosis as possible (*Appendix 1)*. Following two consecutive normal screening results, screening was recommended annually thereafter. In 2013, the guidelines were modified to recommend co-testing as an alternative to cytology testing for FLWHIV 30 years and older, with all other recommendations identical to the 2009 guidelines. In 2015, the guidelines were further revised to recommend that FLWHIV under 30 years begin screening within one year of onset of sexual activity or at the time of diagnosis if already sexually active. Screening could be extended annually following a normal cytology result and three-yearly following three consecutive normal results. Another change from the 2009 guidelines was the extension to three-yearly screening following a single negative co-test from those 30 years and older. In each iteration of these cervical cancer screening guidelines for FLWHIV, screening was recommended to continue throughout the lifespan. Our observed decrease in total screening

rates during the study period aligns with more recent guidelines recommending longer re-screening intervals. The decrease in total screening rates also aligns with KPWA and MGB implementing co-testing, a screening modality that allows for longer re-screening intervals, during the study period. Finally, as females with prevalent HIV (84.4 % of the study population entering the cohort) became eligible for longer re-screening intervals following the requisite number of negative screening results, we would also expect to observe a decrease in total screening rates over time.

The lower cervical cancer screening rates that we observed in older FLWHIV in this study are consistent with a 2009 study of 2,417 FLWHIV that found that females 50 years and older had a higher odds of not receiving cervical cancer screening in the past year compared to 18-29-year-olds (Odds Ratio (OR): 2.6, 95% CI: 1.8-3.7).[9] Although literature is limited, the variation in total screening rates by race and ethnicity among FLWHIV shown by our data is not supported by a recent study examining patterns of cervical cancer screening among 2,270 FLWHIV.[10] This study found no difference in screening rates between non-Hispanic Black women, Hispanic/Latino women, non-Hispanic white women, and women of other races. However, this study relied on self-report of receipt of cytology testing and may have also been subject to selection bias. Study subjects were included if they participated in two HIV case interviews one year apart making it likely that those included in the study were more likely to utilize health care. The disparity with race and ethnicity we observed in FLWHIV is well-documented among average-risk females.[11, 12, 13] Similar to our study results, a recent study of 57,814 average-risk females found that Black and Hispanic females were more likely to have received cervical cancer screening in the last three years compared to white females.[14] We also observed that FLWHIV with high comorbidity scores (9+) were less likely to be screened compared to those with lower scores (0-6). Existing data on average-risk women are mixed for the association between cervical cancer screening and comorbidity burden. Research in populations screening for colorectal and breast cancer have found that higher comorbidity burden is associated with a lower likelihood of receiving cancer screening.[15,16,17] Few relevant data exist for FLWHIV, but one study of screening uptake among 2,271 FLWHIV in Ontario, Canada found that higher comorbidity burden was associated with greater likelihood to screen.[18] Although the population of FLWHIV in our study have health care coverage, differences in the health care ecosystems and care delivery in the two settings may explain the different findings.

Our study suggests that rates of cervical cancer screening decreased from 2010-2019 among FLWHIV receiving care at three healthcare systems across the US, aligning with guideline changes recommending longer screening intervals, implementation of co-testing at two of the healthcare systems, and females with prevalent HIV extending to longer re-screening intervals following the requisite number of normal screening results during the study period. Future research should examine whether FLWHIV are up to date with screening and whether up to date FLWHIV are appropriately extending to longer re-screening intervals. Our finding that FLWHIV who are white or have greater comorbidity burden have lower screening rates should be confirmed in other US settings, and the disparity we observed in cervical cancer screening rates by age also warrants further investigation. Screening disparities suggest the potential for unequal cervical morbidity and mortality outcomes among FLWHIV, a population at higher risk of cervical cancer and therefore important to address.

REFERENCES

[1] Stelzle D, Tanaka LF, Lee KK, et al. Estimates of the global burden of cervical cancer associated with HIV. Lancet Glob Health. 2021; 9(2):e161-e169. doi:10.1016/S2214-109(20)30459-9

[2] Abraham AG, D'Souza G, Jing Y, et al. Invasive Cervical Cancer Risk Among HIV-Infected Women: A North American Multicohort Collaboration Prospective Study. JAIDS J Acquir Immune Defic Syndr. 2013;62(4):405-413. doi:10.1097/QAI.0b013e31828177d7

[3] Ahdieh L, Klein RS, Burk R, Cu-Uvin S., Schuman P, Duerr A, Safaeian M, Astemborski J, Daniel R, Shah K, Prevalence, Incidence, and Type-Specific Persistence of Human Papillomavirus in Human Immunodeficiency Virus (HIV)-Positive and HIV-Negative Women, The Journal of Infectious Diseases, Volume 184, Issue 6, 15 September 2001, Pages 682–690, https://doi.org/10.1086/323081

[4] Centers for Disease Control and Prevention. What should I know about cervical cancer screening? 2023. https://www.cdc.gov/cancer/cervical/basic_info/screening.htm

[5] Oster AM, Sullivan PS, Blair JM. Prevalence of cervical cancer screening of HIV-infected women in the United States. J Acquir Immune Defic Syndr. 2009 Aug 1;51(4):430-6. doi: 10.1097/QAI.0b013e3181acb64a. PMID: 19474756.

[6] Barnes A, Betts AC, Borton EK, Sanders JM, Pruitt SL, Werner C, Bran A, Estelle CD, Balasubramanian BA, Inrig SJ, Halm EA, Skinner CS, Tiro JA. Cervical cancer screening among HIV-infected women in an urban, United States safety-net healthcare system. AIDS. 2018 Aug 24;32(13):1861-1870. doi: 10.1097/QAD.0000000000001881. PMID: 29762164; PMCID: PMC6059987.

[7] Beaber EF, Kamineni A, Burnett-Hartman AN, et al. Evaluating and Improving Cancer Screening Process Quality in a Multilevel Context: The PROSPR II Consortium Design and Research Agenda. Cancer Epidemiol Biomark Prev Publ Am Assoc Cancer Res Cosponsored Am Soc Prev Oncol. 2022;31(8):1521-1531. doi:10.1158/1055-9965.EPI-22-0100

[8] Kamineni A, Tiro JA, Beaber EF, et al. Cervical cancer screening research in the PROSPR I consortium: Rationale, methods and baseline findings from a US cohort. Int J Cancer. 2019;144(6):1460-1473. doi:10.1002/ijc.31940

[9] Oster, Alexandra M MD; Sullivan, Patrick S DVM, PhD; Blair, Janet M PhD, MPH. Prevalence of Cervical Cancer Screening of HIV-Infected Women in the United States. JAIDS Journal of Acquired Immune Deficiency Syndromes 51(4):p 430-436, August 2009. | DOI: 10.1097/QAI.0b013e3181acb64a

[10] Frazier, EL, Sutton, Y, Tie, Y., McNaghten, A, Blair, J, Skarbinski, J. Screening for Cervical Cancer and Sexually Transmitted Diseases Among HIV-Infected Women. Journal of Women's Health.Feb 2016.124-132. http://doi.org/10.1089/jwh.2015.5368

[11] Ford S, Wassim T, Williams K. P., Roman L. A., Leach R. Differences in cervical cancer screening and follow-up for black and white women in the United States, Gynecologic Oncology, Volume 160, Issue 2, 2021, 369-374. https://doi.org/10.1016/j.ygyno.2020.11.027.

[12] Datta GD, Pana MP, M-H Mayrand, Glenn B. Racial/ethnic inequalities in cervical cancer screening in the United States: An outcome reclassification to better inform interventions and benchmarks. Preventive Medicine, Volume 159, 2022.107055. ISSN 0091-7435, https://doi.org/10.1016/j.ypmed.2022.107055.

[13] Miles-Richardson S., Allen S., Claridy M.D. et al. Factors Associated with Self-Reported Cervical Cancer Screening Among Women Aged 18 Years and Older in the United States. J Community Health 42, 72–77 (2017). https://doi.org/10.1007/s10900-016-0231-5

[14] Zanwar PP, Davis MM, Horner-Johnson W. Assessing Intersectional Disparities in Cervical Cancer Screening by Disability Status, Race, and Ethnicity. AJPM Focus. 2022 Aug 5;1(2):100019. doi: 10.1016/j.focus.2022.100019. PMID: 37791247; PMCID: PMC10546533.

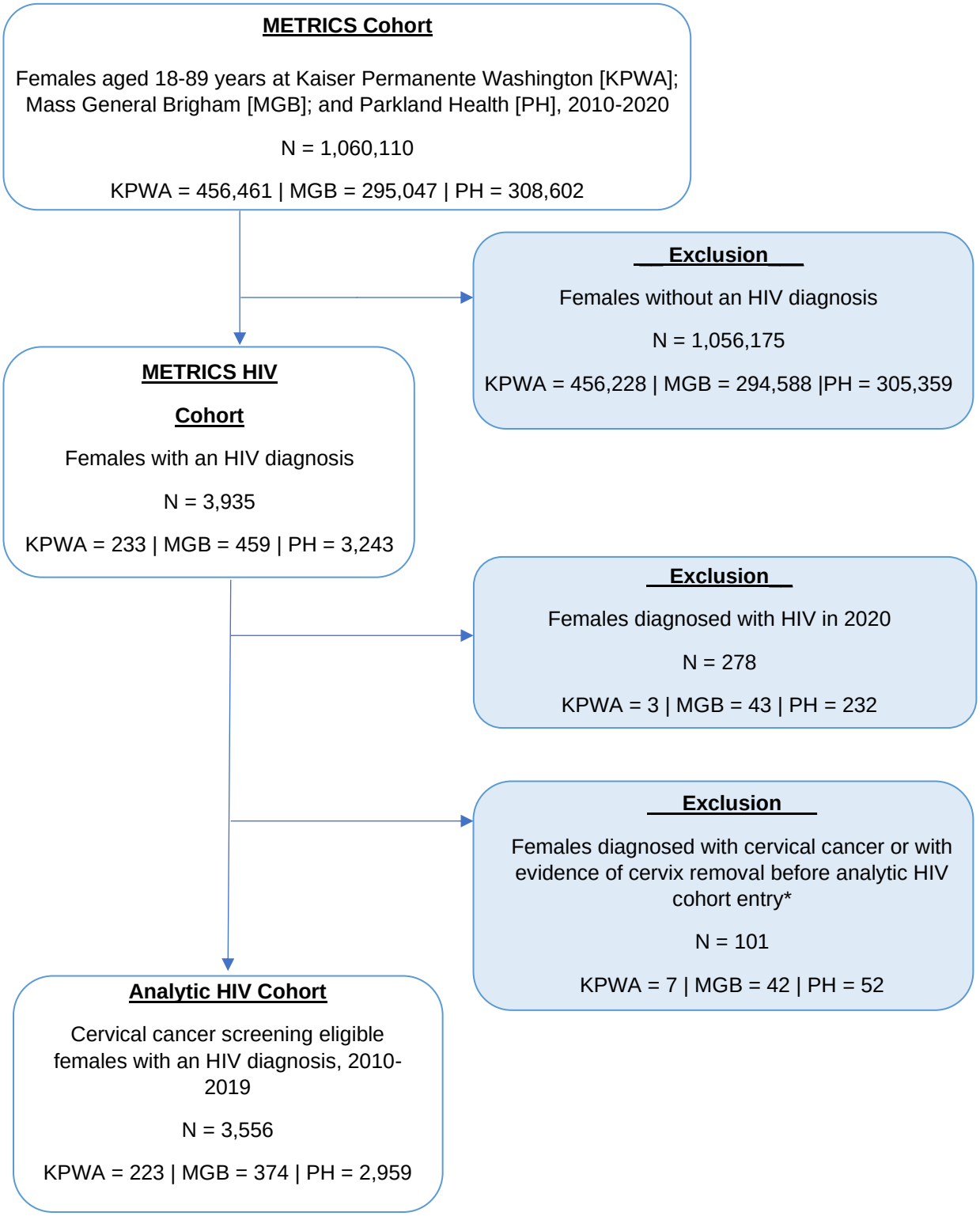
[15] Coronado, G.D., Nielson, C.M., Keast, E.M. et al. The influence of multi-morbidities on colorectal cancer screening recommendations and completion. Cancer Causes Control 32, 555–565 (2021). https://doi.org/10.1007/s10552-021-01408-2

[16] Makedonov I, Gu S, Paszat LF; investigators of Ontario Cancer Screening Research Network. Organized breast screening improves reattendance compared to physician referral: a case control study. BMC Cancer. 2015 Apr 26;15:315. doi: 10.1186/s12885-015-1346-2. PMID: 25928416; PMCID: PMC4417301.

[17] Jensen LF, Pedersen AF, Andersen B, Vestergaard M, Vedsted P. Non-participation in breast cancer screening for women with chronic diseases and multimorbidity: a population-based cohort study. BMC Cancer. 2015 Oct 26;15:798. doi: 10.1186/s12885-015-1829-1. PMID: 26502879; PMCID: PMC4623919.

[18] Burchell AN, Kendall CE, Cheng SY, Lofters A, Cotterchio M, Bayoumi AM, Glazier RH, Antoniou T, Raboud J, Yudin MH, Loutfy M. Cervical cancer screening uptake among HIV-positive women in Ontario, Canada: A population-based retrospective cohort study. Prev Med. 2018 Feb;107:14-20. doi: 10.1016/j.ypmed.2017.11.023. Epub 2017 Nov 29. PMID: 29197533.

Figure 1. Identification of the study population: cervical cancer screening-eligible females living with HIV at three US healthcare settings during 2010-2019.



*Analytic cohort entry was the date of the first evidence of an HIV diagnosis on or after METRICS cohort entry. Females with evidence of an HIV diagnosis prior to METRICS cohort entry were assigned an analytic cohort entry date equal to the METRICS cohort entry date.

Table 1. Characteristics of cervical cancer screening-eligible females living with HIV at three US healthcare settings during 2010-2019.

	Kaiser Permanente Washington N = 223	**Parkland Health** N = 2,959	**Mass General Brigham** N = 374	**Total** N = 3,556
	n (%)	n (%)	n (%)	n (%)
Calendar year[1]				
2010 - 2013	96 (43.1)	1,934 (65.4)	275 (73.5)	2,305 (64.8)
2014 - 2016	27 (12.1)	524 (17.7)	66 (17.6)	617 (17.4)
2017 - 2019	100 (44.8)	501 (16.9)	33 (8.8)	634 (17.8)
Follow-up time (years)				
Mean [SD]	*2.8 [2.9]*	*5.5 [3.3]*	*6.4 [3.0]*	*5.4 [3.3]*
Median [25th, 75th percentiles]	*1.7 [0.2, 3.3]*	*5.1 [2.2, 8.1]*	*6.7 [3.7, 9.7]*	*5.0 [1.9, 8.1]*
0 - <1 years	92 (41.3)	308 (10.4)	10 (2.7)	410 (11.5)
1 - <3 years	65 (29.2)	440 (14.9)	42 (11.2)	547 (15.4)
3 - <5 years	23 (10.3)	704 (23.8)	86 (23.0)	813 (22.9)
≥5 years	43 (19.3)	1,507 (50.9)	236 (63.1)	1,786 (50.2)
Age (years)[1]				
Mean [SD]	*41.6 [10.7]*	*39.8 [11.8]*	*45.7 [11.4]*	*40.5 [11.8]*
Median [25th, 75th percentiles]	*41.5 [34.7, 48.3]*	*39.0 [30.4, 47.7]*	*45.7 [38.3, 53.2]*	*40.0 [31.3, 48.7]*
18 - 29	27 (12.1)	697 (23.6)	36 (9.6)	760 (21.4)
30 - 39	70 (31.4)	874 (29.5)	77 (20.6)	1,021 (28.7)
40 - 49	81 (36.3)	767 (25.9)	125 (33.4)	973 (27.4)
50 - 65	40 (17.9)	579 (19.6)	126 (33.7)	746 (21.0)
66 - 89	5 (2.2)	42 (1.4)	10 (2.7)	56 (1.6)
Race and ethnicity				
Hispanic	22 (11.8)	484 (16.5)	110 (29.7)	616 (17.7)
Non-Hispanic Black	94 (50.3)	2,088 (71.3)	176 (47.4)	2,358 (67.6)
Non-Hispanic White	56 (30.0)	301 (10.3)	69 (18.6)	426 (12.2)
Non-Hispanic Asian/Pacific Islander	6 (3.2)	50 (1.7)	8 (2.2)	64 (1.8)
Non-Hispanic Multiracial/ Other	9 (4.8)	6 (0.2)	8 (2.2)	23 (0.7)
Unknown[2]	*36 [16.1]*	*30 [1.0]*	*3 [0.8]*	*69 [1.9]*
Comorbidity score[3]				
0-6	119 (84.4)	1,505 (50.9)	212 (56.7)	1,836 (52.8)
7-8	16 (11.4)	1,070 (36.2)	129 (34.5)	1,215 (35.0)
9+	6 (4.3)	384 (13.0)	33 (8.8)	423 (12.2)
Unknown[2]	*82 [36.8]*	*0.0 [0.0]*	*0 [0.0]*	*82 [2.3]*

[1]Calendar year and age were reported as of analytic cohort entry.
[2]Percentages were calculated excluding the unknown category. The percentage unknown is shown in square brackets.
[3]Comorbidity score was based on the Charlson comorbidity index and was calculated using comorbidities recorded at health care encounters in the calendar year of analytic cohort entry (KPWA), or analytic cohort entry year and preceding calendar years (PH and MGB). For KPWA, the comorbidity score was set to missing for individuals not enrolled in the health plan for the full calendar year of analytic cohort entry. For the Charlson comorbidity index, a diagnosis of HIV/AIDS is assigned a value of 6.

Table 2. Cytology screening, co-testing, and total cervical cancer screening rates among females living with HIV, overall and by healthcare setting, calendar year, age, race and ethnicity, and comorbidity score, 2010-2019.

	Number of cervical cancer screening tests during follow-up[1,3]			Person-years	Screening rate per 100 person-years			Crude total screening rate ratio (95% CI)[4]	Adjusted total screening rate ratio (95% CI)[4,5]
	Cytology	Co-tests	Total		Cytology	Co-tests	Total		
Total	6,078	1,600	7,704	18,605	32.7	8.6	41.4	-	-
Healthcare setting									
Kaiser Permanente Washington	161	158	345	604	26.7	26.2	57.1	1.0 (Ref)	1.0 (Ref)
Mass General Brigham	485	629	1,114	2,334	20.8	26.9	47.7	0.83 (0.74, 0.93)	0.88 (0.79, 0.99)
Parkland Health	5,432	813	6,245	15,667	34.7	5.2	39.9	0.70 (0.63, 0.77)	0.69 (0.63, 0.76)
Calendar year									
2010-2013	2,777	357	3,141	6,285	44.2	5.7	50.0	1.0 (Ref)	1.0 (Ref)
2014-2016	1,957	446	2,411	6,114	32.0	7.3	39.4	0.79 (0.76, 0.82)	0.80 (0.77, 0.83)
2017-2019	1,344	797	2,152	6,206	21.7	12.8	34.7	0.69 (0.66, 0.73)	0.71 (0.68, 0.75)
Age (years)									
18-29	870	120	990	2,236	38.9	5.4	44.3	1.0 (Ref)	1.0 (Ref)
30-39	1,638	399	2,050	4,450	36.8	9.0	46.1	1.03 (0.96, 1.11)	1.04 (0.97, 1.11)
40-49	1,920	514	2,445	5,354	35.9	9.6	46.0	1.04 (0.94, 1.09)	1.02 (0.94, 1.09)
50-65	1,541	532	2,075	5,732	26.9	9.3	36.2	0.82 (0.75, 0.89)	0.82 (0.74, 0.89)
66-89	109	35	144	784	13.9	4.5	18.4	0.42 (0.34, 0.52)	0.43 (0.34, 0.54)
Race and ethnicity[2]									
Non-Hispanic Black	3,951	1,014	4,969	12,412	31.8	8.2	40.0	1.0 (Ref)	1.0 (Ref)
Hispanic	1,306	345	1,652	3,427	28.1	10.1	48.2	1.21 (1.13, 1.29)	1.19 (1.11, 1.28)
Non-Hispanic White	624	181	816	2,203	28.3	8.2	37.0	0.93 (0.84, 1.02)	0.89 (0.81, 0.98)
Non-Hispanic Asian/ Pacific Islander	138	39	178	324	42.6	12.0	54.9	1.37 (1.09, 1.73)	1.33 (1.08, 1.65)
Non-Hispanic Multiracial & Other	26	15	41	103	25.2	14.6	39.8	1.0 (0.70, 1.41)	0.86 (0.63, 1.17)
Comorbidity score[2]									

0-6	2,634	715	3,367	7,521	35.0	9.5	44.8	1.0 (Ref)	1.0 (Ref)
7-8	2,409	597	3,009	7,245	33.3	8.2	41.5	0.93 (0.88, 0.98)	0.99 (0.93, 1.04)
9+	1,015	273	1,288	3,781	26.9	7.2	34.1	0.76 (0.69, 0.83)	0.89 (0.82, 0.98)

[1]Receipt of cervical cancer screening was defined as receipt of a cytology test, co-test, or cervical cancer screening test of unknown modality. Cytology tests received on the same day as a biopsy, colposcopy, or excision were excluded as they were considered diagnostic tests. Repeat cytology tests (i.e., those that occurred within four months of an unsatisfactory cytology test) were included only if the repeat test was the first cervical cancer screening test received during follow up.

[2]n=48 cervical cancer screening tests with missing race and ethnicity data were not included in the race and ethnicity-specific estimates and n=40 cervical cancer screening tests with missing comorbidity scores were not included in the comorbidity-specific estimates.

[3]The number of cytology tests and co-tests do not necessarily sum to the total number of cervical cancer screening tests because the total number of tests includes screening tests of unknown modality.

[4]Generalized estimating equation (GEE) models with Poisson regression were used to estimate screening rate ratios and 95% confidence intervals. GEE was used to account for within-person correlation due to females receiving more than one cervical cancer screening test during follow up.

[5]Screening rate ratios were adjusted for age, calendar year, and healthcare setting.

Appendix

Guideline Source	Date Issued	Screening Recommendations
CDC, NIH, HIV-MA[1]	April 2009	Two cytology screenings in the first year after HIV diagnosis, prioritizing the first screening as close to time of diagnosis as possible. After two consecutive negative screens, screen annually. Screening continues throughout their life.
CDC, NIH, HIV-MA[2]	July 2013	Two cytology screenings in the first year after HIV diagnosis, ideally at 6-month intervals and prioritizing first screening as close to time of diagnosis as possible. Screening continues throughout their life. **FLWHIV < 30 years:** Co-testing is not recommended. **FLWHIV ≥30 years:** • Co-testing or cytology screening recommended. • After two consecutive negative tests, screen annually thereafter (both modalities).
CDC, NIH, HIV-MA[3]	September 2015	**FLWHIV < 30 years:** • Co-testing is not recommended. • Begin screening within one year of onset of sexual activity. • If the initial cytology test is normal, they can screen annually thereafter (optional: one additional follow-up screening 6 months after the first test). • If the results of 3 consecutive screenings are normal, screening every 3 years. **FLWHIV ≥30 years:** • Either cervical cytology testing or co-testing is recommended. *If cervical cytology screening:* • All guidelines are the same as for FLWHIV < 30 years. *If co-testing*: • Co-testing can be done at the time of diagnosis or at age 30. • If the first co-test is negative, patients can screen again in 3 years. Screening continues throughout their life.
CDC, NIH, HIV-MA[4]	May, 2019	All guidelines are the same as for 2015, except: • For an ASC-US cervical cytology test result, if reflex HPV testing is positive, a repeat cervical cytology test in 6-12 months or repeat co-testing in 12 months is recommended.

[1] Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. MMWR 2009;58(No. RR-4):[68-69].

[2] Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Available at https://clinicalinfo.hiv.gov/sites/default/files/guidelines/archive/Adult_OI003389.pdf. [p 1-2]

[3] Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Available at https://clinicalinfo.hiv.gov/sites/default/files/guidelines/archive/Adult_OI003407.pdf. [p 1-2]

[4] Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Available at https://clinicalinfo.hiv.gov/sites/default/files/guidelines/archive/Adult_OI003615.pdf. [Q1-4]

Supplemental Table 2a. Cytology screening, co-testing, and total cervical cancer screening rates among females living with HIV, overall and by calendar year, age, race and ethnicity, and comorbidity score at Kaiser Permanente Washington, 2010-2019.

	Number of cervical cancer screening tests during follow-up[1,5]			Person-years	Screening rates per 100 person-years			Crude total screening rate ratio (95% CI)[3]	Adjusted total screening rate ratio (95% CI)[3,4]
	Cytology	Co-tests	Total		Cytology	Co-tests	Total		
Total	161	158	345	604	26.7	26.2	57.1	-	-
Calendar Years									
2010-2013	103	3	113	193	53.4	1.6	58.5	1.0 (Ref)	1.0 (Ref)
2014-2016	47	37	92	169	27.7	21.8	54.1	0.93 (0.78, 1.10)	0.96 (0.81, 1.14)
2017-2019	11	118	140	242	4.6	49.0	58.1	0.99 (0.83, 1.17)	1.02 (0.86, 1.22)
Age (Years)									
18-29	16	3	19	41	39.0	7.3	46.3	1.0 (Ref)	1.0 (Ref)
30-39	42	48	103	133	31.6	36.1	77.4	1.68 (0.99, 2.85)	1.67 (0.98, 2.84)
40-49	73	53	137	239	30.5	22.2	57.3	1.24 (0.73, 2.12)	1.24 (0.73, 2.12)
50-65	30	52	84	176	17.1	29.6	47.7	1.04 (0.61, 1.78)	1.03 (0.60, 1.77)
66-89	0	2	2	15	0.0	13.3	13.3	0.30 (0.07, 1.26)	0.30 (0.07, 1.27)
Race and Ethnicity[2]									
Non-Hispanic Black	65	81	150	241	27.0	33.6	62.2	1.0 (Ref)	1.0 (Ref)
Hispanic	14	16	31	62	22.6	25.8	50.0	0.81 (0.63, 1.04)	0.84 (0.65, 1.09)
Non-Hispanic White	63	48	112	223	28.3	21.5	50.2	0.88 (0.71, 1.08)	0.92 (0.75, 1.12)
Non-Hispanic Asian/ Pacific Islander	7	5	13	24	29.2	20.8	54.2	0.88 (0.55, 1.39)	0.91 (0.57, 1.43)
Non-Hispanic Multiracial & Other	7	3	10	20	35.0	15.0	50.0	0.81 (0.42, 1.56)	0.87 (0.47, 1.60)
Comorbidity Score[2]									
0-6	117	115	250	444	26.4	25.9	56.3	1.0 (Ref)	1.0 (Ref)
7-8	16	22	41	67	23.9	32.8	61.2	1.09 (0.86, 1.38)	1.15 (0.91, 1.46)
9+	8	6	14	36	22.2	16.7	38.9	0.70 (0.32, 1.50)	0.83 (0.42, 1.62)

[1]Receipt of cervical cancer screening was defined as receipt of a cytology test, co-test, or unknown modality of cervical screening test. This definition did not include vaginal cytology tests, nor cytology tests received on the same day as a biopsy, colposcopy, or excision as they were considered to be diagnostic tests. Cytology tests designated as repeat tests, i.e., occurred within four months after an unsatisfactory screening test, were included in the definition of receipt of cervical cancer screening only if the repeat test was the first cervical cancer screening test received during analytic cohort follow up.

[2]Not included in the analyses according to race and ethnicity were n=29 cervical cancer screening tests with missing race and ethnicity data; and not included in analyses according to comorbidity score were n=40 cervical cancer screening tests with missing comorbidity score.

[3]Generalized estimating equation (GEE) models with Poisson regression was used to estimate screening rate ratios and 95% confidence intervals. GEE was used to account for within-person correlation due to females receiving more than one cervical cancer screening test during follow up.

[4]Total screening rate ratios were adjusted for age, calendar year, and healthcare setting.

[5]The number of cytology and co-tests do not necessarily sum to the total number of cervical cancer screening tests because the total number of tests includes tests with unknown modality.

Supplemental Table 2b. Cytology screening, co-testing, and total cervical cancer screening rates among females living with HIV, overall and by calendar year, age, race and ethnicity, and comorbidity score at Mass General Brigham, 2010-2019

	Number of cervical cancer screening tests during follow-up[1,5]			Person-years	Screening rates per 100 person-years			Crude total screening rate ratio (95% CI)[3]	Adjusted total screening rate ratio (95% CI)[3,4]
	Cytology	Co-tests	Total		Cytology	Co-tests	Total		
Total	485	629	1,114	2,334	20.8	27.0	47.8	-	-
Calendar Years									
2010-2013	279	152	431	756	36.9	20.1	57.0	1.0 (Ref)	1.0 (Ref)
2014-2016	132	205	337	777	17.0	26.4	43.4	0.76 (0.68, 0.84)	0.77 (0.69, 0.86)
2017-2019	74	272	346	801	9.2	34.0	43.2	0.75 (0.66, 0.85)	0.79 (0.69, 0.89)
Age (Years)									
18-29	35	11	46	94	37.2	11.7	48.9	1.0 (Ref)	1.0 (Ref)
30-39	77	110	187	335	23.0	32.8	55.8	1.11 (0.85, 1.44)	1.08 (0.83, 1.40)
40-49	162	190	352	682	23.8	27.9	51.7	1.05 (0.81, 1.36)	1.02 (0.79, 1.31)
50-65	199	302	501	1,063	18.7	28.4	47.1	0.96 (0.74, 1.24)	0.95 (0.74, 1.22)
66-89	12	16	28	161	7.5	9.9	17.4	0.35 (0.21, 0.59)	0.36 (0.22, 0.59)
Race and Ethnicity[2]									
Non-Hispanic Black	241	328	569	1,121	21.5	29.3	50.8	1.0 (Ref)	1.0 (Ref)
Hispanic	133	177	310	671	19.8	26.4	46.2	0.92 (0.78, 1.08)	0.94 (0.80, 1.11)
Non-Hispanic White	72	92	164	416	17.3	22.1	39.4	0.78 (0.62, 1.00)	0.83 (0.65, 1.04)
Non-Hispanic Asian/ Pacific Islander	20	22	42	52	38.5	42.3	80.8	1.61 (0.96, 2.68)	1.56 (0.92, 2.65)
Non-Hispanic Multiracial & Other	13	10	23	58	22.4	17.2	39.7	0.79 (0.49, 1.27)	0.85 (0.59, 1.25)
Comorbidity Score									
0-6	262	278	540	1,076	24.4	25.8	50.2	1.0 (Ref)	1.0 (Ref)
7-8	171	246	417	911	18.8	27.0	45.8	0.91 (0.80, 1.04)	0.94 (0.82, 1.08)
9+	52	105	157	347	45.2	30.3	45.2	0.87 (0.67, 1.14)	1.00 (0.77, 1.30)

[1]Receipt of cervical cancer screening was defined as receipt of a cytology test, co-test, or unknown modality of cervical screening test. This definition did not include vaginal cytology tests, nor cytology tests received on the same day as a biopsy, colposcopy, or excision as they were considered to be diagnostic tests. Cytology tests designated as repeat tests, i.e., occurred within four months after an unsatisfactory screening test, were included in the definition of receipt of cervical cancer screening only if the repeat test was the first cervical cancer screening test received during analytic cohort follow up.

[2]Not included in the analyses according to race and ethnicity were n=6 cervical cancer screening tests with missing race and ethnicity data.

[3]Generalized estimating equation (GEE) models with Poisson regression was used to estimate screening rate ratios and 95% confidence intervals. GEE was used to account for within-person correlation due to females receiving more than one cervical cancer screening test during follow up.

[4]Total screening rate ratios were adjusted for age, calendar year, and healthcare setting.

[5]The number of cytology and co-tests do not necessarily sum to the total number of cervical cancer screening tests because the total number of tests includes tests with unknown modality.

Supplemental Table 2c. Cytology screening, co-testing, and total cervical cancer screening[1] rates among Females Living with HIV, overall and by calendar year, age, race and ethnicity, and comorbidity score at Parkland Health, 2010-2019

[1]Receipt of cervical cancer screening was defined as receipt of a cytology test, co-test, or unknown modality of cervical screening test. This definition did not include vaginal cytology tests, nor cytology tests received on the same day as a biopsy, colposcopy, or excision as they were considered to be diagnostic tests. Cytology tests designated as repeat tests, i.e., occurred within four months after an unsatisfactory screening test, were included in the definition of receipt of cervical cancer screening only if the repeat test was the first cervical cancer screening test received during analytic cohort follow up.

	Number of cervical cancer screening tests during follow-up[1,4]			Person-years	Screening rates per 100 person-years			Crude total screening rate ratio (95% CI)[3]	Adjusted total screening rate ratio (95% CI)[3,4]
	Cytology	Co-tests	Total		Cytology	Co-tests	Total		
Total	5,432	813	6,245	15,667	34.7	5.2	39.9	-	-
Calendar Years									
2010-2013	2,395	202	2,597	5,336	44.9	3.8	48.7	1.0 (Ref)	1.0 (Ref)
2014-2016	1,778	204	1,982	5,167	34.4	3.9	38.4	0.79 (0.75, 0.82)	0.80 (0.77, 0.84)
2017-2019	1,259	407	1,666	5,164	24.3	7.9	32.2	0.66, 0.63, 0.70)	0.68 (0.65, 0.72)
Age (Years)									
18-29	819	106	925	2,101	39.0	5.1	44.0	1.0 (Ref)	1.0 (Ref)
30-39	1,519	241	1,760	4,031	37.7	6.0	43.7	1.01 (0.93, 1.08)	1.02 (0.94, 1.09)
40-49	1,685	271	1,956	4,433	38.0	6.1	44.1	1.01 (0.93, 1.09)	1.03 (0.95, 1.11)
50-65	1,312	178	1,490	4,494	29.2	4.0	33.2	0.76 (0.69, 0.83)	0.79 (0.72, 0.86)
66-89	97	17	114	608	16.0	2.8	18.8	0.43 (0.33, 0.55)	0.46 (0.36, 0.60)
Race and Ethnicity[2]									
Non-Hispanic Black	3,645	605	4,250	11,049	33.0	5.5	38.5	1.0 (Ref)	1.0 (Ref)
Hispanic	1,159	152	1,311	2,695	43.0	5.6	48.6	1.27 (1.17, 1.37)	1.27 (1.18, 1.37)
Non-Hispanic White	489	41	530	1,564	31.3	2.6	33.9	0.88 (0.78, 0.99)	0.89 (0.79, 1.00)
Non-Hispanic Asian/ Pacific Islander	111	12	123	249	44.6	4.8	49.4	1.29 (1.00, 1.66)	1.34 (1.07, 1.68)
Non-Hispanic Multiracial & Other	6	2	8	26	23.1	7.7	30.8	0.81 (0.34, 1.92)	0.77 (0.34, 1.76)
Comorbidity Score									
0-6	2,255	322	2,577	6,001	37.6	5.4	43.0	1.0 (Ref)	1.0 (Ref)
7-8	2,222	329	2,551	6,268	35.5	5.2	40.7	0.95 (0.89, 1.01)	0.99 (0.93, 1.05)
9+	955	162	1,117	3,398	28.1	4.8	32.9	0.76 (0.70, 0.83)	0.88 (0.81, 0.97)

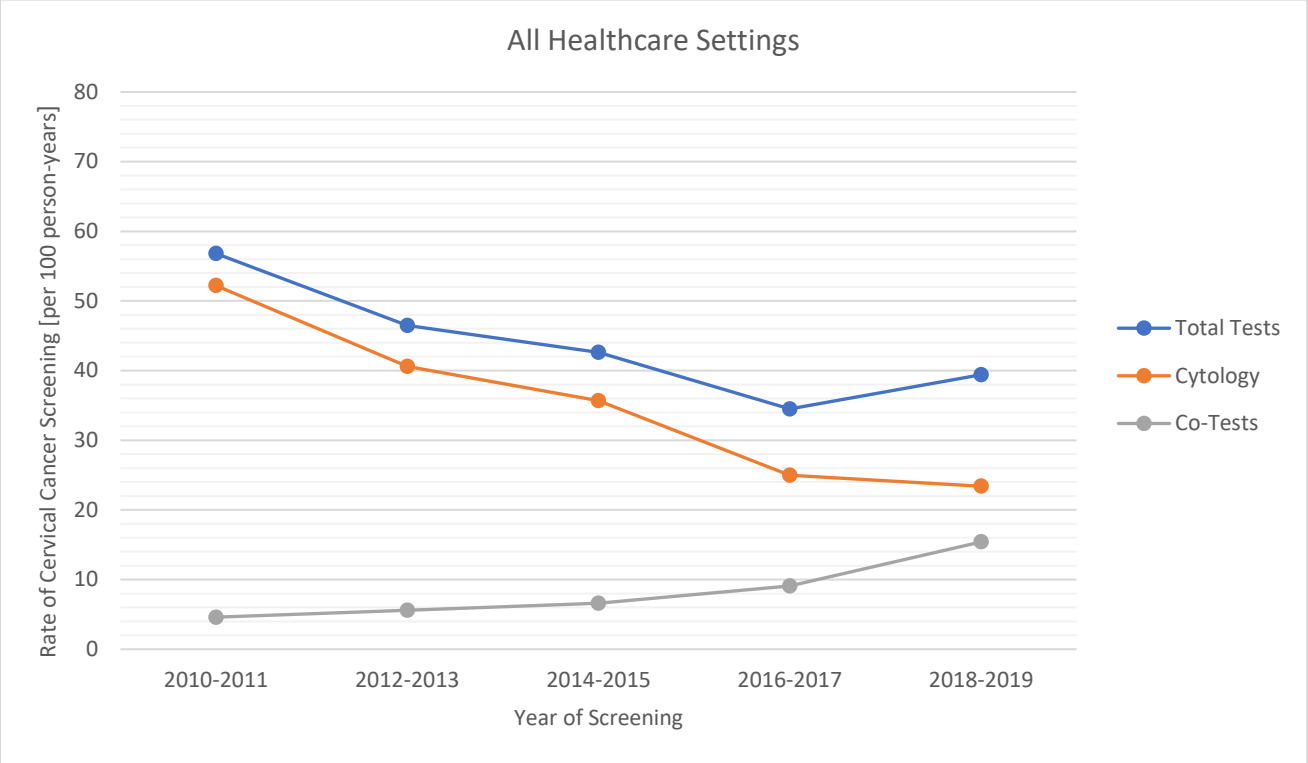
[2]Not included in the analyses according to race and ethnicity were n=23 cervical cancer screening tests with missing race and ethnicity data.

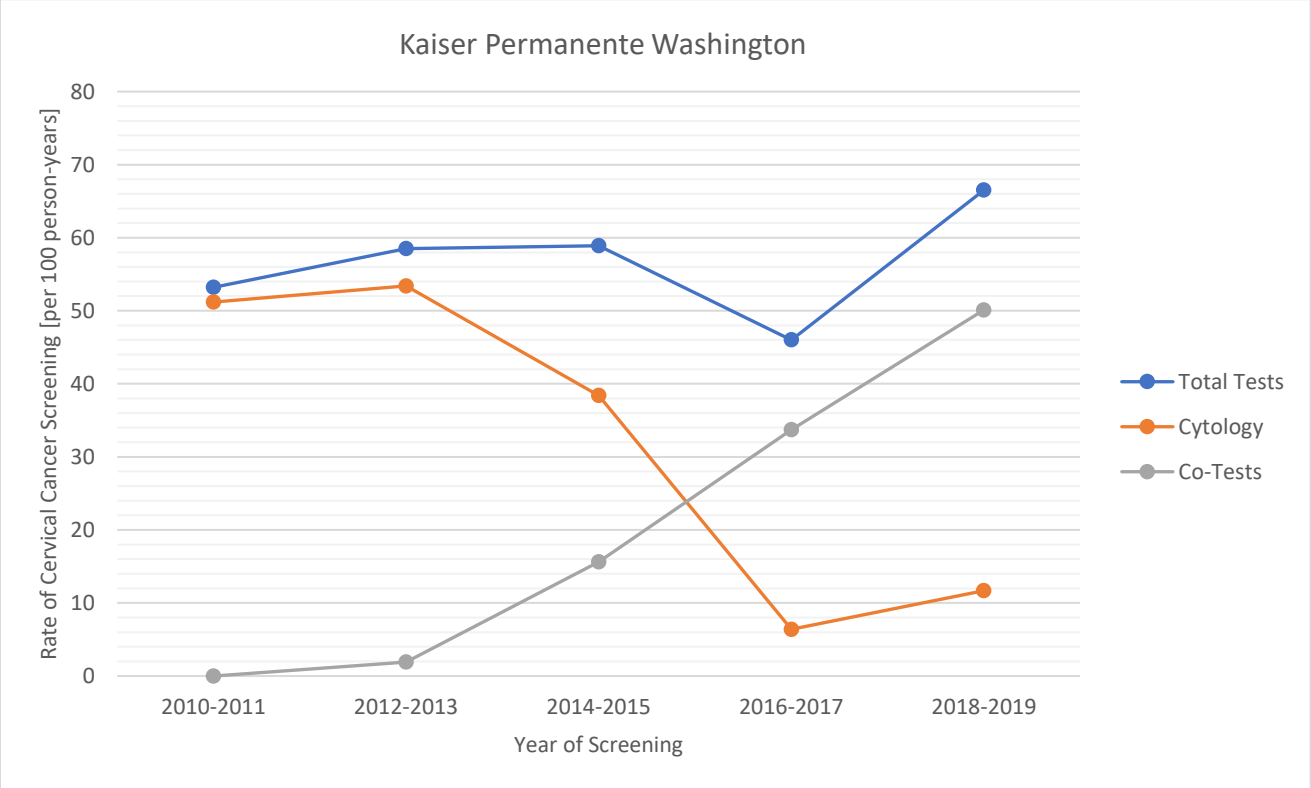
[3]Generalized estimating equation (GEE) models with Poisson regression was used to estimate screening rate ratios and 95% confidence intervals. GEE was used to account for within-person correlation due to females receiving more than one cervical cancer screening test during follow up.

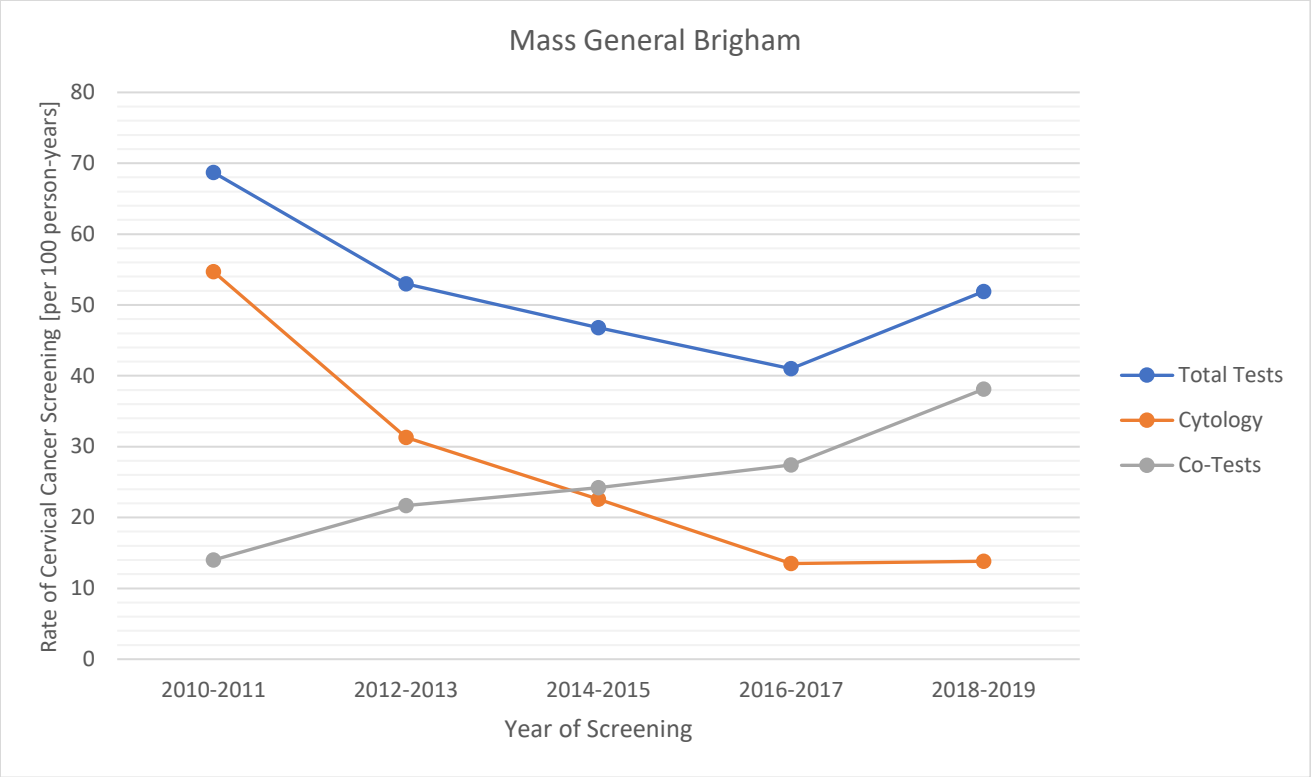
[4]Total screening rate ratios were adjusted for age, calendar year, and healthcare setting.

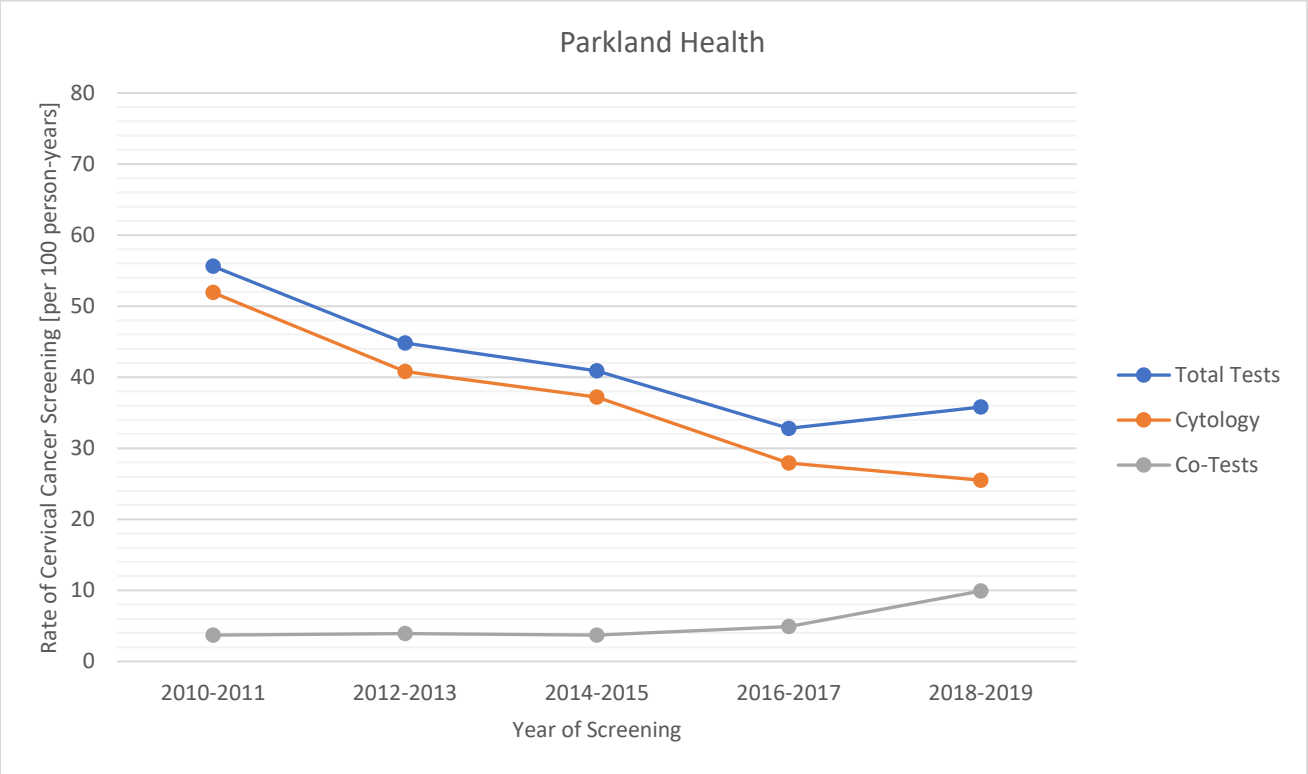
[5]The number of cytology and co-tests do not necessarily sum to the total number of cervical cancer screening tests because the total number of tests includes tests with unknown modality.

Supplemental Figure 2. Age-adjusted rates of cervical cancer screening among females living with HIV at three US healthcare settings during 2010-2019, overall and by screening modality.[1]









[1]Rates were age-adjusted to the age distribution of the total study population during 2010-2019.