Identifying opportunities to reduce cervical cancer prevention disparities in Western Washington

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Abstract

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Cervical cancer screening (CCS) and human papillomavirus (HPV) vaccination are at the heart of the global cervical cancer elimination movement. However, in the United States (US), less than two thirds of age-eligible adolescents are up to date for HPV vaccination, and screening coverage among minorities and immigrants is still low. This dissertation addressed critical knowledge gaps in CCS adherence among East African immigrants and the association of maternal screening adherence with adolescent HPV vaccination. In addition, it predicted the impact of screening by self-sampling on the burden of cervical cancer among East African immigrants in Washington State.

The first chapter examined cervical cancer screening adherence and its correlates among 1,664 East African immigrant females aged 25-65 years with ≥1 primary care clinic visit(s) between 2017 and 2018, using electronic health record (EHR) data from University of Washington (UW) Medicine. It also included an analysis of the screening uptake of overdue women who were retrospectively followed for 12 months. Adherence to cervical cancer screening was 63%, and older age, longer duration of care, higher visit frequency, index visit in an obstetrics and

gynecology clinic, having an assigned primary care provider, and breast and colorectal cancer screening adherence were associated with higher CCS adherence. Low body mass index was associated with lower screening adherence. Only 9% of overdue women were screened within 12 months of follow-up, and having commercial health insurance compared to having Medicare/Medicaid was associated with higher screening uptake.

The second chapter also used EHR data and assessed the association between maternal CCS and adolescent HPV vaccination among adolescent-mother pairs who had ≥1 primary care visit at UW Medicine between 2018 and 2020. It also assessed the associations between maternal breast cancer screening adherence and HPV vaccination, and maternal receipt of a recent wellness visit with HPV vaccination. For the association of maternal CCS and adolescent HPV vaccination, effect modifications by adolescent sex, maternal language interpreter use, and provider characteristics were further evaluated. Of 4,121 identified adolescents, 3,395 (82%) initiated HPV vaccination, and 2,020 (49%) completed the series. CCS adherence and recent maternal wellness visit were associated with higher HPV vaccination. There was no statistically significant association between maternal breast cancer screening and HPV vaccination. The associations of maternal CCS and adolescent HPV vaccination were stronger for male vs. female adolescents, adolescents with a primary care provider with a specialty in Family Practice vs. Pediatrics, and adolescents with the same primary care provider as their mother's vs. not.

The third chapter estimated the impact of screening by self-sampling relative to primary HPV testing via provider collection as the standard of care on cervical cancer incidence and mortality among East African immigrants using a Markov cohort state-transition model for the natural history of high-risk HPV. A hypothetical cohort of 10,000 East African immigrant women aged 25 years was followed until age 80, and outcomes for various scenarios of screening coverage and colposcopy adherence were compared across the screening strategies. Keeping the colposcopy adherence for self-sampling lower than the standard of care based on empirical evidence balanced out the potential gains in screening coverage; cancer incidence and mortality

were not significantly different across the strategies except when self-sampling coverage increased to 100%. Screening by self-sampling yields lower incidence and mortality of cervical cancer relative to the standard of care when both strategies have equal colposcopy adherence.

Overall, cervical cancer screening adherence among East African immigrants was lower than the national average of 80%, and patients with frequent and long-term connections to the health system had higher screening coverage. As our model predicted, self-sampling can be a better alternative for CCS if followed by increased screening coverage and high compliance for follow-up testing. Nevertheless, it can still be an option for under-screened people who could not get screened otherwise. More importantly, since maternal adherence to cervical cancer screening along with attendance to wellness visits had a positive association with HPV vaccination, leveraging healthcare encounters in addition to designing culturally tailored interventions could potentially improve both CCS adherence and adolescent HPV vaccination.

Table of Contents

List of tables

List of figures

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Chapter 1: Adherence and correlates of cervical cancer screening among East African immigrants in Washington State

Abstract

Introduction: East African immigrants in the United States have persistently low cervical cancer screening (CCS) rates. To inform future interventions to increase screening, we investigated adherence and correlates of adherence to CCS among East African immigrants in western Washington State.

Method: University of Washington (UW) Medicine electronic health records were examined to identify females aged 25-65 years with ≥1 primary care clinic visit(s) between 2017 and 2018. East African immigrants were identified based on self-reported language, country of birth and/or ethnicity. CCS adherence was defined as a documented Pap test within ≤3 years or human papillomavirus (HPV) and Pap co-testing within ≤5 years. Potential correlates of adherence included age, requiring a language interpreter, comorbidity, social vulnerability, provider sex, duration of care, primary care visit frequency, body mass index (BMI), health insurance type, type of clinic for the index visit, having an assigned primary care provider (including provider type and specialty), and (if age-eligible) screening for breast and colorectal cancers. We further assessed screening uptake by following overdue women for 12 months. We imputed missing data using the Multiple Imputation by Chained Equation method. We used Poisson regression with robust standard errors to identify correlates of adherence and uptake and explore effect modification by provider sex.

Results: We identified 1,664 women, including 851 (57%) born in Ethiopia, 458 (30%) born in Somalia, and 156 (10%) born in Eritrea. About two-thirds (63%) were adherent to cervical cancer screening. Variables associated with higher CCS adherence included older age (adjusted prevalence ratio (APR) - 1.47: 95% confidence interval (CI) 1.14, 1.90 and 1.38: 95%CI: 1.05, 1.80, respectively, for patients ages 30-39 and 40-49 vs 25-29 years), longer duration of care

(APR - 1.22: 95%CI: 1.03, 1.45, comparing >10 vs <5 years), higher visit frequency (APR - 1.23: 95%CI: 1.04, 1.44 and 1.46: 95%CI: 1.24, 1.72, respectively, for 3-5 and ≥6 vs 1-2 visits), index visit in an obstetrics and gynecology clinic (APR - 1.26: 95%CI: 1.03, 1.55, compared to family practice), having an assigned primary care provider (APR - 1.35: 95%CI: 1.02, 1.79), breast cancer screening adherence (APR - 1.66: 95%CI: 1.27, 2.17), and colorectal cancer screening adherence (APR - 1.59: 95%CI: 1.24, 2.03). Low BMI was associated with lower screening adherence (APR - 0.50: 95%CI: 0.26, 0.96, comparing <18.5 kg/m^2 vs 18.5-24.5 kg/m^2). The use of a language interpreter was associated with lower screening adherence in the crude model (crude prevalence ratio (CPR) - 0.85: 95%CI: 0.75, 0.96), but not when it was adjusted for the duration of care (APR - 0.91: 95%CI: 0.79, 1.05). There was no effect modification by provider sex. In the analysis for correlates of screening uptake among the 608 (37%) overdue women, only 9% were screened in 12 months. Only health insurance type – having commercial health insurance compared to having Medicare/Medicaid was associated with higher uptake (adjusted risk ratio (ARR) - 2.44: 95%CI: 1.15, 5.18).

Conclusion: More than one third of East African immigrants were overdue for CCS. Women who interacted more frequently or had longer-term relationship with the healthcare system were more likely to get screened. Interventions focused on increasing healthcare access and utilization could potentially increase CCS, as could leveraging health encounters to address barriers faced by younger patients or those who have less familiarity with the health system.

Introduction

As a result of widespread expansion of cervical cancer screening programs, cervical cancer in high-income countries has decreased by 80% over the last several decades (1,2). In the US, 80.5% of women are up to date for cervical cancer screening, close to the 84.3% target of the Healthy People 2030 plan (3). However, of the more than 13,000 cases and 4,000 deaths annually, most are diagnosed among under-screened or never screened people (4). Also, screening coverage is inconsistent across subpopulations, and ethnic minorities and immigrants have lower healthcare utilization and the highest disease burden (5,6). Reducing disparities in cervical cancer screening in these populations will be essential to eliminating the burden of cervical cancer.

Evidence shows that cervical cancer screening adherence among Black or African American women is 85% - higher than the national average of 80% (7). However, non-US-born Black women are less likely to be screened for cervical cancer than US-born Black women (8,9). Amuta-Jimenez et al reported that US-born African American women are seven times more likely to adhere to cervical cancer screening than Black immigrant women (9). Black immigrants also have the lowest screening uptake compared with other immigrants (10), and immigrants from East Africa have the lowest screening uptake compared with other Black immigrants (11). A community-based survey done in Minnesota has reported that cervical cancer screening uptake among Somali immigrants was 32% lower than among other African immigrants and other studies conducted among Somali immigrants reported that only 45-50% of age-eligible women are ever screened for cervical cancer (12–14). Nevertheless, most of the evidence has been largely qualitative, based on surveys and self-reports, conducted among people in refugee camps, focused on only the Somali community, and/or limited by small sample sizes (13–16)

Prior studies have reported that barriers to screening for East African immigrants (EAIs) include language, acculturation, health insurance/cost, fear of abnormal results, poor awareness, cultural beliefs and traditions, and gender of healthcare providers (17–22). However, since most of these studies have involved people who had recently immigrated, there is a substantial gap in knowledge of barriers and facilitators of cervical cancer screening among EAIs who established their lives in the US and access health care. Most studies that have assessed the association between race and screening uptake have ignored participants' immigration status, and others that have considered immigration tend to merge people irrespective of their differences in country of origin (10,23). Importantly, immigrants are expected to be healthier during the early periods of immigration, but health benefits decline over time living in the US (24) . EAIs come from a region of the world with the highest cervical cancer incidence (40 cases per 100,000 per year (25)), a high HPV prevalence, and without routine screening (16,26,27). Due to the possibly high HPV infection rate, they have an increased risk of developing cervical cancer while staying longer in the US (28,29). As a result, there is a critical need to specifically target this population with interventions to increase screening and reduce the burden of cervical cancer.

However, few studies have evaluated cervical cancer-related prevention efforts specifically addressing EAI women (10,30), and EAIs have been underrepresented in most studies and national surveys. Therefore, estimating cervical cancer screening adherence and identifying barriers is crucially important to inform decision-making. In this study, using electronic health record (EHR) data from a large healthcare system in Washington State, we estimated adherence to cervical cancer screening among EAI women and identified possible barriers and facilitators.

Methods

We used both cross-sectional and retrospective cohort designs to evaluate cervical cancer screening adherence among 25- to 65-year-old EAI women. Using 2017-2019 electronic health record (EHR) data from the University of Washington (UW) Medicine, a large healthcare system, we first conducted a cross-sectional study to estimate adherence to cervical cancer screening and its correlates. Then, as a secondary analysis, we used a retrospective cohort study to evaluate 12-month screening uptake among overdue women. (Figure 1).

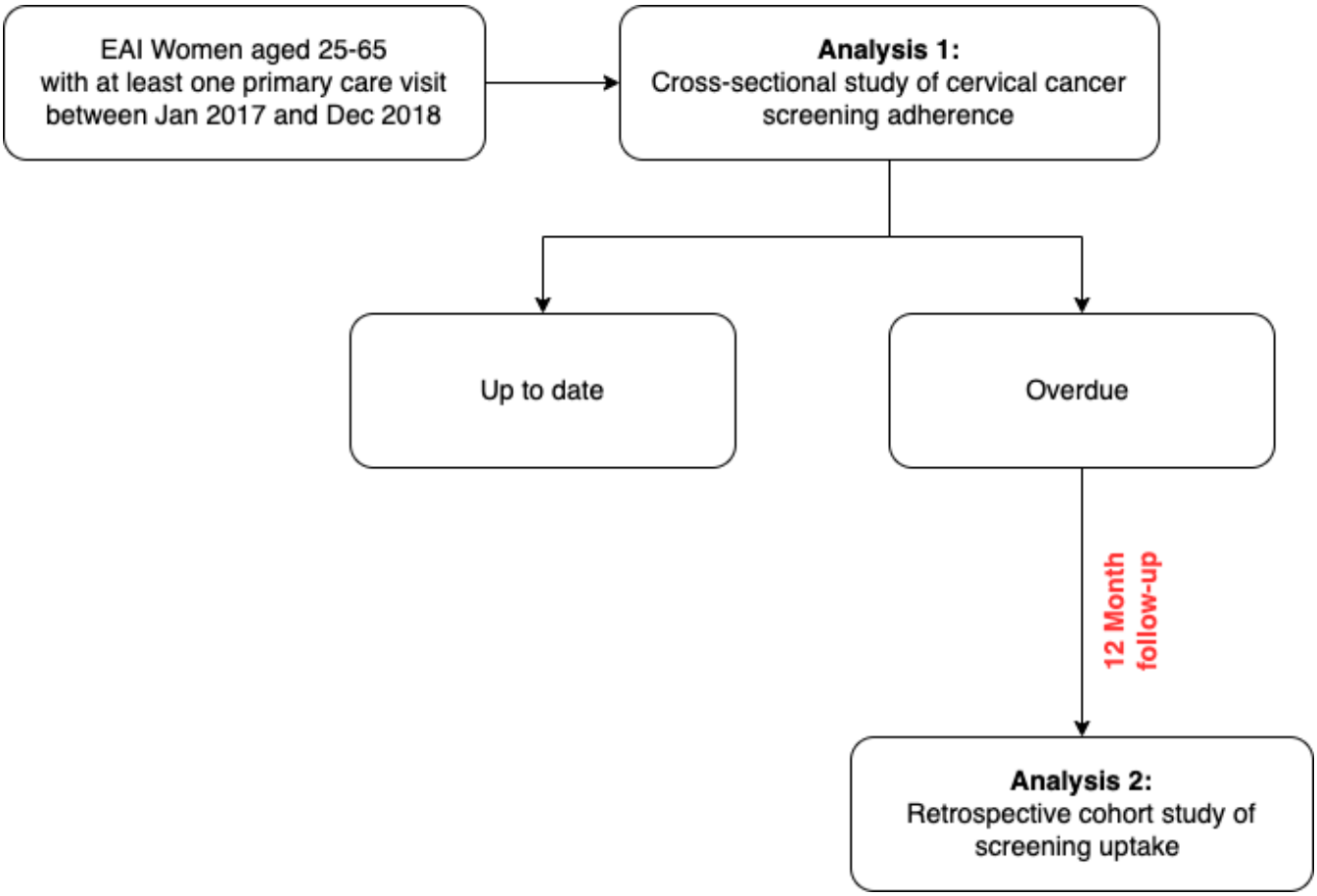


Figure 1. 1. Depiction of the study design for adherence and correlates of CCS among EAIs

Study setting, population, and procedure

UW Medicine is the largest health system in Washington State, incorporating three hospitals and 16 neighborhood clinics encompassing over 300 outpatient care sites, providing over 1.6 million annual outpatient visits (31). We identified EAI women aged 25-65 who had ≥1 primary care visit at the UW Medicine hospitals and neighborhood clinics between January 1, 2017, and December 31, 2018. A primary care clinic visit was defined as a completed in-person visit in either obstetrics and gynecology (OBGY), family medicine, or internal medicine and provided by an MD (Medical Doctor), DO (Doctor of Osteopathic Medicine), MBBS/ MBChB/ MBBCH (Bachelor of Medicine, Bachelor of Surgery), NP (Nurse Practitioner), DNP (Doctor of Nursing Practice), or PA (Physician Assistant). The last primary care visit was considered the index visit. Our operational definition of EAI included meeting ≥1 of the following criteria: country of birth recorded as Somalia, Ethiopia, or Eritrea; primary language as Amharic, Oromo, Somali, Tigrigna, Maay Maay, Afar, Hadiyya, Harari, Kunama, Saho, or Ethiopian (unspecified dialect); or self-identified ethnicity as Ethiopian, Somali, Eritrean, Amhara, Oromo, or Tigre. Individuals who had documented hysterectomy were excluded. The study was approved by the Institutional Review Board (IRB) of the University of Washington.

Outcome and correlates

We identified cervical cancer screening status from the EHR using the Current Procedure Terminology (CPT) and International Classification of Disease (ICD)-10 diagnostic codes. The recommendation for cervical cancer screening per the contemporary guideline was cytology (Pap test) every three years for women aged 25-65 or co-testing (Pap test and HPV testing) every five years for women aged 30-65 years (32). Therefore, the outcome for the cross-sectional analysis, screening adherence, was defined as a Pap test within three years or a co-test (Pap and HPV tests) within five years before the index visit. For individuals with HIV, screening adherence was

defined as co-testing or Pap within three years (33). Women who had no screening record, or no Pap test within three years and no co-test within five years (within three years in the case of HIV positive patients) prior to the index visit were considered overdue. The outcome of the secondary longitudinal analysis was the uptake of cervical cancer screening within 12 months after the index visit among women who were overdue.

The correlates of interest were sociodemographic variables including age (25-29, 30-39, 40-49, and 50-65 years), using a language interpreter (yes/no), and neighborhood socioeconomic status (NSES - defined based on the participant's address linked with the 2018 CDC estimated geocoded neighborhood deprivation index, classified in terciles as poorest, middle, and least poor (34)); health-related variables including body mass index (BMI) (<18.5, 18.5-24.9, 25-29.9, and ≥30 kg/m^2), HIV status, comorbidity (0, 1, 2, 3+; based on Charlson's comorbidity index) (35); healthcare access-related variables including health insurance type (Medicare/Medicaid, commercial, self-pay or other), duration of care at UW Medicine (time since intitial encounter classified as <5 years, 5-10 years, and >10 years), frequency of clinic visits within the prior two years (classified as 1 to 2, 3 to 5, and more than 5), type of clinic visited during the index visit (family medicine, internal medicine, infectious diseases, or OB/GYN), and having an assigned primary care provider (PCP) (yes, no); and primary care provider-related variables including primary care provider sex (male, female, unknown), provider type (physician, nurse practitioner, physician assistant), and specialty. The primary care provider was either most recently assigned or the index visit provider if there was no assigned primary care provider.

We also explored associations of guideline-recommended screening for breast cancer (adherent if had mammography within two years, restricted to age ≥52 years) and colorectal cancers (Fecal Occult Blood Test (FOBT) or Fecal Immunochemical Test (FIT) within one-year, flexible sigmoidoscopy or colonography within 5 years, or colonoscopy within ten years, restricted to age ≥51 years) (36,37).

Statistical analysis

For the cross-sectional analysis, we fitted Poisson regression models with robust standard errors to estimate prevalence ratios for the associations of screening adherence with the correlates. We fitted a model incorporating all the correlates. The only exception was for HIV/AIDS and comorbidity where we fitted separate adjusted models for comorbidity that included all the other correlates except HIV/AIDS and vice versa. We also separately fitted models for the association of breast cancer and colorectal cancer screening adherence with CCS adherence among age-eligible women, adjusting for all the correlates.

Variables with missing observations were identified, and Multiple Imputation by Chained Equation (MICE) method was used to impute the selected variables with missing observations (38). We ran the imputation to get 10 imputed datasets for 50 iterations. Before the imputation was run, categorical variables were labeled as factors. The imputed variables were NSES and BMI (*Supplemental Table 1.1)*. The analysis from the multiple imputation datasets was considered the primary approach. We also conducted a complete case analysis and compared estimates as a sensitivity analysis.

As part of the sensitivity analysis, we evaluated associations after redefining the outcome – CCS adherence – as having a Pap test in 3.5 years or a co-test within 5.5 years of the index visit (i.e., adding a 6-month grace period). We also did additional analysis restricting the population to only individuals who received care from UW Medicine for at least five years.

For the retrospective cohort analysis, we calculated the uptake of screening within 12 months after the index visit among overdue women. We fitted Poisson regression models with robust standard errors to assess the association of uptake with the correlates. We applied the same

approach as the cross-sectional analysis, except we adjusted for baseline cervical cancer screening history (categorized as ever screened or never screened).

In all analyses, we used an alpha value of 0.05 to determine statistical significance.

Results

Sociodemographic characteristics

We identified 1,664 EAI women aged 25-65 who had at least one primary care visit between 2017 and 2018 and no documented history of hysterectomy (Figure 2).

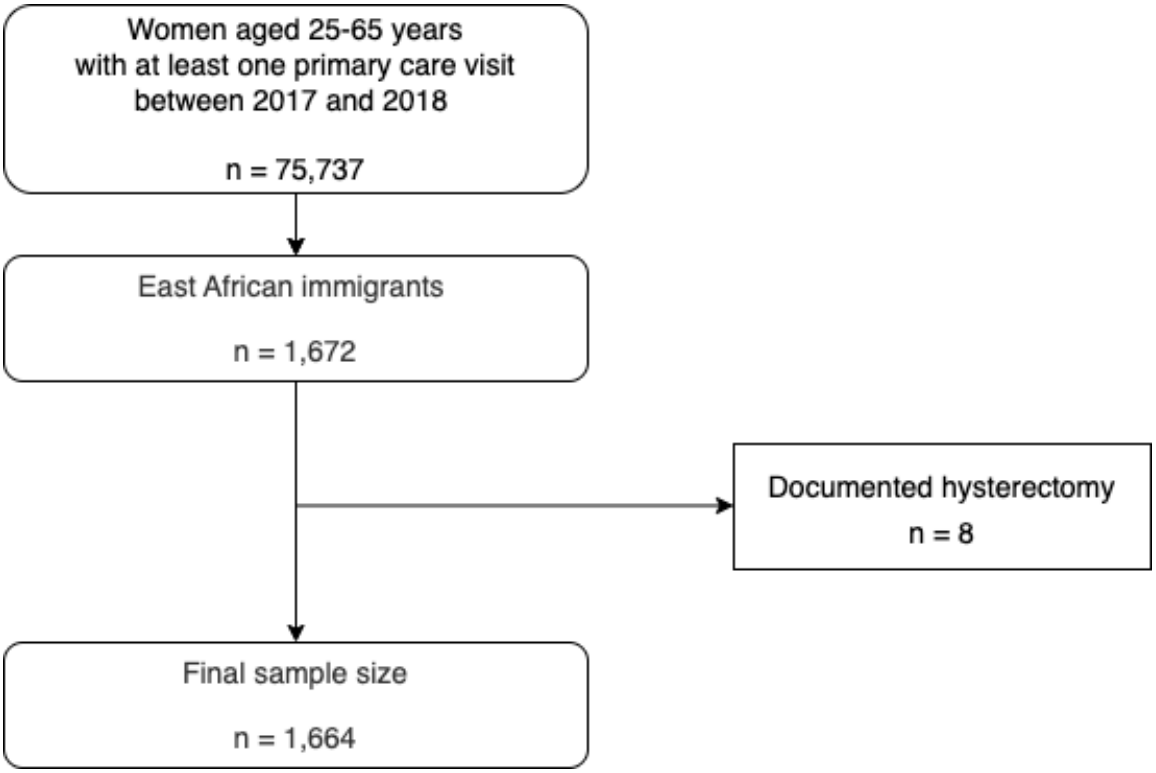


Figure 1. 2. Flow diagram for the selection and inclusion of eligible EAI women

The mean age of patients was 44 (standard deviation (SD) ±11) years. More than two thirds (69%) received care from UW Medicine for at least five years. The majority (57%) were born in Ethiopia, 30% in Somalia, and 10% in Eritrea. More than half of the patients (53%) used a language interpreter to get medical care (Table 1).

Cervical Cancer Screening Adherence

Of the 1,664 women, 1,056 (63%) were adherent to cervical cancer screening (95%CI: 61%, 66%) . Among the 608 who were overdue for screening, 397 (65%) had no prior history of screening documented - 60% of those without documented history of screening received care for less than 5 years. Women aged 25-29 had the lowest CCS adherence (45%), and those aged 40-49 had the highest adherence (71%). Fifty-nine percent of women who used a language interpreter were adherent, compared to 69% of those who did not use a language interpreter (Table 1).

Table 1. 1. Sociodemographic and healthcare-related characteristics of individuals

Characteristic		N = 1,664	Up to date***, N = 1,05 6
Age			
	25-29	159	72 (45%)
	30-39	528	365 (69%)
	40-49	414	294 (71%)
	50-65	563	325 (58%)
NSES quintile*			
	Least poor	146	98 (67%)
	Middle	1,090	692 (63%)
	Poorest	329	202 (61%)
	Missing	99	64
Language interpreter flag			
	No	790	544 (69%)

	Yes	874	512 (59%)
Country of birth			
	Ethiopia	851	574 (67%)
	Somalia	458	288 (63%)
	Eritrea	156	97 (62%)
	Others	39	21 (54%)
	Missing	160	76
Body mass index (BMI)			
	<18.5 Kg/m^2	26	7 (27%)
	18.5-24.5 Kg/m^2	365	238 (65%)
	24.5-30 Kg/m^2	601	390 (65%)
	>30 Kg/m^2	524	340 (65%)
	Missing	148	81
Charlson's comorbidity index			
	0	1,099	702 (64%)
	1	387	249 (64%)
	2	123	69 (56%)
	3+	55	36 (65%)
HIV/AIDS			
	No	1,578	996 (63%)
	Yes	86	60 (70%)
Health insurance type			
	Medicare/Medicaid	876	558 (64%)
	Commercial	454	306 (67%)
	Self-Pay/Other	334	192 (57%)
Duration of care at the UW			
	< 5 years	512	266 (52%)
	5-10 years	385	247 (64%)
	>10 years	767	543 (71%)
Frequency of primary care visits in prior two years			
	1 to 2	586	311 (53%)
	3 to 5	520	333 (64%)
	≥6	558	412 (74%)
Index visit clinic type			
	Family Medicine	667	398 (60%)
	Infectious Diseases	78	49 (63%)
	Internal Medicine	326	207 (63%)
	International Medicine	284	180 (63%)
	Obstetrics and Gynecology	309	222 (72%)

Have assigned primary care provider		
No	148	70 (47%)
Yes	1,516	986 (65%)
Sex of primary care provider		
Female	1,317	858 (65%)
Male	347	198 (57%)
Primary care provider type		
Physician	1,390	880 (63%)
Nurse Practitioner	183	115 (63%)
Physician Assistant	49	32 (65%)
Other	42	29 (69%)
Primary care provider specialty		
Family Practice	729	447 (61%)
Internal Medicine	594	403 (68%)
Obstetrics/Gynecology	131	92 (70%)
Other	210	114 (54%)

* *Neighborhood socioeconomic status* (34)
***Charlson's comorbidity index* (35)*;*
****The percentages are row percentages for adherence to cervical cancer screening for categories under each variable.*

Associations with cervical cancer screening adherence

The variables that had a statistically significant association with CCS adherence in the adjusted model were age, duration of care at UW Medicine, BMI, frequency of primary care visits in the prior two years, clinic type and having an assigned primary care provider. Compared to individuals aged 25-29, those aged 30-39 had a 42% higher adherence (APR - 1.42: 95% CI:1.10, 1.83), and those aged 40-49 had a 41% higher adherence (APR - 1.41: 95% CI: 1.08, 1.85). Compared to individuals who had established care for less than five years, those who had received care for more than 10 years had a 22% higher adherence (APR - 1.22: 95% CI: 1.03, 1.45). Individuals with a BMI of less than 18.5 Kg/m^2 had 50% lower adherence than those with a normal BMI (18.5-24.5 kg/m^2) (APR - 0.47: 95% CI: 0.24, 0.93). Compared to individuals who had 1 to 2 primary care visits in the prior two years, those who had 3 to 5 visits had a 23% higher adherence (APR - 1.23: 95% CI: 1.03, 1.45) and those with more than five visits had a 47% higher adherence (APR

- 1.47: 95% CI: 1.25, 1.74). Individuals whose index visit was in an obstetrics and gynecology clinic had a 27% higher adherence (APR - 1.27: 95% CI: 1.03, 1.55) than those who visited a family medicine clinic. Individuals with an assigned primary care provider had a 35% higher adherence (APR - 1.35: 95% CI: 1.02, 1.79) than those without an assigned provider. Language interpreter flag had a statistically significant association with adherence in the crude model (CPR - 0.85: 95% CI: 0.75, 0.96), but in the adjusted model, the association became attenuated and nonsignificant (APR - 0.91: 95% CI: 0.78, 1.05) (Figure 3).

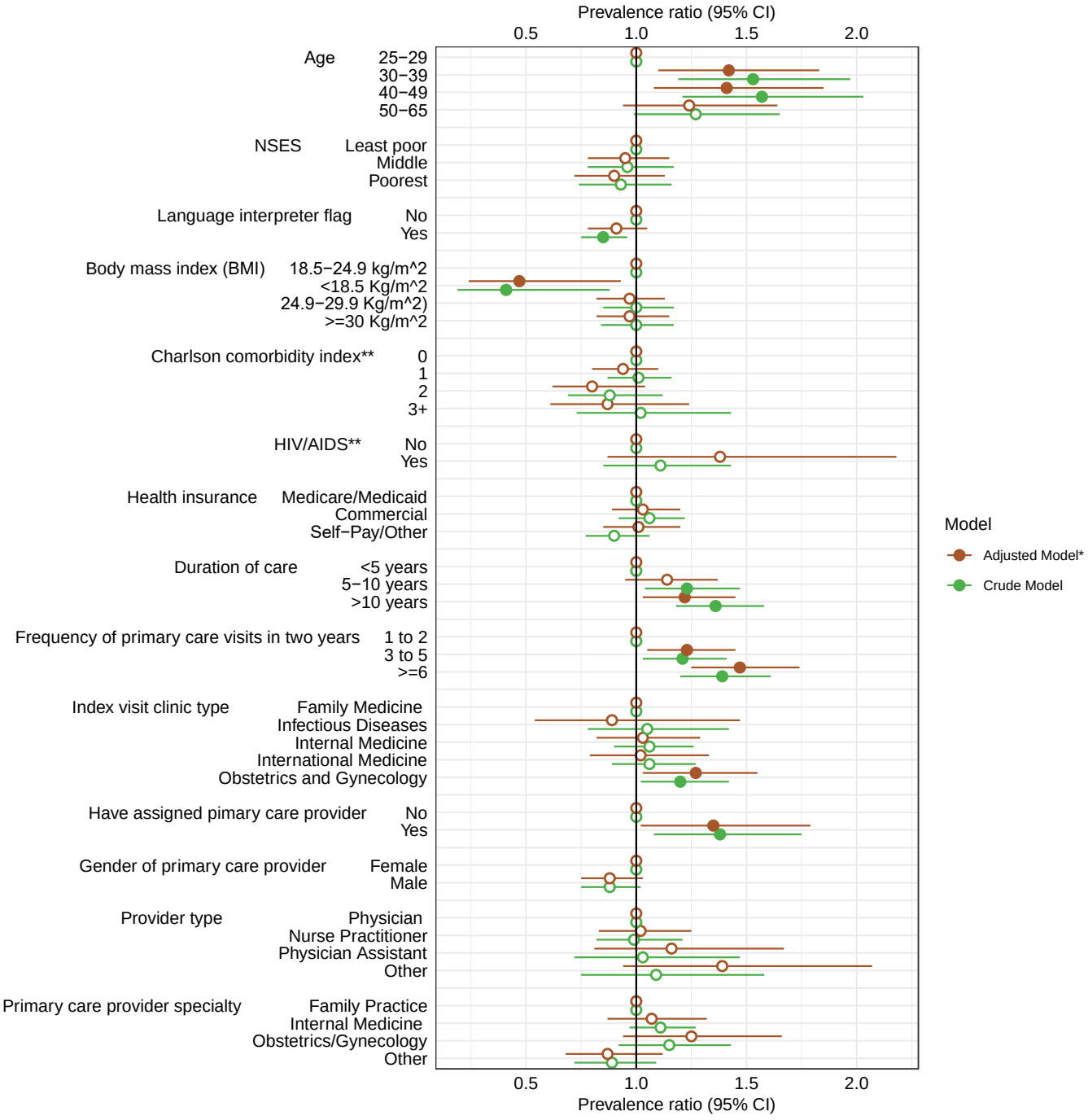


Figure 1. 3. Correlates of CCS adherence among EAIs in western Washington State.

**The adjusted model was fitted by including all the variables in a single model.*
***In the adjusted models for HIV and comorbidity, one was not included on the adjusted model of the other, but all the other variables were included.*

In a separate analysis among age-eligible women, breast cancer and colorectal cancer screening adherence each had a statistically significant association with CCS adherence. Among women aged ≥52 years (n=484), breast cancer screening adherence was associated with a 65% higher CCS adherence (APR - 1.65: 95% CI: 1.25, 2.17), and colorectal cancer screening adherence (n=524, age ≥51) was associated with a 56% higher CCS adherence (APR – 1.56: 95% CI: 1.21, 2.00) (Table 2).

Table 1. 2. The association of breast and colorectal cancer screening with CCS adherence

Characteristic	Overdue	Up to date	CPR	95% CI	APR	95% CI
Breast cancer screening (N=484, Age≥52)						
Overdue	153 (57%)	117 (43%)	ref.	ref.	ref.	ref.
Up to date*	56 (26%)	158 (74%)	1.70	1.34, 2.16	1.65	1.25, 2.17
Colorectal cancer screening (n=524, Age≥51)						
Overdue	168 (54%)	142 (46%)	ref.	ref.	ref.	ref.
Up to date**	56 (26%)	158 (74%)	1.61	1.28, 2.02	1.56	1.21, 2.00

CPR= Crude prevalence ratio; APR = Adjusted prevalence ratio (adjusted for age, language interpreter flag, duration of care, NSES, health insurance, comorbidity, HIV, BMI, frequency of visit, index visit clinic type, having an assigned primary care provider sex, provider type, and provider specialty).
**Women who had mammography within two years were considered up to date for breast cancer screening.*
***Women who had Fecal Occult Blood Test (FOBT) or Fecal Immunochemical Test (FIT) within one-year, flexible sigmoidoscopy or colonography within 5 years, or colonoscopy within ten years were considered up to date for colorectal cancer screening* (36,37).

Sensitivity analysis

There was no substantial difference in the estimates from the complete case analysis and the multiple imputation models (Figure 1.4). Likewise, estimates for cervical cancer screening adherence and correlates were not different when the definition of adherence was extended with a six-month grace period (*Supplemental Table 1.2*). The estimates for adherence to cervical cancer screening in the analysis restricted to individuals who received care for at least 5 years was 68%, and except for minimal changes in the effect sizes, there was not substantial difference in the correlates associated with screening adherence (*Supplemental Table 1.3)*

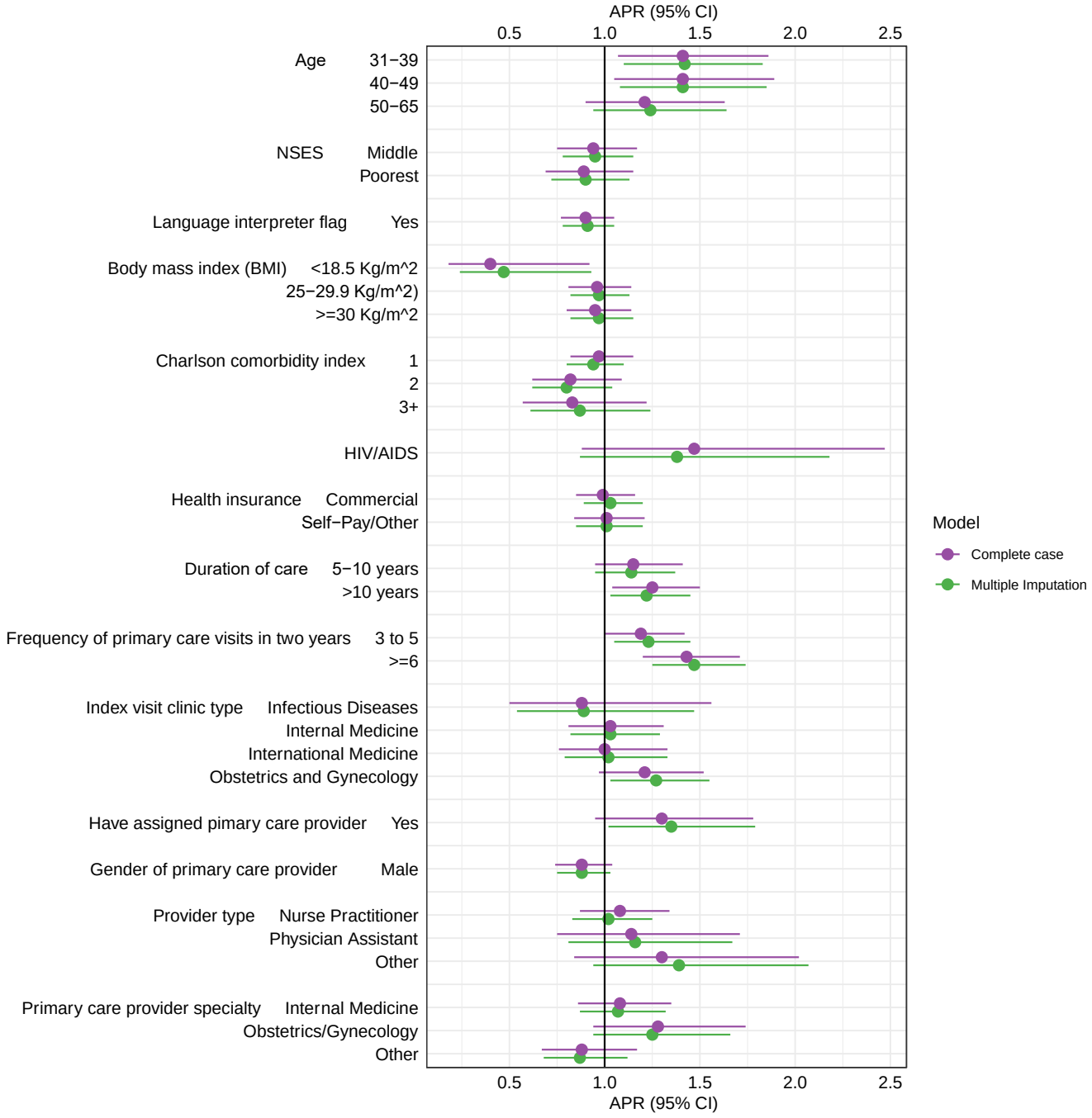


Figure 1. 4. Comparing estimates of complete case analysis and multiple imputation models for the correlates of cervical cancer screening adherence.

Uptake of screening among overdue women

Women who were overdue during the initial assessment at the index visit were further followed for 12 months after the index visit to assess cervical cancer screening uptake. Among the 608 overdue women, only 54 (9%) received screening within 12 months (Figure 5).

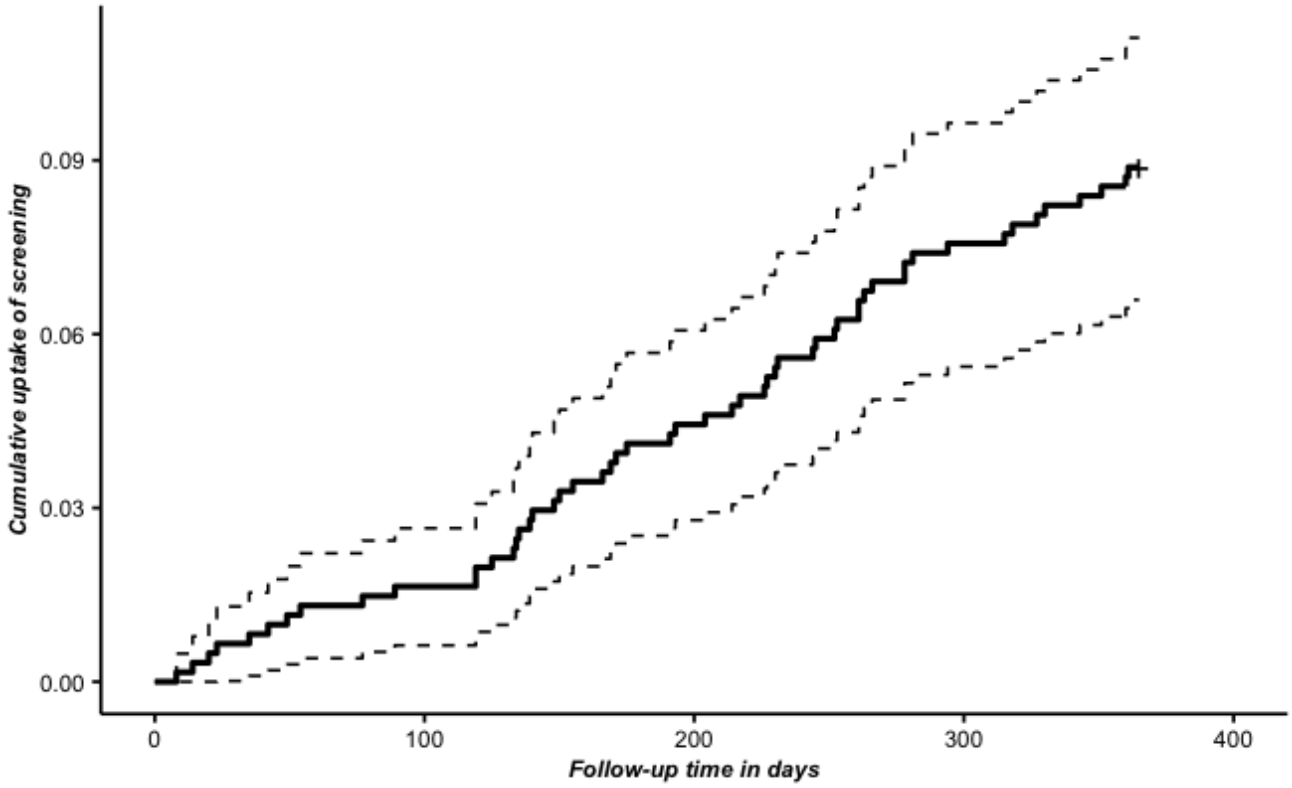


Figure 1. 5. Kaplan Meier curve for the uptake of cervical cancer screening over time since the index visit.

NB. Time 0 is the index visit, and the dotted lines show the 95% confidence interval.

Stratifying by screening history, 9% of the 397 never screened women and 9% of the 211 ever-screened women were screened within 12 months (Figure 6).

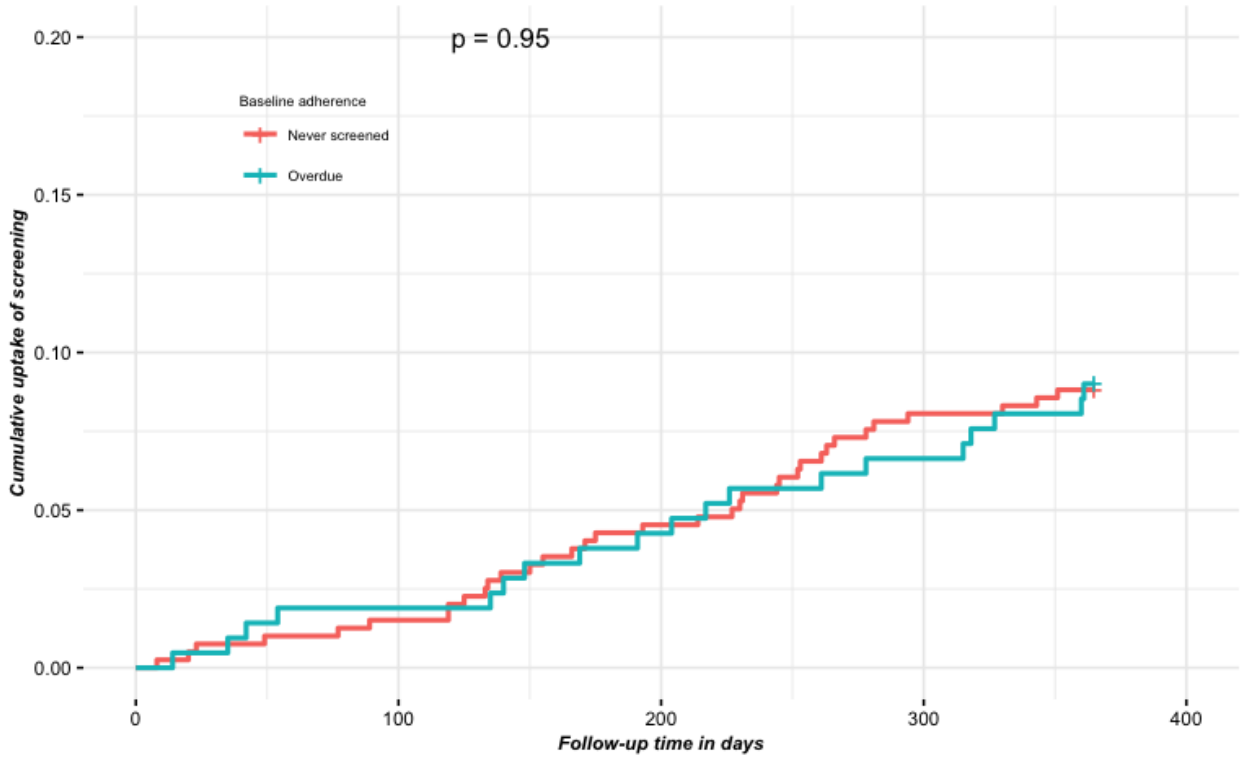


Figure 1. 6. Uptake of cervical cancer screening over a 12-month period comparing overdue (ever-screened) and never-screened women.

NB: The p-value is from a Kaplan Meier test comparing the two curves.

Individuals with no comorbidity had the lowest uptake of screening (6.5%) compared to those with 1 or more comorbidities (11% to 17%). Most screened individuals (68%) had more than three primary care visits within two years before the index visit. About 35% of HIV-positive individuals were screened over the 12-month follow-up period, but only 8% of the HIV-negative individuals were screened (Table 3).

Table 1. 3. Correlates of uptake of screening among overdue women

Characteristic		Total overdue N = 608	Screening uptake (Yes), N = 54 (row %)
Age			
	25-29	87	7 (8%)
	30-39	163	11 (7%)
	40-49	120	13 (11%)
	50-65	238	23 (10%)
Neighborhood socioeconomic status quintile			
	Least poor	48	4 (8%)
	Middle	398	32 (8%)
	Poorest	127	16 (13%)
	Missing	35	2
Language interpreter flag			
	No	246	17 (7%)
	Yes	362	37 (10%)
Body mass index (BMI)			
	<18.5 Kg/m^2	127	2 (11%)
	18.5-24.5 Kg/m^2	19	9 (7%)
	24.5-30 Kg/m^2	211	17 (8%)
	>30 Kg/m^2	184	21 (11%)
	Missing	67	5
Charlson's comorbidity index			
	0	397	26 (7%)
	1	138	17 (12%)
	2	54	9 (17%)
	3+	19	2 (11%)
HIV/AIDS		0	
	No	582	45 (8%)
	Yes	26	9 (35%)
Health insurance type			
	Medicare/Medicaid	318	19 (6%)
	Commercial	148	20 (14%)
	Self-Pay/Other	142	15 (11%)
Duration of care at the UW			
	< 5 years	246	26 (11%)

	5-10 years	138	9 (7%)
	>10 years	224	19 (9%)
Frequency of primary care visits in two years			
	1 to 2	275	17 (6%)
	3 to 5	187	19 (10%)
	≥6	146	18 (12%)
Index visit clinic type			
	Family Medicine	269	18 (7%)
	Infectious Diseases	29	9 (31%)
	Internal Medicine	119	7 (6%)
	International Medicine	104	12 (12%)
	Obstetrics and Gynecology	87	8 (9%)
Have assigned primary care provider			
	No	78	8 (10%)
	Yes	530	46 (9%)
Sex of primary care provider			
	Female	459	40 (8%)
	Male	149	14 (9%)
Provider type			
	Physician	510	44 (9%)
	Nurse Practitioner	68	6 (9%)
	Physician Assistant	17	1 (6%)
	Other	13	3 (23%)
Primary care provider specialty			
	Family Practice	282	18 (6.4%)
	Internal Medicine	191	21 (11%)
	Obstetrics/Gynecology	39	3 (7.7%)
	Other	96	12 (12%)

Correlates of screening uptake

In the model that included all the correlates, only health insurance type had a statistically significant association with screening uptake. Compared to individuals with Medicare/Medicaid, those with commercial health insurance had a 144% higher uptake (ARR - 2.44: 95%CI: 1.20, 4.97) (Figure 7).

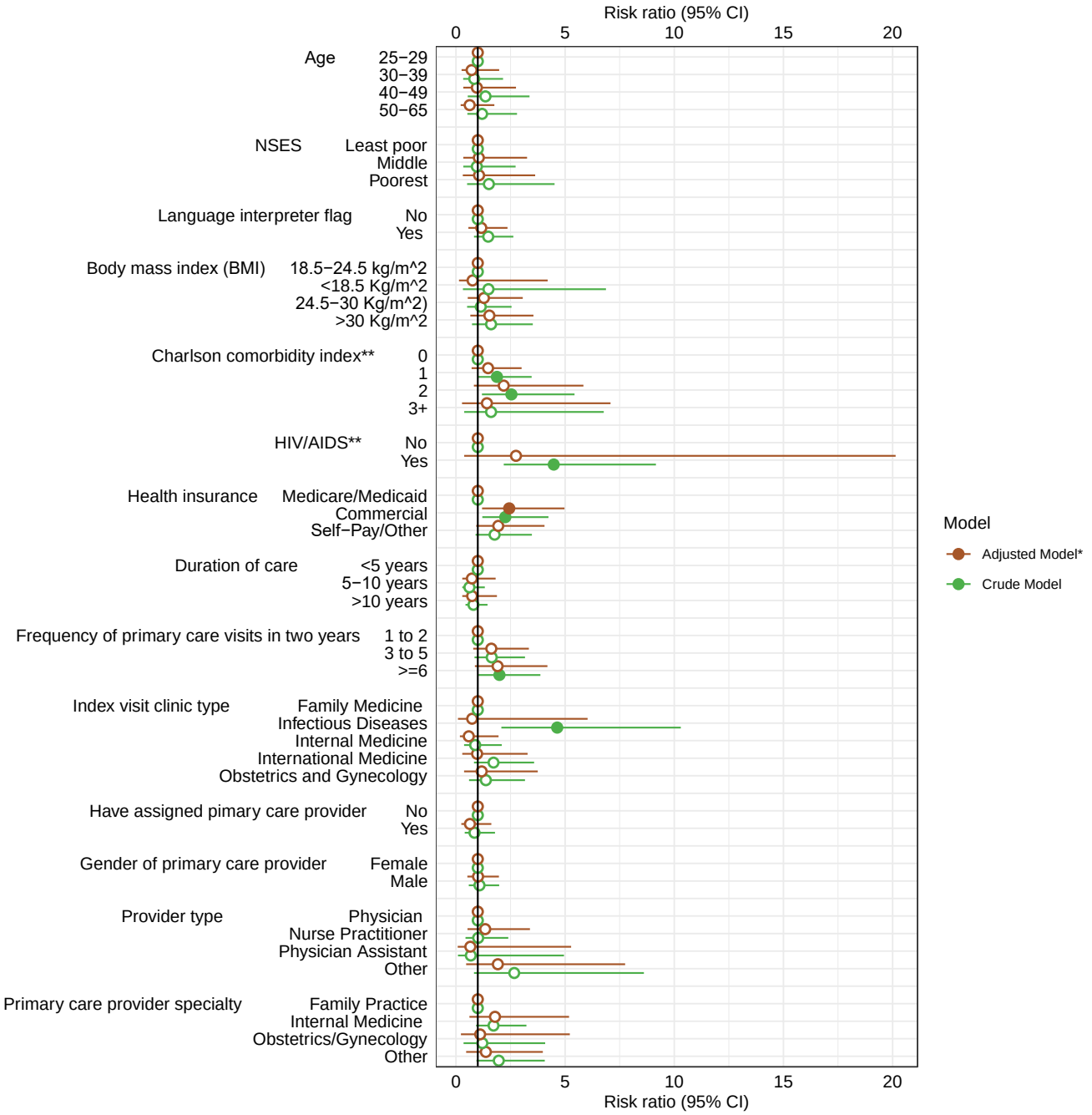


Figure 1. 7. Correlates of the uptake of cervical cancer screening within 12 months after the index visit of overdue women.

**The adjusted model was fitted by including all the variables in a single model. The exception was for HIV and comorbidity where one was not included on the adjusted model of the other.*

In a separate analysis among age-eligible women, breast cancer and colorectal cancer screening adherence were not significantly associated with uptake of CCS over a 12-month period among overdue participants (Table 4).

Table 1. 4. Association of adherence to breast and colorectal cancer screening with CCS uptake

	Uptake of screening					
Characteristic	No	Yes	CRR	95%CI	ARR	95%CI
Breast cancer screening (N=209, Age≥52)						
Overdue	139 (91%)	14 (9%)	ref.	ref.	ref.	ref.
Up to date*	52 (93%)	4 (7%)	0.78	0.26, 2.37	0.34	0.05, 2.14
Colorectal cancer screening (n=224, Age≥51)						
Overdue	152 (90%)	16 (10%)	ref.	ref.	ref.	ref.
Up to date**	51 (91%)	5 (9%)	0.94	0.34, 2.56	0.45	0.08, 2.62

CRR= Crude risk ratio; ARR = Adjusted risk ratio(adjusted for age, language interpreter flag, duration of care, NSES, health insurance, comorbidity, HIV, BMI, frequency of visit, index visit clinic type, having an assigned primary care provider sex, provider type, and provider specialty).
**Women who had mammography within two years were considered up to date for breast cancer screening.*
***Women who had Fecal Occult Blood Test (FOBT) or Fecal Immunochemical Test (FIT) within one-year, flexible sigmoidoscopy or colonography within 5 years, or colonoscopy within ten years were considered up to date for colorectal cancer screening* (36,37)*.*

Discussion

This study estimated cervical cancer screening adherence and its correlates among East African immigrants in Washington state who are engaged in primary care. We found that 63% of women aged 25-65 were up to date for cervical cancer screening. Older age, longer duration of care within the healthcare system, more frequent clinic visits, having an assigned primary care provider, getting care at a gynecology and obstetrics clinic and adherence to screening for breast and colorectal cancers each had a positive association with higher adherence. We also estimated screening uptake among overdue women and found that only 9% were screened over 12 months. Having commercial health insurance was associated with higher screening uptake as compared to having Medicare/Medicaid coverage.

Our estimated screening adherence of 63% (95%CI: 61%, 66%) is higher than prior studies done among East African immigrants. Based on two studies that Morrison et al conducted in 2008 among Somali immigrants attending primary care clinics in Minnesota, 49% and 51% of 18-65-year-old women were adherent for cervical cancer screening (12,13). A community-based survey by the New Americans Community Services (NACS) from 2006-2007 also reported that only 37% of 18-65-year-old Somali immigrants in Minnesota were ever screened for cervical cancer (14). Excluding Ethiopian and Eritrean immigrants, Somali immigrants in our study had a CCS adherence of 60%. All the previous studies were done in Minnesota - more than a decade ago – indicating possible differences associated with the settings and time of the studies. Including women who have been actively accessing primary care clinics and aged 25 years or above (instead of 18 in the previous studies) could also explain some of the differences. Even if estimates from the current study are higher than the previous few studies, it is still lower than the US national average. Based on CDC data, CCS adherence among Black or African American women in the US is 85% – showing that aggregating African immigrants with US-born African American could obscure important differences (7). In addition, our study may have included individuals with better access to and familiarity with the health system. About 69% of the individuals in our study had established care for at least five years; similarly, the prior studies conducted among Somali immigrants have also reported that the majority of the participants lived in the US for at least five years (12,13). Nevertheless, the estimates could be lower among the large pool of immigrants who do not have access to primary healthcare due to limited healthcare awareness, lack of acculturation, and/or immigration-related issues.

The way acculturation impacts adherence to cervical cancer screening was also observed in our study. Adjusted for all possible confounders, a longer duration of care was associated with higher cervical cancer screening adherence. The duration of care is a proxy indicator of acculturation and familiarity with the health system. Prior studies among African immigrants had also reported

that people who lived in the US longer and had established care for longer periods have higher adherence to cervical cancer screening (13,14). People receiving care for longer periods are more likely to have an assigned primary care provider, better trust in the health system, and improved knowledge of recommended preventative healthcare services. In addition, the longer they live in the US, there may be fewer immigration-related barriers that impact their access to healthcare, and they may be more likely to have learned English or to have figured out comfortable ways of using a language interpreter service. The latter scenario was suggested in our study, where using a language interpreter had a statistically significant association with lower cervical cancer screening adherence in the crude analysis, but it was not significant when adjusted explicitly for the duration of care - indicating possible mitigation of language interpreter use by the duration of care. On the contrary, newcomers may struggle with adapting to the health system, including scheduling clinic visits, communicating with providers, and using English or a language interpreter service (39). More importantly, the absence of similar preventive health services in their home countries may influence them to perceive the US health system likewise, and they may continue to be unaware of and not seek preventive health services (40,41).

Patients' connection with the health system is also important for adherence to cervical cancer screening. We found that women who had more frequent clinic visits had better screening adherence. Frequent clinic visits are opportunities to interact with healthcare providers and get more health-related information. People who frequently visit healthcare facilities may have comorbidities, may be pregnant, or be seeking contraception, all of which may increase opportunities for screening. In general, the more frequent visits the patients have, the more likely they are to establish a conducive and enabling environment and feel at ease to accept healthcare provider recommendations (42–44). Also, they are more likely to have an assigned primary care provider who takes care of their overall well-being (42,45). Our analysis also showed that women with an assigned primary care provider had higher CCS adherence. Regardless of the

participant's chief complaint or diagnosis, assigned primary care providers are more likely to offer and undertake preventive health services (46,47). The specialty of the providers where patients seek care also appears to matter for their patients' adherence to cervical cancer screening. We found that women who had their index visit in an obstetrics and gynecology clinic had higher screening adherence than those who had a visit in a family medicine clinic. About 80% of women with an index visit in a gynecology clinic had a primary care provider specializing in gynecology and obstetrics. This suggests that the primary reason for seeking medical care for this group of patients might have been issues related to gynecology and obstetrics, including prenatal care, post-natal care, or family planning services. Providers who have specialized in women's health may be more likely to recommend and perform CCS than general practitioners (48). Although having a female provider was mentioned as an important factor in prior studies (21,22), we did not observe a significant difference in screening adherence by provider sex in this study.

Health-seeking behavior in utilizing other preventative services was also an important correlate of cervical cancer screening adherence. Women who were adherent to breast and colorectal cancer screenings had higher adherence to cervical cancer screening. This association has been observed by multiple other studies that evaluated the association across adherence to screenings for these malignancies (36,49–51). As a behavior, screening may indicate increased knowledge and awareness of possible health risks (45,52). As a result, people screened for one type of cancer may better understand the benefit of screening and could be more likely to get screened for others. In addition, people adherent to a specific type of cancer screening may have a family or personal history of cancer-related issues that could alert them to identify problems earlier through better adherence to recommended screening services (53,54). In addition, the analysis for breast and colorectal cancer was restricted to women aged at or above 51 years for both analyses. This includes older women who may be more likely than younger women to have

comorbidities and to be adherent to screening and other health care recommendations by providers(55).

Compared to women aged 25-29 years, those in the older age categories – 30-39 and 40-49 – had higher CCS adherence. Younger women may have a lower perception of risk leading to a lower likelihood of seeking screening (56). Alternatively, women in the middle age category 30-50 might have more exposure to the health system due to other health issues, including pregnancy and other reproductive health encounters, making them more knowledgeable about cervical cancer screening. In addition, risk perception may increase with age and additional familial and societal responsibilities. However, the risk estimate in the oldest age category (50-65) was not statistically significantly different from the youngest age category, suggesting that other factors may be responsible for the age associations with screening observed in this study. Women in the oldest age category could be less sexually active and might have an underestimation of the risk of cervical cancer and lesser recommendation for screening by providers (57,58). Also, frequent normal findings from prior screenings might influence them not to have additional screenings. On the other hand, older individuals could be more likely to have comorbidities that could make CCS less of a priority (58). Furthermore, they could avoid genital examination due to discomfort because of menopause and related vaginal atrophy (59). In the case of our study, older people were more likely to have more comorbidities and use a language interpreter. The difficulty of acculturation and accessing the health system could be much more pronounced among older individuals than the younger population.

Underweight individuals (BMI <18.5 kg/m^2) had lower CCS adherence than those with a normal BMI (18.5-24.5 kg/m2). Although prior studies mostly mention obesity as a major risk factor for lower CCS screening adherence (60–62), there is growing evidence on the association of underweight with lower CCS adherence (63,64). In this study, underweight individuals had higher HIV prevalence, higher language interpreter use, and lower duration of care than normal BMI

individuals (*Supplemental Table 1.5).* However, other potential reasons for the lower adherence of cervical cancer screening may need further investigation.

Over a 12-month follow-up, only 9% of women who were overdue at the index visit were screened. The very low screening uptake may indicate that overdue women are more likely to remain overdue, and that the contemporary approach of advocating or reminding for cervical cancer screening was not well functioning for this group of EAI. Before 2023, UW Medicine did not have an automated system to remind overdue women. Since January 2023, UW Medicine has started sending cervical cancer screening reminders to overdue patients using either paper mail written in English and Spanish or electronic notifications through their medical records. Recently, care managers with access to telephonic interpretation have begun contacting patients due or overdue for screening by phone. However, less than half of individuals in our study use English to get medical care, and the majority are less likely to understand the messages and respond accordingly. It is possible that EAIs have different preferred ways of hearing health messages (65). Not surprisingly, individuals with commercial health insurance had higher screening uptake than Medicaid and Medicare users (66). In the US, commercial insurance can reflect an individual's economic affluence or employment to an organization that pays for their insurance. Individuals with commercial insurance are more likely to be educated and have better familiarity with the health system (67). As a result, identifying alternative ways of health messaging and designing intervention strategies addressing the barriers overdue women encounter could help reach more underserved populations.

This study has a number of key strengths. Firstly, the data come from a health system that serves an ethnically and economically diverse population; as a result, it may have a representation of most of the East African community in western Washington who have access to primary health care (*Supplemental figure 1.1*). Secondly, screening status was based on documented screening

– minimizing possible biases due to recall or under- or over-reporting. Thirdly, it includes variables that represent potential barriers and facilitators from the perspectives of the patients and the health system – which has been less entertained in other similar studies. However, the study does have some limitations. The results might not represent people who do not have healthcare access or who go to health facilities other the UW Medicine. However, the study includes a representative sample of the underserved community that UW Medicine serves as a public institution serving economically and ethnically diverse people. The approaches we used to identify EAIs based on language, ethnicity and country of birth might not have perfectly captured all EAIs or incorrectly classified others as EAIs. In addition, screenings which occurred in other health facilities might not have been completely recorded and could have biased our estimates. In addition, estimating adherence with a three-to-five-year interval for some women who might have been on a different schedule due to a diagnosis of cervical precancer or cancer and immunosuppression might have led to overestimation of screening adherence (68). Finally, the study relied on medical records. Data entry errors by the healthcare staff may have resulted in non-differential misclassification and attenuated the observed associations.

Conclusion

Cervical cancer screening among EAI women with access to healthcare in a large healthcare system in Washington State was lower than the national average among the general population and insufficient to meet global cervical cancer elimination targets. More than one third of EAIs were overdue or had no documented CCS. Women who interacted more frequently with the healthcare system were more likely to get screened. Nevertheless, a large proportion of women are still not getting screened despite frequent interaction with providers and clinics. These disparities could be addressed through interventions calibrated to the people's culture and

tradition and by applying better health communication methods, specifically for those with less familiarity and comfort with the US health system. Interventions focused on increasing healthcare access and utilization, and leveraging health encounters to address barriers faced by younger patients or those less familiar with the health system could potentially increase CCS among EAIs. In addition, healthcare encounters can be better utilized to educate patients about screening and engage them in preventive health services. Services targeting the transition phase when EAIs are getting acculturated, and interventions to ensure that the language interpreter service is more comfortable for new users, may improve screening uptake and facilitate cervical cancer elimination efforts.

Appendix

Supplemental Table 1.1: The distribution of missing observations

Characteristic	Percent Missing	Remark
Age	0%	
Duration of care at the UW	0%	
Primary language	0%	
Language interpreter flag	0%	
Race	2.94%	Not imputed
Ethnicity	10.24%	Not imputed
Country of birth	10.19%	Not imputed
Health insurance type	0%	
Body mass index (BMI)	9.22%	Imputed
HIV/AIDS	0%	
Charlson's comorbidity index	0%	
Frequency of primary care visits in two years	0%	
Index visit clinic type	0%	
Have assigned primary care provider	0%	
Index visit by the assigned primary care provider	0%	
Gender of primary care provider	0%	
Provider type	0%	
Primary care provider degree	0%	
Primary care provider specialty	0%	

Neighborhood socioeconomic status	5.77%	Imputed

Supplemental Table 1.2. Correlates of CCS adherence based on results from defining cervical cancer screening adherence with the addition of a 6-month grace period (3.5 years for Pap test and 5.5 years for co-testing of Pap and HPV)

Characteristic	CPR	95% CI	APR	95% CI[1]
Age				
25-29	ref.	ref.	ref.	ref.
30-39	1.52	1.18, 1.95	1.41	1.07, 1.85
40-49	1.55	1.20, 2.00	1.39	1.04, 1.85
50-65	1.26	0.98, 1.62	1.2	0.89, 1.61
NSES				
Least poor	ref.	ref.	ref.	ref.
Middle	0.96	(0.8, 1.17)	0.96	0.77, 1.19
Poorest	0.92	(0.73, 1.14)	0.92	0.71, 1.18
Language interpreter flag				
No	ref.	ref.	ref.	ref.
Yes	0.86	0.77, 0.97	0.89	0.76, 1.04
Body mass index (BMI)				
18.5-24.5 Kg/m^2	ref.	ref.	ref.	ref.
<18.5 Kg/m^2	0.41	0.19, 0.88	0.46	0.22, 0.98
24.5-30 Kg/m^2)	1	0.85, 1.17	0.95	0.80, 1.12
>30 Kg/m^2	1	0.84, 1.17	0.94	0.79, 1.12
Missing	67	81		
Charlson's comorbidity index				
0	ref.	ref.	ref.	ref.
1	1.03	0.90, 1.19	0.97	0.81, 1.15
2	0.88	0.69, 1.13	0.8	0.60, 1.07
3+	1.07	0.77, 1.48	0.84	0.58, 1.23
HIV/AIDS				
No	ref.	ref.	ref.	ref.
Yes	1.11	0.85, 1.43	1.46	0.88, 2.44
Health insurance type				
Medicare/Medicaid	ref.	ref.	ref.	ref.
Commercial	1.06	0.92, 1.22	0.99	0.85, 1.16

Self-Pay/Other	0.9	0.77, 1.06	0.99	0.83, 1.19
Duration of care at the UW				
< 5 years	ref.	ref.	ref.	ref.
5-10 years	1.23	1.04, 1.47	1.18	0.97, 1.44
>10 years	1.36	1.18, 1.58	1.27	1.06, 1.53
Frequency of primary care visits in two years				
1 to 2	ref.	ref.	ref.	ref.
3 to 5	1.21	1.03, 1.41	1.21	1.02, 1.44
>=6	1.39	1.20, 1.61	1.43	1.20, 1.71
Index visit clinic type				
Family Medicine	ref.	ref.	ref.	ref.
Infectious Diseases	1.05	0.78, 1.42	0.92	0.53, 1.61
Internal Medicine	1.06	0.90, 1.26	1.03	0.82, 1.31
International Medicine	1.06	0.89, 1.27	1.02	0.77, 1.35
Obstetrics and Gynecology	1.2	1.02, 1.42	1.2	0.96, 1.50
Have assigned primary care provider				
No	ref.	ref.	ref.	ref.
Yes	1.38	1.08, 1.75	1.27	0.93, 1.74
Gender of primary care provider				
Female		ref.	ref.	ref.
Male	0.2	0.91	0.88	0.74, 1.05
Provider type				
Physician	ref.	ref.	ref.	ref.
Nurse Practitioner	0.99	0.82, 1.21	1.06	0.86, 1.32
Physician Assistant	1.03	0.72, 1.47	1.14	0.76, 1.71
Other	1.09	0.75, 1.58	1.28	0.83, 1.98
Primary care provider specialty				
Family Practice	ref.	ref.	ref.	ref.
Internal Medicine	1.09	0.95, 1.25	1.05	0.84, 1.32
Obstetrics/Gynecology	1.12	0.89, 1.40	1.24	0.91, 1.68
Hospitalist	0.88	0.72, 1.08	0.87	0.66, 1.15

Supplemental Table 1.3. Correlates of CCS adherence among individuals who received care for at least 5 years.

Characteristic	**Overall**, N = 1,152	**Up to date**, N = 790	**Complete case**		**Multiple imputation**	
			APR	**95% CI**	**APR**	**95% CI**
Age						
25-29	83	35 (42%)	ref.	ref.	ref.	ref.
30-39	363	259 (71%)	1.52	1.19, 1.93	1.59	1.11, 2.27
40-49	336	251 (75%)	1.59	1.24, 2.03	1.66	1.15, 2.39
50-65	370	245 (66%)	1.45	1.12, 1.86	1.52	1.04, 2.23
NSES Quintile						
Least poor	99	72 (73%)	ref.	ref.	ref.	ref.
Middle	764	519 (68%)	0.96	0.84, 1.11	0.96	0.75, 1.22
Poorest	230	160 (70%)	0.97	0.83, 1.14	0.97	0.74, 1.29
Unknown	59	39				
Language interpreter flag						
No	645	455 (71%)	ref.	ref.	ref.	ref.
Yes	507	335 (66%)	0.97	0.82, 1.15	0.94	0.8, 1.12
Body mass index (BMI)						
<18.5 Kg/m^2	12	3 (25%)	ref.	ref.	ref.	ref.
18.5-24.5 Kg/m^2	226	157 (69%)	0.37	0.15, 0.92	0.48	0.18, 1.28
24.5-30 Kg/m^2)	434	304 (70%)	0.97	0.88, 1.08	0.99	0.82, 1.2
>30 Kg/m^2	393	274 (70%)	0.96	0.86, 1.06	0.98	0.8, 1.2
Unknown	87	52				
Charlson's comorbidity index						
0	732	506 (69%)	ref.	ref.	ref.	ref.
1	278	192 (69%)	0.97	0.87, 1.08	0.94	0.78, 1.13
2	93	59 (63%)	0.86	0.73, 1.02	0.85	0.64, 1.12
3+	49	33 (67%)	0.85	0.68, 1.06	0.87	0.6, 1.27
HIV/AIDS						
No	1,097	748 (68%)	ref.	ref.	ref.	ref.
Yes	55	42 (76%)	1.38	1.08, 1.74	1.4	0.85, 2.29
Health insurance type						
Medicare/Medicaid	652	443 (68%)	ref.	ref.	ref.	ref.
Commercial	349	248 (71%)	1	0.91, 1.10	1.03	0.87, 1.22
Self-Pay/Other	151	99 (66%)	1.04	0.92, 1.18	1	0.8, 1.25
Duration of care at the UW						
5-10 years	385	247 (64%)	ref.	ref.	ref.	ref.
>10 years	767	543 (71%)	1.06	0.96, 1.16	1.06	0.89, 1.25
Frequency of primary care visits in two years						

1 to 2	376	228 (61%)	ref.	ref.	ref.	ref.
3 to 5	354	247 (70%)	1.14	1.02, 1.28	1.16	0.96, 1.39
>=6	422	315 (75%)	1.3	1.16, 1.45	1.3	1.07, 1.58
Index visit clinic type						
Family Medicine	487	315 (65%)	ref.	ref.	ref.	ref.
Infectious Diseases	47	31 (66%)	0.84	0.62, 1.13	0.79	0.45, 1.4
Internal Medicine	220	163 (74%)	1.04	0.90, 1.19	1.02	0.79, 1.33
International Medicine	207	135 (65%)	0.95	0.80, 1.12	0.91	0.67, 1.24
Obstetrics and Gynecology	191	146 (76%)	1.22	1.07, 1.39	1.2	0.95, 1.52
Have assigned primary care provider						
No	52	24 (46%)	ref.	ref.	ref.	ref.
Yes	1,100	766 (70%)	1.53	1.13, 2.07	1.61	1.04, 2.49
Sex of primary care provider						
Female	913	641 (70%)	ref.	ref.	ref.	ref.
Male	239	149 (62%)	0.91	0.81, 1.02	0.89	0.74, 1.08
Primary care provider specialty						
Family Practice	537	350 (65%)	ref.	ref.	ref.	ref.
Internal Medicine	431	313 (73%)	1.09	0.96, 1.24	1.11	0.88, 1.42
Obstetrics/Gynecology	70	54 (77%)	1.29	1.08, 1.55	1.25	0.89, 1.75
Other	114	73 (64%)	0.93	0.78, 1.11	0.92	0.68, 1.25

Supplemental Table 1.4. Association of adherence to breast and colorectal cancer screening

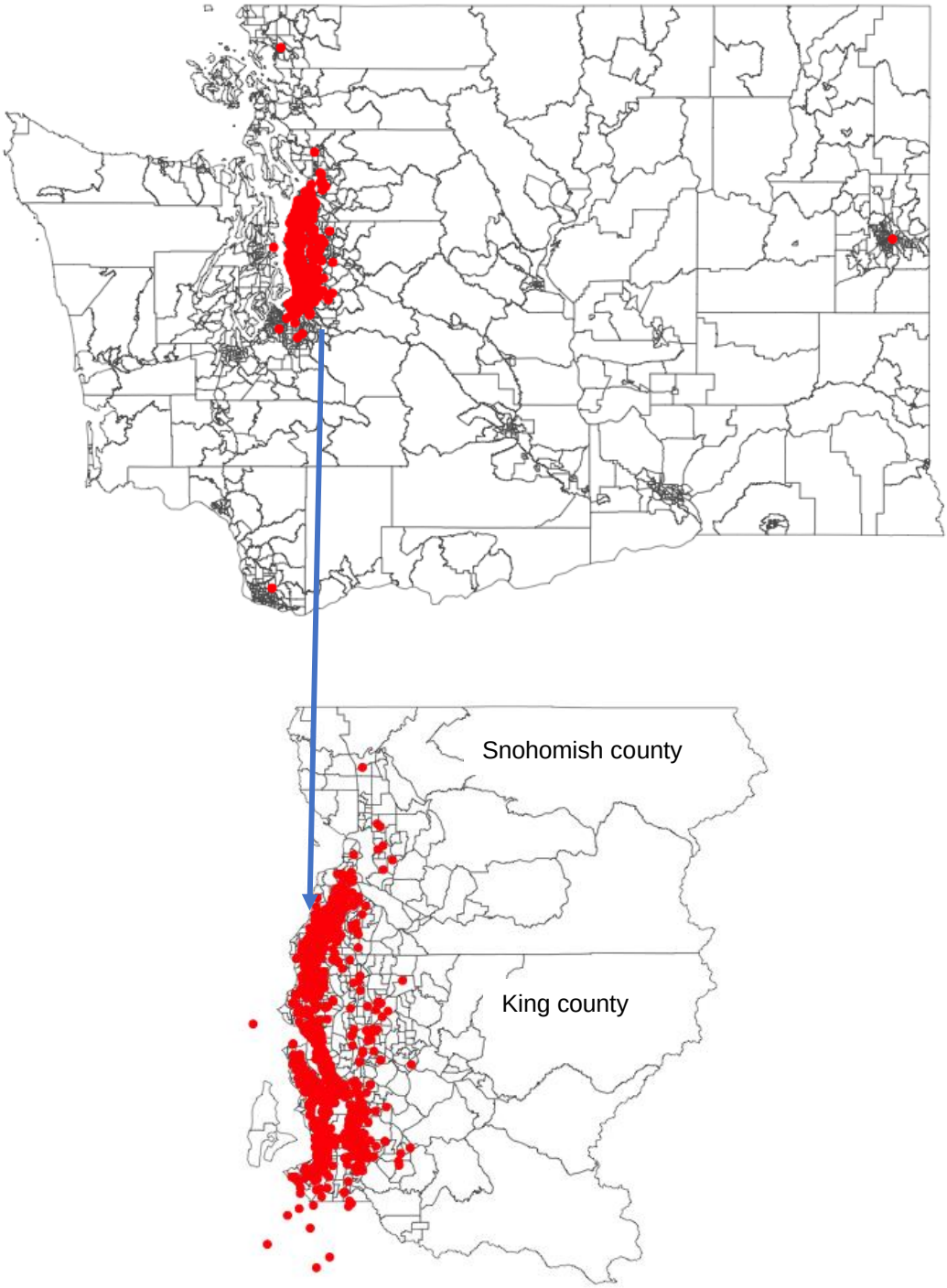
CCS adherence among individuals who received care for at least 5 years.

Breast cancer screening (N=310)			ARR	95%CI	P-value
Overdue	164	89 (54%)	ref.	ref.	
Up to date	146	114 (78%)	1.49	1.25, 1.77	<0.001
Colorectal cancer screening (N=344)					
Overdue	191	107 (56%)	ref.	ref.	
Up to date	153	117 (76%)	1.35	1.15, 1.59	<0.001

Supplemental Table 1.5. The association of BMI with selected sociodemographic and health-related variables

Characteristic	**Overall**, N = 1,516	**BMI Categories**			
		<18.5 Kg/m^2, N = 261	**18.5-24.5 Kg/ m^2**, N = 365	**24.5-30 Kg/ m^2)**, N = 601	**>30 Kg/ m^2**, N = 524
Age					
25-29	146 (9.6%)	9 (35%)	61 (17%)	37 (6.2%)	39 (7.4%)
30-39	475 (31%)	9 (35%)	142 (39%)	192 (32%)	132 (25%)
40-49	375 (25%)	3 (12%)	76 (21%)	141 (23%)	155 (30%)
50-65	520 (34%)	5 (19%)	86 (24%)	231 (38%)	198 (38%)
Comorbidity					
0	999 (66%)	17 (65%)	279 (76%)	406 (68%)	297 (57%)
1	357 (24%)	7 (27%)	54 (15%)	134 (22%)	162 (31%)
2	108 (7.1%)	2 (7.7%)	24 (6.6%)	40 (6.7%)	42 (8.0%)
3+	52 (3.4%)	0 (0%)	8 (2.2%)	21 (3.5%)	23 (4.4%)
HIV/AIDS					
0	1,446 (95%)	23 (88%)	350 (96%)	573 (95%)	500 (95%)
1	70 (4.6%)	3 (12%)	15 (4.1%)	28 (4.7%)	24 (4.6%)
Language interpreter use					
No	715 (47%)	10 (38%)	194 (53%)	279 (46%)	232 (44%)
Yes	801 (53%)	16 (62%)	171 (47%)	322 (54%)	292 (56%)
NSES					
Least poor	134 (9.4%)	2 (8.0%)	37 (11%)	45 (7.9%)	50 (10%)
Middle	990 (69%)	20 (80%)	245 (72%)	406 (71%)	319 (65%)
Poorest	303 (21%)	3 (12%)	59 (17%)	117 (21%)	124 (25%)
Unknown	89	1	24	33	31
Duration of care					
< 5 years	451 (30%)	14 (54%)	139 (38%)	167 (28%)	131 (25%)
5-10 years	354 (23%)	11 (42%)	98 (27%)	145 (24%)	100 (19%)
>10 years	711 (47%)	1 (3.8%)	128 (35%)	289 (48%)	293 (56%)
Health insurance type					
Medicare/Medicaid	802 (53%)	10 (38%)	171 (47%)	334 (56%)	287 (55%)
Commercial	416 (27%)	8 (31%)	117 (32%)	156 (26%)	135 (26%)
Self-Pay/Other	298 (20%)	8 (31%)	77 (21%)	111 (18%)	102 (19%)
Frequency of visit					
1 to 2	521 (34%)	13 (50%)	149 (41%)	203 (34%)	156 (30%)
3 to 5	476 (31%)	6 (23%)	114 (31%)	186 (31%)	170 (32%)
>=6	519 (34%)	7 (27%)	102 (28%)	212 (35%)	198 (38%)
Having as assigned primary care provider					
No	120 (7.9%)	1 (3.8%)	39 (11%)	43 (7.2%)	37 (7.1%)
Yes	1,396 (92%)	25 (96%)	326 (89%)	558 (93%)	487 (93%)

Supplemental figure 1.1. The geographical distribution of study patients across the state of Washington



Chapter 2. Association of maternal cervical cancer screening adherence with adolescent HPV vaccination among adolescent-mother pairs in Washington State

Abstract

Introduction: Less than two thirds of US adolescents are up to date with HPV vaccination. In general, mothers engaged in preventive care are more likely to seek preventive care for their children. However, the association between maternal cervical cancer screening (CCS) and adolescent HPV vaccination is underexplored.

Method: To assess the association between maternal CCS and adolescent HPV vaccination, we conducted a cross-sectional study using electronic health record data from a large health system in Seattle, USA (UW Medicine). We included adolescents (11-17 years) and their mothers if each had ≥1 primary care visit between 2018-2020. The outcomes were initiation and completion of the adolescent HPV vaccine series. The primary exposure was maternal CCS adherence, defined as up-to-date with US guideline-recommended intervals. Secondary exposures were maternal breast cancer screening adherence (restricted to adolescents with mothers ≥52 years) and maternal receipt of ≥1 wellness visit within two years. We used Generalized Estimating Equation (GEE) with a Poisson link and exchangeable correlation matrix to account for the clustering of adolescents within the same mother and estimate prevalence ratios and 95% CIs, adjusted for adolescent age and sex and maternal age, duration of care at UW Medicine, and use of a language interpreter. We further evaluated effect modification for the association of maternal CCS and adolescent HPV vaccination by adolescent sex (male vs. female), adolescent provider specialty (Pediatrics vs. Family Practice), maternal language interpreter use (yes/no), and having the same primary care provider for both adolescents and mothers (yes/no).

Results: Of 4,121 adolescents, 2,687 (66%) had a CCS-adherent mother, 3,395 (82%) initiated HPV vaccination, and 2,020 (49%) completed the HPV vaccination series. CCS adherence was associated with higher HPV vaccine initiation (adjusted prevalence ratio (APR): 1.10, 95%CI:

1,06, 1.13) and completion (APR: 1.16, 95%CI: 1,08, 1.23). Also, recent maternal wellness visit was associated with higher vaccine initiation (APR: 1.04, 95%CI: 1.01, 1.07) and completion (APR: 1.12, 95%CI: 1.05, 1.20). Maternal breast cancer screening adherence (n=511 eligible) had no statistically significant association with HPV vaccination (initiation: APR: 1.01, 95%CI: 0.96, 1.07, completion: APR: 1.09: 95%CI: 0.95, 1.25). The associations of maternal CCS and adolescent HPV vaccine initiation and completion were stronger for male vs female adolescents (initiation: APR – 1.13 [1.08, 1.19] vs 1.06 [1.02, 1.11] : p =0.03; completion: APR – 1.28 [1.15, 1.43] vs 1.08 [0.98, 1.18] : p =0.017), for adolescents who had a primary care provider with a specialty in Family Practice vs Pediatrics (initiation: APR – 1.14 [1.09, 1.20] vs 1.02 [0.98, 1.07]: p <0.001; completion: APR – 1.23 [1.11, 1.36] vs 1.05 [0.94, 1.16]: p= 0.026) , and for adolescents who had the same primary care provider as their mother's vs not (initiation: APR – 1.26 [1.16, 1.37] vs 1.05 [1.01, 1.09]]: p <0.001; completion: APR – 1.38 [1.17, 1.63] vs 1.11[1.03, 1.21]]: p =0.019).

Conclusion: The observed association between maternal preventive service utilization and adolescent HPV vaccination suggests that delivering healthcare through a family-centered approach and engaging mothers in broad preventive care could increase adolescent HPV vaccination coverage.

Introduction

Human papillomavirus (HPV) vaccination is one of the key strategies to prevent cervical cancer-related morbidity and mortality (64–66). Since its introduction in 2006, it has played a vital role in the over 80% reduction of the prevalence of HPV infections in the US (67). Annually in the US, about 25,000 women and 20,000 men get diagnosed for HPV-related cancers (68). Currently, the 9-valent vaccine, which prevents infection from nine different HPV types, is the only vaccine given in the US (69). The vaccine covers HPV genotypes (6, 11, 16, 18, 31, 33, 45, 52, and 58)

responsible for most genital warts and linked with six types of cancers, including cervical, oropharyngeal, anal, penile, vaginal, and vulvar cancers (70). It is recommended to be given to all adolescents starting at the age of 9. Two doses of the vaccine given six months apart are recommended if vaccination started between 9 to 14 years. An additional third dose is required if vaccination began after age 14 or if the two doses were delivered less than five months apart (69). As part of the global cervical cancer elimination goal, the World Health Organization (WHO) recommended to vaccinate 90% of girls by 2030 (71). Similarly, the US targets to reach 80% coverage in both boys and girls, according to the Healthy People 2030 plan (3). However, only 61% of 13-17 years old adolescents nationally and 68% of adolescents in Washington state have completed the recommended doses of HPV vaccine as of 2020 (72–74) - still far below the target goals (3,65,75).

In order to improve HPV vaccination coverage among adolescents, understanding parental influence is essential. Since adolescents under 18 years old require parental consent for medical care, their uptake of HPV vaccination depends on their parents' perception and attitude toward the vaccine (76). Barriers mothers experience in their own health-seeking could also negatively impact adolescent HPV vaccination and hinder cervical cancer prevention efforts (71,77). Prior studies reported poor maternal health-seeking behavior is associated with a lower uptake of HPV vaccination (18,78). However, most studies assessing the relationship between maternal health-seeking behavior and adolescent HPV vaccination were done more than a decade ago, around the time when HPV vaccination was first introduced (15,21–27). In addition, prior studies were mainly concentrated on HPV vaccination among girls, and some of them were done even before approval for vaccinating boys (18,79–85). As a result, updated studies to assess the impact of maternal preventive care service utilization on adolescent HPV vaccination uptake and evaluate possible sex differences in the association are important for designing future interventions to improve adolescent HPV vaccine coverage. As healthcare encounters are potential opportunities

to disseminate health information, maternal health encounters could be leveraged to include HPV vaccine advocacy and improve coverage (19–26).

In this study, we used electronic health record (EHR) data from the University of Washington (UW) Medicine health system to determine the association between maternal preventive care service utilization and adolescent HPV vaccination coverage and to evaluate potential effect modification by adolescent sex, maternal language interpreter use, and primary care provider characteristics.

Methods

We conducted a cross-sectional study among adolescents paired with their respective mothers who received primary care at UW Medicine. We evaluated the associations of HPV vaccine initiation and completion with maternal cervical and breast cancer screening adherence and attendance at wellness visits.

Study setting, population, and data collection procedure

We used data from the UW Medicine EHR. UW Medicine is a large health system in Washington State with three hospitals and 16 primary care clinics (31). We included adolescents aged 11-17 years who had ≥1 primary care visit between March 2018 and February 2020, with a mother who also received primary care at UW Medicine during the same period. A primary care clinic visit was defined as a completed in-person visit in either Pediatrics (only for adolescents), Obstetrics and Gynecology (OBGY), Family Medicine, or Internal Medicine and provided by an MD (Medical Doctor), DO (Doctor of Osteopathic Medicine), MBBS/ MBChB/ MBBCH (Bachelor of Medicine, Bachelor of Surgery), NP (Nurse Practitioner), DNP (Doctor of Nursing Practice), or PA (Physician Assistant).

Adolescents and mothers were linked using the combinations of maternal patient ID (identified as a parent in the medical records), health insurance membership details, and home address. A mother was defined as a female client with a patient ID mentioned in the adolescent medical record or with the same insurance coverage or who lives in the same address as the adolescent and is at least 16 years older than the respective adolescent(s) (to exclude siblings) (79,86). Adolescents with multiple potential mothers, no-matching mothers, or mothers older than 65 years were excluded (Figure 2.1). Ethical approval with waiver of consent and HIPPA authorization was received from the UW IRB.

Outcomes and exposures

All outcomes and exposures were anchored on an index visit, defined as the adolescent's last primary care visit between March 2018 and February 2020. The primary outcomes of interest were adolescent HPV vaccine initiation and completion at or before the index visit. HPV vaccine initiation was defined as receiving at least one dose of the HPV vaccine. HPV vaccine completion was defined as receiving the recommended two doses if vaccination was initiated between 9 to 14 years of age. Three doses were required if vaccination was initiated on or after the age of 15 or if the interval between two doses was less than five months regardless of age at initiation or if the first dose was given before October 2016 (three doses were recommended for all ages before then) (69). The primary exposure was maternal cervical cancer screening (CCS) adherence. Cervical cancer screening adherence was assessed among mothers with no documented hysterectomy history before the index visit. Mothers with a Pap test within three years or a Pap and HPV co-test within five years before the index visit were considered adherent to cervical cancer screening (32). Secondary exposures were maternal utilization of wellness visits and adherence to breast cancer screening. Wellness visit attendance was defined as at least one wellness visit within two years before the index visit. Breast cancer screening was evaluated only

among adolescents with mothers ≥52 years of age, and adherence was defined as screening mammography within two years of the index visit (87).

The covariates considered were grouped as adolescent characteristics (age, sex, race, ethnicity, language interpreter use, neighborhood socioeconomic status (NSES), health insurance type), adolescent primary care provider characteristics (primary care provider sex, type, and specialty), and maternal characteristics (age, race, ethnicity, language interpreter use, duration of care, and maternal primary care provider sex, type, and specialty). NSES was defined based on the participant's address linked with the 2018 CDC estimated geocoded neighborhood deprivation index measuring the census tract level vulnerability of communities for various social situations, including public health crisis (34).

Statistical analysis

First, we calculated the distribution of the sociodemographic characteristics of adolescents with HPV vaccine initiation and completion and compared differences across categories of adolescent and maternal characteristics using Chi-square tests. To estimate the association between maternal CCS and adolescent HPV vaccine initiation and completion, we used univariable and multivariable Generalized Estimating Equation (GEE) with a Poisson link and exchangeable correlation matrix to account for the clustering of adolescents within the same mother. We evaluated effect modification by adolescent sex (male vs. female), adolescent provider specialty (Pediatrics vs. Family Practice), maternal language interpreter use (yes/no), and having the same primary care provider for both adolescents and mothers (yes/no). Wald tests and associated p-values for the interaction terms were used to determine the strength of evidence for effect modification. As a secondary analysis, we fitted a model to evaluate the associations between maternal wellness visit attendance and adherence to screenings for breast cancer with adolescent HPV vaccination. All the models were adjusted for adolescent age (continuous), sex, maternal

age (continuous), maternal duration of care at the UW (continuous, time from first encounter to index visit), and maternal language interpreter use (yes/no) unless the covariates were being evaluated for effect modification. We reported prevalence ratios (PR) with the respective 95% confidence intervals, and an alpha value of 0.05 was used to determine statistical significance. As a sensitivity analysis, we explored vaccination coverage by duration of care and estimated its association with maternal preventative service use only among adolescents who has received care from UW Medicine since their 9th birthday (the minimum recommended age to initiate HPV vaccination).

Results

A total of 9,694 adolescents had a primary care clinic visit between March 2018 and February 2020. Of them, 4,121 (43%) had an eligible mother identified and were included in the study (*Figure 2.1, Supplemental Table 2.1)*.

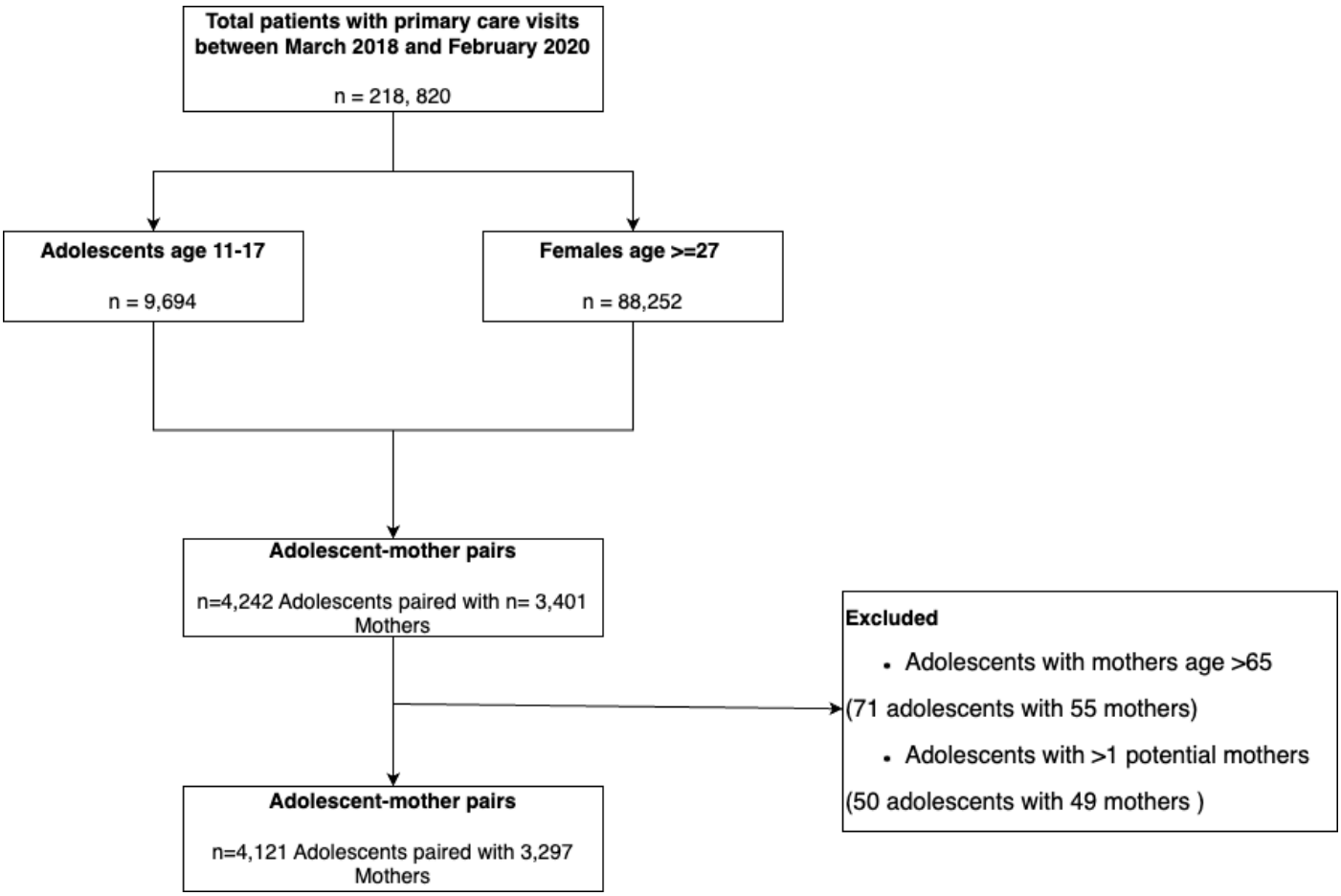


Figure 2. 1. Flow diagram for the selection of eligible adolescent-mother pairs

Characteristics of adolescents by HPV vaccination status

Half of the 4,121 adolescents (49%) were males, and 47% were aged 15 or older. English was the primary language for 93% of them. About 26% had missing data on race; among those with non-missing data, the documented race was White for 61%, Black or African American for 15%, and Asian for 16%.

Of the 4,121 adolescents, 3,395 (82%) had ever initiated HPV vaccination, and 2,020 (49%) had completed the series. The majority (57%) initiated HPV vaccination at the age of 11 years, and only 173 (5%) adolescents initiated it before their 11th birthday. Vaccine completion among

females and males was 52% vs. 46%, respectively (p<0.001). Individuals with a recorded race of White had 50% HPV vaccine completion, Black or African American Individuals had 53% completion, and Asian Individuals had 56% completion (P=0.1). Adolescents with a female primary care provider had 51% completion, and those with a male provider had 44% completion (p<0.001). Similarly, adolescents with a provider in Pediatrics had 56% completion, and those in Family Practice had 45% completion (p<0.001) (Table 1.1).

Table 2. 1. Adolescent characteristics and the distribution of HPV vaccination status

		HPV Vaccination**		
Characteristic	N = 4,121	Never initiated, N = 726 n (row %)	Ever initiated, N = 3,395 n (row %)	Completed, N = 2,020 n (row %)
Age				
11	303	102 (34%)	201 (66%)	39 (13%)
12	590	116 (20%)	474 (80%)	282 (48%)
13	614	104 (17%)	510 (83%)	344 (56%)
14	669	117 (17%)	552 (83%)	309 (46%)
15	654	102 (16%)	552 (84%)	321 (49%)
16	670	92 (14%)	578 (86%)	363 (54%)
17	621	93 (15%)	528 (85%)	362 (58%)
Sex				
Female	2,101	344 (47%)	1,757 (52%)	1,092 (54%)
Male	2,014	381 (52%)	1,633 (48%)	925 (48%)
Unknown	6	1 (0%)	5 (0%)	3 (0%)
Primary language				
English	3,849	696 (18%)	3,153 (82%)	1,874 (49%)
Non-English	272	30 (11%)	242 (89%)	146 (54%)
Language interpreter flag				
Yes	201	23 (11%)	178 (89%)	108 (54%)
No	3455	620 (18%)	2835 (82%)	1684 (49%)
Missing	465	83	382	228
Race				
American Indian or Alaska Native	27	5 (19%)	22 (81%)	12 (44%)
Asian	499	79 (16%)	420 (84%)	280 (56%)

Black or African American	459	52 (11%)	407 (89%)	244 (53%)
Multi-racial	160	31 (19%)	129 (81%)	75 (47%)
Native Hawaiian or Other Pacific Islander	41	3 (7.3%)	38 (93%)	24 (59%)
White	1,853	323 (17%)	1,530 (83%)	926 (50%)
Missing	1,082	233	849	459
Ethnicity				
Hispanic	346	43(12%)	303 (88%)	188 (54%)
Non-Hispanic	2,814	466(17%)	2,348 (83%)	1,429 (51%)
Missing	961	217	744	403
Health insurance type				
Commercial	2,896	517 (18%)	2,379 (82%)	1,424 (49%)
Medicare/Medicaid	1,045	181 (17%)	864 (83%)	498 (48%)
Self-Pay	155	23 (15%)	132 (85%)	81 (52%)
Missing	25	5	20	17
NSES *				
Least poor	595	84 (14%)	511 (86%)	305 (51%)
Middle	1,436	238 (17%)	1,198 (83%)	715 (50%)
Poorest	1,903	363 (19%)	1,540 (81%)	914 (48%)
Missing	187	41	146	86
Gender of primary care provider				
Female	3,103	535 (17%)	2,568 (83%)	1,572 (51%)
Male	1,013	190 (19%)	823 (81%)	447 (44%)
Missing	5	1	4	1
Provider type				
Physician	3,264	566 (17%)	547 (82%)	322 (48%)
Nurse Practitioner	669	122 (18%)	2,698 (83%)	1,626 (50%)
Physician Assistant	181	34 (19%)	147 (81%)	72 (40%)
Other	7	4 (57%)	3 (43%)	0 (0%)
Primary care provider specialty				
Family Practice	2,433	509 (21%)	1,924 (79%)	1,103 (45%)
Pediatrics	1,466	161 (11%)	1,305 (89%)	827 (56%)
Others	222	56 (25%)	166 (75%)	90 (41%)

** Neighborhood socioeconomic status* (34)

*** HPV vaccination never-initiated and ever-initiated percentages add up to 100% across each row. HPV vaccination completion overlaps with ever-initiation because individuals who have completed the recommended doses are included in each column.*

Characteristics of mothers by adolescent HPV vaccination status

There were 3,297 mothers paired with the 4,121 adolescents. The number of adolescents under a single mother ranged from 1 to 5; 2,556 (78%) of the mothers had one child, 668 (20%) had two children, 73 (2%) had more than two children. For 91% of adolescents, the primary language of their mothers was English; mothers of 65% self-identified as White, 18% as Asian, and 13% as Black or African American. About 4 out of 5 adolescents had a mother who received care from UW Medicine for at least five years.

Adolescents with a mother using a language interpreter had higher initiation (89% vs. 82%, p <0.001) and higher completion (56% vs. 48%, p =0.01) than those with a mother who did not use a language interpreter. Adolescents with a mother who had received care from UW Medicine for more than 10 years had higher initiation (85% vs. 82% & 74%, p=0.022) and higher completion (53% vs. 45% & 42%, p<0.001) than those who received care for 5-10 years and less than five years respectively (Table 1.2).

Table 2. 2. Maternal characteristics and adolescent HPV vaccination status

		HPV Vaccination**		
Maternal characteristics	N = 4,121	Never vaccinated, N = 726	Ever initiated, N = 3,395	Completed, N = 2,020
Maternal age				
27-35	274	50 (18%)	224 (82%)	124 (45%)
36-45	1,776	355 (20%)	1,421 (80%)	828 (47%)
46-55	1,829	286 (16%)	1,543 (84%)	942 (52%)
56-65	242	35 (14%)	207 (86%)	126 (52%)
Maternal language interpreter flag				
No	3,812	693 (18%)	3,119 (82%)	1,847 (48%)
Yes	309	33 (11%)	276 (89%)	173 (56%)
Maternal language				
English	3,744	676 (18%)	3,068 (82%)	1,811 (48%)
Non-English	377	50 (13%)	327 (87%)	209 (55%)

Maternal race				
American Indian or Alaska Native	43	5 (12%)	38 (88%)	19 (44%)
Asian	656	108 (16%)	548 (84%)	349 (53%)
Black or African American	469	63 (13%)	406 (87%)	238 (51%)
Native Hawaiian or Other Pacific Islander	53	4 (8%)	49 (92%)	25 (47%)
Two or more races	71	16 (23%)	55 (77%)	28 (39%)
White	2,363	409 (17%)	1,954 (83%)	1,156 (49%)
Missing	466	121	345	205
Maternal ethnicity				
Hispanic	248	38 (15%)	210 (85%)	133 (54%)
Non-Hispanic	3,501	606 (17%)	2,895 (83%)	1,714 (49%)
Missing	372	82	290	173
Maternal duration of care*				
< 5 years	929	238 (26%)	691 (74%)	388 (42%)
5-10 years	670	122 (18%)	548 (82%)	301 (45%)
>10 years	2,522	366 (15%)	2,156 (85%)	1,331 (53%)
Maternal provider sex				
Female	3,434	583 (17%)	2,851 (83%)	1,707 (50%)
Male	687	143 (21%)	544 (79%)	313 (46%)
Maternal provider type				
Nurse Practitioner/CNM	646	122 (19%)	524 (81%)	316 (49%)
Physician	3,265	564 (17%)	2,701 (83%)	1,610 (49%)
Physician Assistant	210	40 (19%)	170 (81%)	94 (45%)
Maternal provider specialty				
Family Practice	2,953	568 (19%)	2,385 (81%)	1,378 (47%)
Internal Medicine	948	127 (13%)	821 (87%)	539 (57%)
Others	220	31 (14%)	189 (86%)	103 (47%)
Mother and adolescent with same primary care provider				
No	2,982	484 (16%)	2,498 (84%)	1,506 (51%)
Yes	1,139	242 (21%)	897 (79%)	514 (45%)

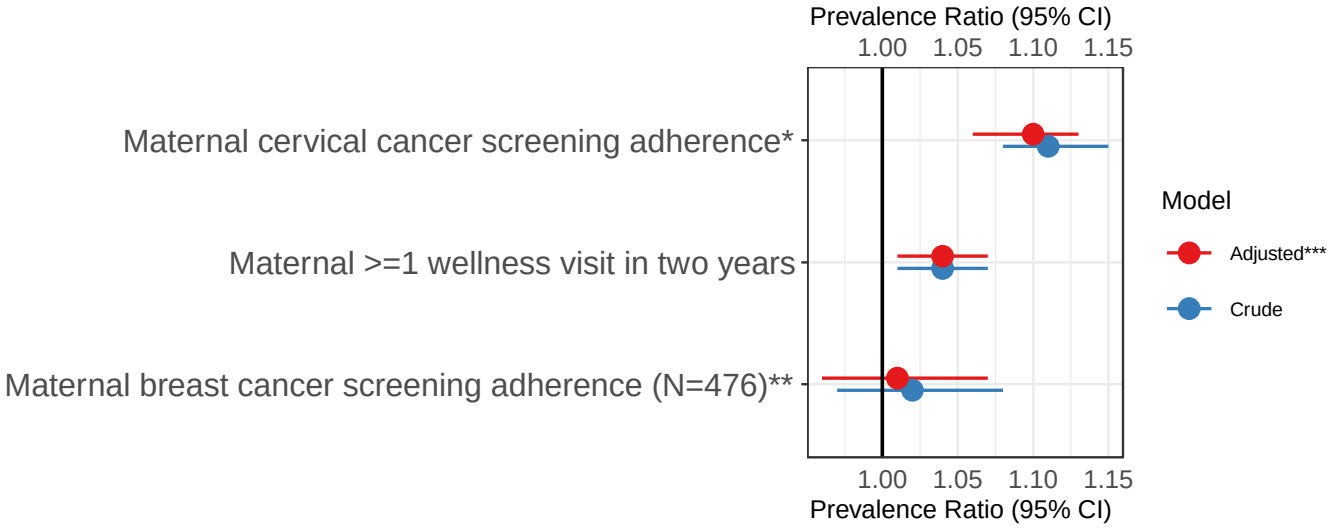
**Time between initial encounter to UW Medicine and the index visit*

*** HPV vaccination never-initiated and ever-initiated percentages add up to 100% across each row. HPV vaccination completion overlaps with ever-initiation because individuals who have completed the recommended doses are included in each column.*

Association of maternal preventative service utilization with adolescent HPV vaccination

HPV vaccine initiation among adolescents with a mother who was up to date for cervical cancer screening was 85%, and it was 77% among those who had a screening overdue mother.

Adolescents with a mother who had at least one wellness visit in two years had an 84% initiation, and it was 81% among those who had no wellness visit. Also, adolescents with a mother up to date for breast cancer screening and those with a mother overdue for breast cancer screening both had 89% HPV vaccine initiation. In the adjusted models, maternal cervical cancer screening adherence was associated with a 10% higher HPV vaccination initiation (APR: 1.10, 95%CI: 1,06, 1.13) than being overdue. Having at least one wellness visit in two years was associated with a 4% higher HPV vaccine initiation (APR: 1.04, 95%CI: 1.01, 1.07) than not having at least one wellness visit. Among mothers ≥52 years of age, breast cancer screening adherence was not significantly associated with HPV vaccine initiation (Figure 2.2).

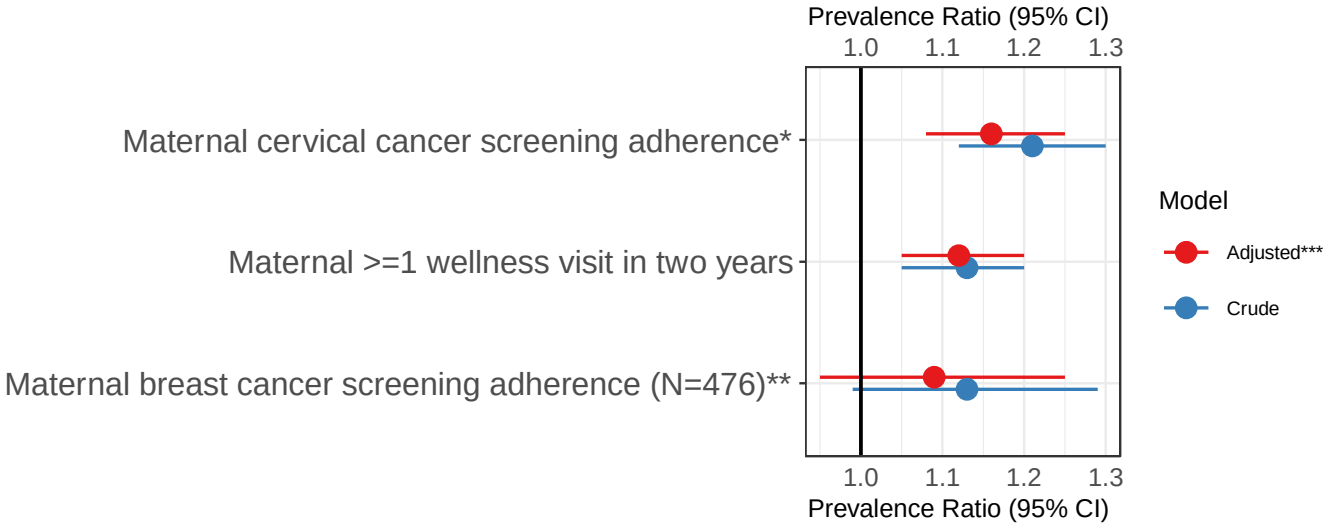


**CCS adherence evaluated among mothers with no documented history of hysterectomy*
***Breast cancer screening was evaluated among mothers age>=52*
****Adjusted for adolescent age and sex, and maternal age, duration of care, and language interpreter use*

Figure 2. 2. The association of maternal CCS, breast cancer screening, and wellness visits with adolescent HPV vaccine initiation

Adolescents with a mother who was up to date for cervical cancer screening had higher completion (52% vs. 43%) than those with an overdue mother. Adolescents with a mother who had at least one wellness visit in two years had higher completion (51% vs. 46%) than those

without. Similarly, adolescents with a mother who was up to date for breast cancer screening had higher completion (58% vs. 49%) than those with an overdue mother. In the adjusted models, maternal cervical cancer screening adherence was associated with a 16% higher vaccine completion (APR: 1.16, 95%CI: 1,08, 1.23) compared with being overdue for cervical cancer screening. Also, having at least one wellness visit in two years was associated with a 12% higher HPV vaccine completion (APR: 1.12, 95%CI: 1.05, 1.20) than not having at least one wellness visit. Among mothers ≥52 years of age, breast cancer screening adherence was not significantly associated with HPV vaccine completion (Figure 2.3).



**CCS adherence evaluated among mothers with no documented history of hysterectomy*
***Breast cancer screening was evaluated among mothers age>=52*
****Adjusted for adolescent age and sex, and maternal age, duration of care, and language interpreter use*

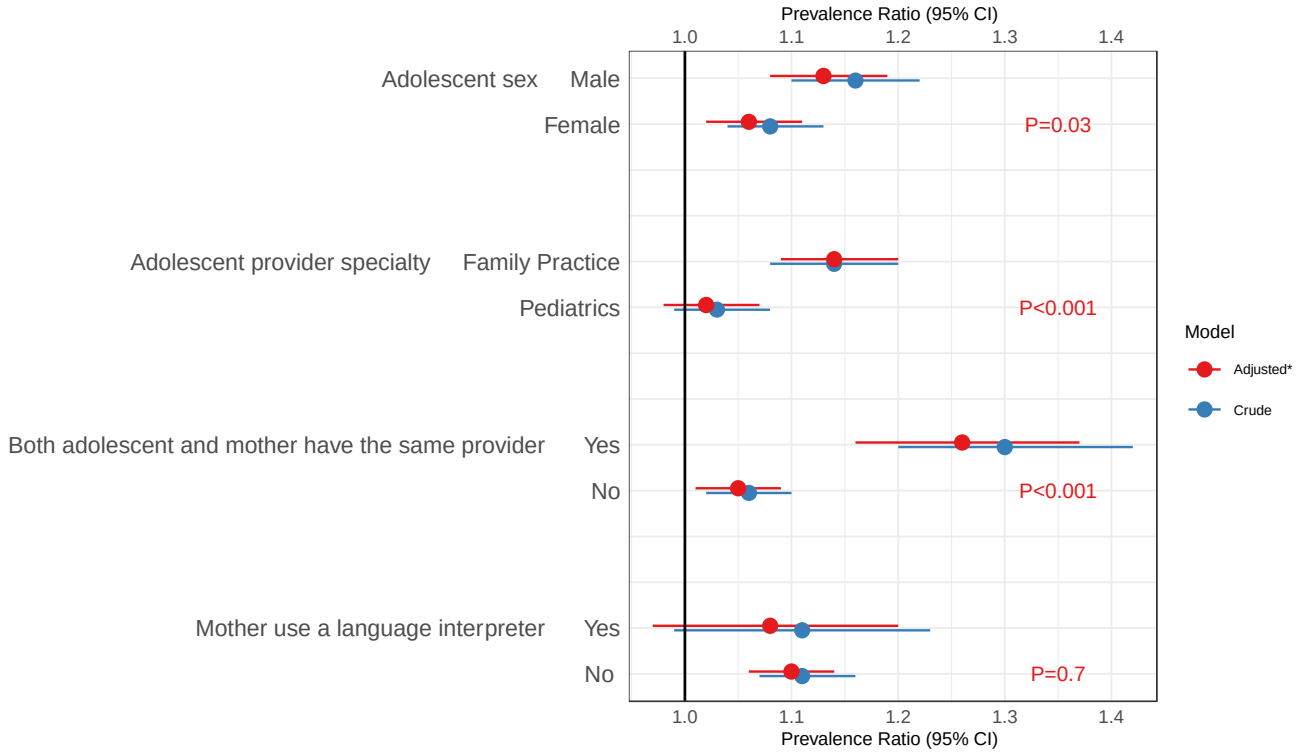
Figure 2. 3. The association of maternal CCS, breast cancer screening, and wellness visits with adolescent HPV vaccine completion

Except small changes in HPV vaccination coverage, the sensitivity analysis provided very similar estimates (*Supplemental Table 2.5 & 2.6*).

Effect modification

HPV vaccine initiation

The observed associations between maternal cervical cancer screening adherence and adolescent HPV vaccine initiation were stronger for male vs. female adolescents (APR_{males} – 1.13 [95%CI: 1.08, 1.19] vs. $APR_{females}$ 1.06 [95%CI: 1.02, 1.11], p=0.03), for adolescents who had a primary care provider with a specialty in Family Practice vs. Pediatrics ($APR_{Family\ Practice}$ – 1.14 [95%CI: 1.09, 1.20] vs. $APR_{Pediatrics}$ 1.02 [95%CI: 0.98, 1.07]:, p<0.001), and for adolescents who had the same primary care provider as their mother vs. not (APR_{same} – 1.26 [95%CI: 1.16, 1.37] vs. $APR_{different}$ 1.05 [95%CI: 1.01, 1.09], p<0.001) (Figure 3).



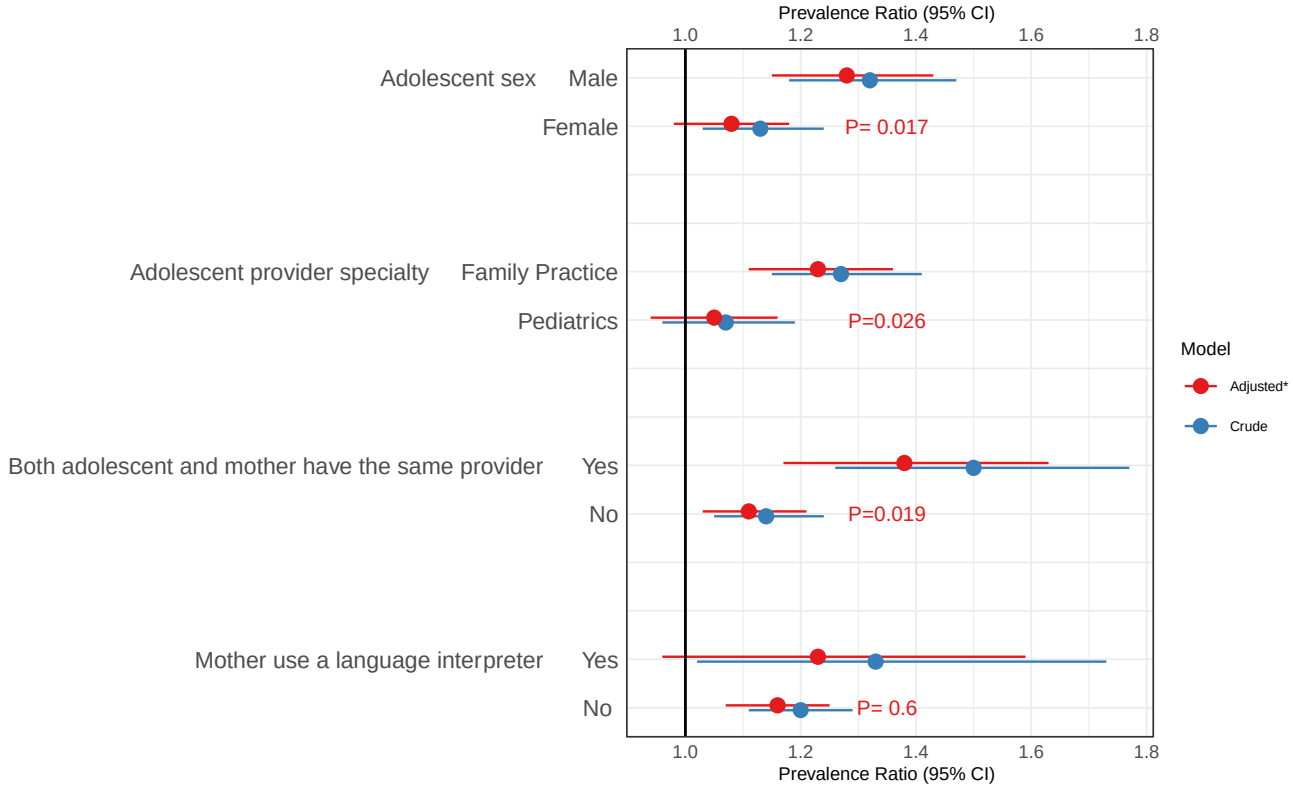
**Adjusted for adolescent age, and maternal age, duration of care, and language interpreter use (when it was not considered as an effect modifier).*

NB: The p−values come from the Wald test used for assessing effect modification

Figure 2. 4. Effect modification for the association of maternal CCS adherence with adolescent HPV vaccine initiation

HPV vaccine completion

The observed associations between maternal cervical cancer screening adherence and adolescent HPV vaccine completion were stronger for male vs. female adolescents (APR_{males} – 1.28 [95%CI: 1.15, 1.43] vs. $APR_{females}$ 1.08 [95%CI: 0.98, 1.18], p=0.017), for adolescents who had a primary care provider with a specialty in Family Practice vs. Pediatrics ($APR_{Family\ Practice}$ – 1.23 [95%CI: 1.11, 1.36] vs. $APR_{Pediatrics}$ 1.05 [95%CI: 0.94, 1.16], p=0.026), and for adolescents who had the same primary care provider as their mother vs. not (APR_{same} – 1.38 [95%CI: 1.17, 1.63] vs. $APR_{different}$ 1.11 [95%CI: 1.03, 1.21], p=0.019) (Figure 3).



**Adjusted for adolescent age, and maternal age, duration of care, and language interpreter use (when it was not considered as an effect modifier).*

NB: The p−values come from the Wald test used for assessing effect modification

Figure 2. 5. Effect modification for the association of maternal CCS adherence with adolescent HPV vaccine completion

Discussion

This study evaluated the association of maternal preventive service utilization with adolescent HPV vaccination. We found that maternal adherence to cervical cancer screening and attendance to wellness visits were associated with higher adolescent HPV vaccine initiation and completion. Maternal breast cancer screening was non-significantly associated with higher vaccine completion in the subset of adolescents with age-eligible mothers. The association between maternal cervical cancer screening adherence and adolescent HPV vaccination was more pronounced for male adolescents, adolescents with the same primary care provider as their mothers, and adolescents with a primary care provider specializing in Family Practice.

The positive association between maternal cervical cancer screening and HPV vaccine initiation and completion has been also reported by several studies done in the US and Europe using various data sources (18,79,84,86). Similarly, there has been evidence of the association of primary care visits with higher HPV vaccine initiation and completion (82). Despite variations in demographics and vaccination uptake over time, the consistencies across studies may suggest the central role of maternal preventive attitude in screening and vaccination (88).

However, most of the evidence so far has been from studies done almost a decade ago when HPV vaccination coverage was very low. For example, Hechter et al. found that maternal CCS adherence was associated with a 13% higher HPV vaccine initiation by using electronic health records from Kaiser Permanente Southern California between 2007-2009; nevertheless, less than 2% of the boys initiated the vaccine during that time (as opposed to 81% in our study) (86). Estimates of other prior US-based studies reporting a positive association between maternal cervical cancer screening adherence and HPV vaccination have reported odds ratios ranging from 1.07 to 1.9 and relative risks ranging from 1.1 to 1.5 (*Supplemental Table 2.4*) (20,23,32). Besides the consistencies across studies, our study provides updated evidence with further

exploration of important effect modifiers such as adolescent sex, provider specialty, having the same provider with a mother, and maternal language interpreter use.

Having a cervical cancer screening encounter may create an opportunity for mothers to learn more about HPV vaccination (89). Particularly, HPV testing has been part of the routine cervical cancer screening test since 2012 (71), and the results from our study might also provide evidence on the potential role HPV testing has played in creating better education opportunities about the virus and subsequent improvement of HPV vaccination. Another potential explanation could be mothers' health seeking behavior and knowledge of preventive healthcare. Women adherent to cervical cancer screening are more likely to have better educational status and better knowledge of the preventive mechanisms of the disease (45), which could make them more likely to get their children vaccinated (90,91). Likewise, wellness visits are mechanisms in which apparently healthy people proactively seek medical care for the early identification of silent medical problems (92,93). The primary purpose of wellness visits is to discuss preventive services and undertake necessary examinations (94,95), creating an opportunity to enhance mothers' knowledge of HPV vaccination and other health issues. On the other hand, the association may be confounded by maternal factors that increase preventative behaviors. For instance, cervical cancer screening adherent mothers may have a personal or family history of cancer and may better understand the consequences of HPV (53,54). The association we observed for breast cancer screening adherence was not statistically significant. The non-significant association may be due to the smaller sample size since we assessed the association only among adolescents with a mother above 52 years. In addition, breast cancer screening may not provide the same educational opportunity about HPV vaccination as cervical cancer screening,

The association of maternal cervical cancer screening adherence with adolescent HPV vaccination was stronger for male than female adolescents. HPV is not only responsible for

cancers of the female genital organs, such as cervical, vaginal, and vulvar cancers, but it also impacts both boys and girls by causing oropharyngeal and anal cancers, and boys by causing penile cancers (68). Even for the diseases among girls, boys play a substantial role in the transmission of HPV. Nevertheless, the long-standing societal awareness of cervical cancer might enable mothers to get their girls vaccinated regardless of their cervical cancer screening adherence. In addition, providers are more likely to recommend the vaccine to girls than boys (96,97). As a result, getting boys vaccinated may require more effort and comprehensive knowledge of the impacts of HPV infection. Our results suggest that mothers who are adherent to cervical cancer screening may be better informed about HPV and its consequences – so they are more likely to bring their boy adolescents for vaccination than non-adherent mothers (98). This implies that efforts to improve cervical cancer screening may subsequently improve HPV vaccination through the opportunities they open up for discussing cervical cancer prevention and available interventions, including HPV vaccination. Nevertheless, potential mechanisms of vaccinating adolescent boys beyond education during cervical cancer screening encounters may need further investigation.

We also observed a stronger association between CCS adherence and HPV vaccination when both mothers and adolescents had the same primary care provider than not. Adolescents are under the influence of their parents, and their healthcare encounters may depend on their parents' convenience (76,77). Mothers adherent to CCS are more likely to have a long-term and trusting relationship with their primary care providers (46,47). Also, mothers interacting frequently with their providers are more likely to vaccinate their children (99). Primary care providers responsible for more family members are more likely to approach things comprehensively and integrate recommendations for cervical cancer screening with HPV vaccination (100). Our analysis also showed that maternal CCS adherence had a higher association with adolescent HPV vaccination when the primary care providers of adolescents were in Family Practice than in Pediatrics. Unlike

Family Practitioners, Pediatricians primarily target adolescents and are more likely to recommend HPV vaccination regardless of maternal cervical cancer screening adherence (97,101). Not surprisingly, adolescents with a provider in Pediatrics had the highest proportions of HPV initiation and completion, but it was not modified by maternal cervical cancer screening adherence.

The HPV vaccine initiation in this study was 82% (close to the national average of 89%). Still, the completion was unacceptably low (49%) - indicating about half of the patients who initiated vaccination did not complete the series. Even among age 13-17 years old adolescents who started receiving care at UW medicine before their 9th birthday, vaccine completion was 56% *(Supplemental Table 2.5)*. In general, our estimates for vaccine completion are lower than the national rate of 61% and much lower than the 2030 Healthy People target of 80% (3,74). The coverage among people not seeking medical care could be even lower than among our sample of individuals engaged in care. Since the national estimates are based on surveys, some differences could be explained by overreporting (102). Despite that, the consistent discrepancy between initiation and completion needs further attention. Since most misconceptions about HPV vaccination may get resolved when adolescents initiate the HPV vaccine series, the failure to complete the series may be due to other potential barriers from both the health system and the patients' side (103). From the health system side, this points to a need for improved engagement and follow-up. In the usual practice at UW Medicine, patients do not routinely receive a reminder when they are due for the next HPV vaccine dose. Most of the ever-vaccinated adolescents in our study (80%) initiated the vaccine series more than 12 months before their index visit. Still, only a subset of them completed the series, suggesting a potential missed opportunity to fully vaccinate more adolescents. On the patient side, almost all adolescents in the HPV vaccine recommendation age group spend most of their weekdays in school. To have a clinic visit, they may have to miss school or go to the clinic after school. Parents' schedules also may not align with their adolescents' or the available clinic appointments (104). However, the interplay of system

and patient barriers needs further exploration. If recent advocacies on the sufficiency of a single-dose HPV vaccination come into reality, completion will be less of an issue (105). But in general, HPV vaccination coverage can be improved by leveraging available maternal and adolescent encounters to provide recommended vaccine doses.

This study has several strengths, including highlighting the role of maternal health-seeking behavior on adolescent HPV vaccination using large health system data. Using data from electronic health records minimizes potential recall bias and over-reporting inherent in most surveys. We also evaluated the role of different types of maternal preventative services and effect modification by patient and provider characteristics. Furthermore, using data from a large health system – UW Medicine – that serves an ethnically and economically diverse population enhances its generalizability. Despite that, it has some limitations. Firstly, we included only adolescents and mothers who had at least one primary care visit in two years, and thus the findings might not represent the rest of the population that do not seek health care or seek care elsewhere. More specifically, the racial and socioeconomic distribution of the included adolescents is different from those who were excluded – limiting the generalizability of the study (*Supplemental Table 2.1*). Secondly, we used residential addresses, insurance subscriptions, and maternal patient IDs to link adolescents with their respective mothers. Although this approach might have captured most of them correctly, there could have been mismatched adolescent-mother pairs that could have biased the observed association. Thirdly, younger adolescents who initiated the vaccination around the index visit might not have had enough time to complete the series, leading to an underestimation of the overall completion status. In addition, we could not establish a temporal relationship between maternal screening and adolescent vaccination due to the study's cross-sectional nature. As a result, decision makers may need to scrutinize potential mechanisms that can be targeted for future interventions. Lastly, despite their inclusion in the routine medical record system and UW Medicine’s bidirectional approach of pulling and pushing data to/from Washington

state immunization information systems (111), screening and vaccinations in other health facilities might not have been fully recorded and could have caused a non-differential misclassification. Beyond that, EHR data on race and ethnicity were missing for a considerable number of patients, limiting our ability to fully describe the characteristics of the study population.

Conclusion

Maternal cervical cancer screening adherence and recent wellness visits were positively associated with adolescent HPV vaccination. Delivering healthcare through a family-centered approach and engaging mothers in broad preventative care may increase HPV vaccination coverage. Maternal cervical cancer screening appointments and other healthcare encounters could be leveraged as opportunities to follow up and recommend adolescent HPV vaccination. Moreover, HPV vaccination can be enhanced by engaging providers of all types in promoting both cervical cancer screening and HPV vaccination.

Appendix

Supplemental Table 2.1. Comparison of the sociodemographic distribution of included and excluded adolescents.

Characteristic		Total, N = 9,694 (column %)	Excluded, N=5573 (column %)	Included N = 4,121 (column %)
Age			N	
	11	680 (7.0%)	377(7%)	303 (7%)
	12	1,396 (14%)	806(14%)	590 (14%)
	13	1,375 (14%)	761(14%)	614 (15%)
	14	1,535 (16%)	866(16%)	669 (16%)
	15	1,485 (15%)	831 (15%)	654 (16%)
	16	1,641 (17%)	971(17%)	670 (16%)
	17	1,582 (16%)	961(17%)	621 (15%)
Sex				
	Female	5,063 (52%)	2962(53%)	2,101 (51%)
	Male	4,619 (48%)	2605(47%)	2,014 (49%)
	Missing	12	6	6
Primary language				
	English	8,598 (89%)	4749(85%)	3,849 (93%)
	Non-English	1,096 (11%)	824 (15%)	272 (7%)
Language interpreter flag				
	Yes	870 (10%)	669 (12%)	201 (5%)
	No	7720(90%)	4265(96%)	3455 (95%)
	Missing	1104	639	465
Race				
	American Indian or Alaska Native	84 (1.2%)	57(2%)	27 (1%)
	Asian	1,105 (16%)	606 (16%)	499 (16%)
	Black or African American	1,305 (19%)	846(22%)	459 (15%)
	Multi-racial	339 (5.0%)	179(5%)	160 (5%)
	Native Hawaiian or Other Pacific Islander	145 (2.1%)	104(3%)	41 (1%)
	White	3,850 (56%)	1997 (53%)	1,853 (61%)
	Missing	2866	1784	1,082
Health insurance type				
	Commercial	5,473 (57%)	2577 (47%)	2,896 (71%)
	Medicare/Medicaid	3,595 (37%)	2550(46%)	1,045 (26%)
	Self-Pay	457 (4.8%)	302 (5%)	155 (4%)
	Other	95 (1.0%)	70 (1%)	25
	Missing	74	74	
NSES				
	Least poor	1,686 (19%)	1091 (22%)	595 (15%)
	Middle	3,304 (37%)	1868 (38%)	1,436 (37%)

	Poorest	3,849 (44%)	1946 (40)	1,903 (48%)
	Missing	855	668	187
Primary care provider sex				
	Female	7,224 (75%)	4121 (74%)	3,103 (75%)
	Male	2,460 (25%)	1447 (26%)	1,013 (25%)
	Missing	10	5	5
Provider type				
	Physician	7,787 (80%)	4523 (81%)	3,264 (79%)
	Nurse Practitioner	1,539 (16%)	870 (16%)	669 (16%)
	Physician Assistant	356 (4%)	175 (3%)	181 (4%)
	Other	12 (0.1%)	5 (0.1%)	7 (0.2%)
Primary care provider specialty				
	Family Practice	4,564 (47%)	2131 (38%)	2,433 (59%)
	Pediatrics	4,473 (46%)	3007 (54%)	1,466 (36%)
	Others	657(7%)	435 (8%)	222 (5%)

Supplemental Table 2.2. The association of maternal CCS adherence with adolescent HPV vaccine initiation stratified by adolescent sex, maternal language interpreter flag, and provider characteristics.

	HPV vaccine initiation													
	Adolescent sex													
	Female (N = 2,101)							Male (N = 2014)						
CCS adherence		CPR	95% CI	p	APR[1]	95% CI	p		CPR	95% CI	p	APR[1]	95% CI	p
Overdue	557 (79%)	ref.	ref.		ref.	ref.		505 (74%)	ref.	ref.		ref.	ref.	
Up to date	1,181 (86%)	1.08	1.04, 1.13	<0.001	1.06	1.01, 1.10	0.014	1,111 (85%)	1.16	1.10, 1.22	<0.001	1.15	1.09, 1.21	<0.001
	Maternal language interpreter flag													
	No (N = 3,812)							Yes (N = 309)						
CCS adherence		CPR	95% CI	p	APR[2]	95% CI	p		CPR	95% CI	p	APR[2]	95% CI	p
Overdue	990 (76%)	ref.	ref.		ref.	ref.		75 (83%)	ref.	ref.		ref.	ref.	
Up to date	2,096 (85%)	1.11	1.07, 1.16	<0.001	1.10	1.06, 1.14	<0.001	198 (92%)	1.11	0.99, 1.23	0.071	1.08	0.97, 1.21	0.14
	Adolescents and mothers with the same primary care provider													
	No (N = 2,982)							Yes (N = 1,139)						
CCS adherence		CPR	95% CI	p	APR[3]	95% CI	p		CPR	95% CI	p	APR[3]	95% CI	p
Overdue	834 (81%)	ref.	ref.		ref.	ref.		231 (65%)	ref.	ref.		ref.	ref.	
Up to date	1,638 (85%)	1.06	1.02, 1.10	0.001	1.05	1.01, 1.09	0.011	656 (85%)	1.30	1.20, 1.42	<0.001	1.27	1.17, 1.38	<0.001
	Adolescent primary care provider specialty													
	Family Practice (N = 2,433)							Pediatrics (N = 1,466)						
CCS adherence		CPR	95% CI	p	APR[4]	95% CI	p		CPR	95% CI	p	APR[4]	95% CI	p
Overdue	616 (72%)	ref.	ref.		ref.	ref.		393 (87%)	ref.	ref.		ref.	ref.	
Up to date	1,286 (83%)	1.16	1.11, 1.22	<0.001	1.14	1.08, 1.20	<0.001	900 (90%)	1.03	0.99, 1.08	0.12	1.03	0.99, 1.08	0.2

[1]Adjusted for adolescent age, and maternal age, duration of care, and language interpreter use
[2]Adjusted for adolescent age and sex, and maternal age, and duration of care
[3]Adjusted for adolescent age and sex, and maternal age, duration of care, and language interpreter use
[4]Adjusted for adolescent age and sex, and maternal age, duration of care, and language interpreter use

Supplemental Table 2.3. The association of maternal CCS adherence with adolescent HPV vaccine initiation stratified by adolescent sex, maternal language interpreter flag, and provider characteristics.

	HPV vaccine completion – n(%)												
	Adolescent sex												
	Female (N = 2,101)							Male (N = 2014)					
CCS adherence		CPR	95% CI	p	APR[1]	95% CI	p		CPR	95% CI	p	APR[1]	95% CI	p
Overdue	335 (48%)	ref.	ref.		ref.	ref.		262 (38%)	ref.	ref.		ref.	ref.	
Up to date	744 (54%)	1.13	1.03, 1.24	0.011	1.08	0.98, 1.18	0.12	652 (50%)	1.32	1.18, 1.47	<0.001	1.29	1.15, 1.44	<0.001
	Maternal language interpreter flag												
	No (N = 3,812)							Yes (N = 309)					
CCS adherence		CPR	95% CI	p	APR[2]	95% CI	p		CPR	95% CI	p	APR[2]	95% CI	p
Overdue	558 (43%)	ref.	ref.		ref.	ref.		41 (46%)	ref.	ref.		ref.	ref.	
Up to date	1,267 (51%)	1.2	1.11, 1.29	<0.001	1.16	1.08, 1.25	<0.001	130 (60%)	1.33	1.02, 1.73	0.034	1.19	0.93, 1.52	0.2
	Adolescents and mothers with the same primary care provider												
	No (N = 2,982)							Yes (N = 1,139)					
CCS adherence		CPR	95% CI	p	APR[3]	95% CI	p		CPR	95% CI	p	APR[3]	95% CI	p
Overdue	478 (46%)	ref.	ref.		ref.	ref.		121 (34%)	ref.	ref.		ref.	ref.	
Up to date	1,011 (53%)	1.14	1.05, 1.24	0.001	1.11	1.02, 1.20	0.014	386 (50%)	1.5	1.26, 1.77	<0.001	1.45	1.22, 1.72	<0.001
	Adolescent provider specialty												
	Family Practice (N = 2,433)							Pediatrics (N = 1,466)					
CCS adherence		CPR	95% CI	p	APR[4]	95% CI	p		CPR	95% CI	p	APR[4]	95% CI	p
Overdue	332 (39%)	ref.	ref.		ref.	ref.		242 (54%)	ref.	ref.		ref.	ref.	
Up to date	757 (49%)	1.27	1.15, 1.41	<0.001	1.23	1.11, 1.36	<0.001	575 (57%)	1.03	0.99, 1.08	0.12	1.03	0.99, 1.08	0.2

[1]Adjusted for adolescent age, and maternal age, duration of care, and language interpreter use
[2]Adjusted for adolescent age and sex, and maternal age, and duration of care
[3]Adjusted for adolescent age and sex, and maternal age, duration of care, and language interpreter use
[4]Adjusted for adolescent age and sex, and maternal age, duration of care, and language interpreter use

Supplemental Table 2.4. Literature summary for the association of maternal health seeking on adolescent HPV Vaccination

Author (Year)	Country	Study design	Population (age, sample size)	Outcome	Key Findings
(Taylor et al. 2014) (112)	US, Seattle	Cross-sectional	• 9–17-year-old • 89 American Cambodian girls	Vaccination	P-value = 0.002: *mother Pap test vs not*
(Chao et al. 2009) (84)	US, California	Cohort	• 9–17-year-old girls • 148,350: initiation • 19,729: completion	Vaccination	**Vaccine initiation** OR:1.47 (95% CI: 1.43, 1.52): *mother Pap test* OR=1.11(95% CI=1.07, 1.14): *abnormal Pap test* OR=1.19(95% CI=1.10, 1.28): *genital/anal warts* OR=1.13(95% CI=1.04, 1.22): *other STI* **Vaccine completion** OR=1.42(95% CI=1.31,1.54): mother Pap test OR=0.67(95% CI=0.43, 1.04): *STI African American* OR=4.92(95% CI=1.00, 24.25): *STI Asian*
(Hechter et al. 2013) (91)	US, California	Cohort	• 9–17-year-old boys • 254,489	Vaccination	**Vaccine initiation** RR = 1.16(95% CI: 1.07, 1.26): *Influenza vaccine* RR = 1.13(95% CI = 1.01, 1.26): *mother Pap test* RR = 1.47(95% CI = 0.93, 2.34): *genital warts*
(Markovitz et al. 2014a) (113)	US, Michigan	Cross-sectional	• 13-17 years old girls. • 38,604	Vaccination	**Vaccine initiation** OR:1.07(95% CI: 1.06-1.08): *mother Pap test* OR: 1.10(95% CI:1.08-1.11): *mammograms* OR: 1.07(95% CI:1.06-1.09) *primary care visits*
(Monnat and Wallington 2013) (104)	US (BRFSS)	Cross-sectional	• 9–17-year-old girls • 4,776: initiation • 1,270: completion	Vaccination	**Vaccine initiation** OR: 1.34(95% CI: 1.07–1.69): *mother Pap test* **Vaccine completion** OR: 1.90(95% CI: 1.37–2.72): *mother Pap test*
(Steens et al. 2012) (114)	The Netherlands	Cross-sectional	• 13-16-year-old girls • 337,368: initiation • 195,673: completion	Vaccination	**Vaccine initiation** OR: 1.40 (95% CI: 1.38–1.43): *mother Pap test* **Vaccine completion** OR: 1.54 (95% CI: 1.51–1.57): *mother Pap test*
(Lutringer-Magnin et al. 2013) (90)	France	Cross-sectional	• 14-23 years old girls • 501	Vaccination	**Vaccine initiation** OR: 6.2 (95% CI: 1.5–25.8): *mother Pap test* OR: 4.6 (95% CI: 1.6–13.5): *mother never lived with a partner*

					OR: 3.2 (95% CI: 1.6–6.1): *mother's vaccination against hepatitis B*
(Venturelli et al. 2017) (93)	Italy	Quasi-experimental	• 12-13 years old girls • 1,445	Vaccination	**Vaccine initiation** Intervention RR 1.72 95%CI 1.26–2.36): *mother Pap test* Control RR 1.20 95%CI 1.04–1.40): *mother Pap test*
(Spencer et al. 2013) (89)	England	Cohort	• 12-13 years old girls • 117,343: initiation • 58,354: completion	Vaccination	**Vaccine initiation** AOR :3.5 (95% CI: 3.1–4.0): *mother Pap test* AOR: 1.2(95%: 1.1–1.3): *mild abnormal Pap* AOR: 1.3(95%: 1.3–1.4): *moderate-severe neoplasia* **Vaccine completion** AOR routine: 2.2(95%:1.6–2.9): *mother Pap test*
(Hansen et al. 2015) (115)	Norway	Cohort	• 10-12 years old girls • 90, 540: initiation • 70,870: completion	Vaccination	**Vaccine initiation** OR: 0.76(95% CI: 0.64,0.90)-*mothers from Africa* OR: 1.44(95%CI: 1.29, 1.62)-*mothers from Asia* OR: 0.86 (95%CI: 0.81,0.91): *No-Pap screened* OR: 1.28 (95%CI: 1.07,1.53): *Screened, abnormal* OR: 0.19(95%CI: 0.18, 0.21: *Girls MMR vaccine* **Vaccine completion** OR: 0.94 (95%CI: 0.84,1.06): *Not Pap screened* OR: 1.08 (95%CI: 0.76,1.54): *Screened, abnormal*
(Lefevere et al. 2011) (18)	Belgium	Cohort	• 11-18 -years-old girls • 127,854	Vaccination	**Vaccine initiation** OR: 4.5(95% CI: 3.5–5.9): *One Pap test* OR:16.0(95% CI: 12.1–21.2): *3 or more Pap tests*

Supplemental Table 2.5. HPV Vaccination by adolescent duration of care

Characteristics	N	HPV Vaccination Ever initiated	Completed
Adolescents age 11-17			
Overall	4121	3,395 (82%)	2,020 (49%)
Adolescents enrolled at UW Medicine before age 9 (all)	3,001	2,549 (85%)	1,546 (52%)
By age			
11	227	158 (70%)	30 (13%)
12	473	390 (82%)	238 (50%)
13	485	416 (86%)	291 (60%)
14	497	426 (86%)	239 (48%)
15	473	414 (88%)	235 (50%)
16	455	398 (87%)	256 (56%)
17	391	347 (89%)	257 (66%)
Adolescents enrolled at UW Medicine after age 9 (all)	1,112	840 (76%)	471 (42%)
By age			
11	75	42 (56%)	8 (11%)
12	115	82 (71%)	43 (37%)
13	127	93 (73%)	53 (42%)
14	172	126 (73%)	70 (41%)
15	181	138 (76%)	86 (48%)
16	214	180 (84%)	107 (50%)
17	228	179 (79%)	104 (46%)
Adolescent duration of care			
<6 months	280	177 (63%)	82 (29%)
6 to 11 months	95	64 (67%)	31 (33%)
1 to 2 Years	380	296 (78%)	173 (46%)
3 to 5 Years	438	360 (82%)	208 (47%)
>5 Years	2928	2,498 (85%)	1,526 (52%)
Adolescents age 13-17			
Overall	3,228	2,720 (84%)	1,699 (53%)
Initiated care at UW Medicine before age 9 (all)	2,301	2,001 (87%)	1,278 (56%)
By age			
13	485	416 (86%)	291 (60%)
14	497	426 (86%)	239 (48%)
15	473	414 (88%)	235 (50%)
16	455	398 (87%)	256 (56%)
17	391	347 (89%)	257 (66%)
Initiated care at UW Medicine after age 9 (all)	922	716 (78%)	420 (46%)
By age			

13	127	93 (73%)	53 (42%)
14	172	126 (73%)	70 (41%)
15	181	138 (76%)	86 (48%)
16	214	180 (84%)	107 (50%)
17	228	179 (79%)	104 (46%)

Supplemental Table 2.6. The association of maternal preventative care utilization with HPV vaccination among 11-17 years old adolescents who initiated care at UW Medicine before their 9th birthday.

	HPV Vaccine Initiation					
	CPR[1]	**95% CI[1]**	**p-value**	**APR**	**95% CI[1]**	**p-value**
Cervical cancer screening adherence						
Overdue	—	—		—	—	
Up to date	1.07	1.03, 1.11	<0.001	1.06	1.02, 1.10	0.002
≥1 Wellness visit in two years						
No	—	—		—	—	
Yes	1.02	0.98, 1.05	0.4	1.02	0.98, 1.05	0.3
Breast cancer screening adherence						
Overdue	—	—		—	—	
Up to date	1.02	0.93, 1.12	0.7	1.03	0.94, 1.12	0.5
	HPV Vaccine Completion					
Cervical cancer screening adherence						
Overdue	—	—		—	—	
Up to date	1.12	1.03, 1.22	0.007	1.10	1.02, 1.20	0.018
≥1 Wellness visit in two years						
No	—	—		—	—	
Yes	1.08	1.00, 1.16	0.039	1.09	1.01, 1.17	0.027
Breast cancer screening adherence						
Overdue	—	—		—	—	
Up to date	1.20	0.94, 1.54	0.14	1.23	0.97, 1.55	0.086

Chapter 3. Modeling the impact of self-sampling on cervical cancer incidence and mortality among East African Immigrant Women in Washington State

Abstract

Introduction: Cervical cancer screening uptake among East African immigrants in the US has been consistently low. Several studies show that using patient self-collected samples can increase screening coverage among underserved populations, with comparable accuracy to clinician-collected samples for detecting precancers. However, its impact on cervical cancer incidence and mortality is understudied.

Methods: We used a Markov cohort state-transition model of the natural history of high-risk human papillomavirus (HPV) to predict the impact of primary HPV screening with self-sampling compared to standard of care clinician sampling on cervical cancer incidence and mortality among East African immigrant women in Washington state. The model was calibrated to HPV prevalence and age-specific cervical cancer incidence. The primary outcomes were age-specific cervical cancer incidence and mortality. A hypothetical cohort of 10,000 East African immigrant women aged 25 years was followed until the age of 80. The base case scenario was a 63% screening coverage and 83% colposcopy adherence with the standard of care and 70% screening coverage and 67% colposcopy adherence with self-sampling, and 85% treatment adherence with both strategies. We also compared outcomes between the screening strategies for various scenarios of screening coverage, colposcopy and treatment adherence. We used a Poisson regression model to compare differences in age-specific incidence and mortality rates.

Results: With the base case scenario, there is no statistically significant difference in cervical cancer incidence and mortality between the standard of care and self-sampling strategies. In a scenario that increased cervical cancer screening coverage by self-sampling to 90%, the results of the two strategies were comparable. However, increasing only cervical cancer screening coverage of self-sampling up to 100% results a 2% lower cervical cancer incidence and mortality. Moreover, as compared to the standard of care, an increase in self-sampling colposcopy

adherence to the level of standard of care yields a 5% reduction in both incidence and mortality with 80% screening coverage, a 7% reduction in incidence and an 8% reduction in mortality with 90% screening coverage, and a 10% incidence and 11% mortality reduction with 100% screening coverage. When we modify the latter scenario to additionally increase treatment adherence to 100%, we could observe a 12% reduction in incidence and a 13% reduction in mortality.

Conclusion: The implementation of cervical cancer screening by self-sampling for underserved populations needs to be backed by strong follow-up of patients. The impact of a self-collection strategy is optimized if the loss to follow-up can be minimized, and the value increases if screening reaches more people than the standard of care. Therefore, strategies with high patient follow-up and treatment adherence may need to be concurrently implemented to consider self-sampling as a better screening alternative.

Introduction

More than 95% of cervical cancer is caused by human papillomavirus (HPV), which primarily infects the cervix's transformation zone and causes precancer and cancerous lesions, although most infections clear spontaneously within one to two years (116–119). Since the invention of the Pap smear around the mid-20th century, cervical cancer-related morbidity and mortality in high-income countries have declined by over 80% (1,2). Identifying the human papillomavirus (HPV) as a necessary cause of cervical cancer has played a substantial role in the technological advancement of screening techniques (120,121). In addition to including liquid-based cytology in 2000, HPV testing has been part of the routine screening program since the late 1990s as a triage for atypical squamous cells of undetermined significance (ASCUS), then as co-testing with cytology since 2012, and most recently as primary screening (122–124). The current standard of care screening strategies in the US are cytology only every three years, cytology plus HPV co-

testing every five years, or an HPV test only every five years (33,124). All strategies involve clinician-collected samples through pelvic examination.

Most cervical cancer cases and deaths in the US occur among underserved and minority populations, including immigrants (5,6). East African immigrants are one of the underserved populations with lower screening rates and multiple cultural barriers to healthcare seeking (125). In Washington state, the East African immigrant community is one of the fast-growing populations, with an estimated size of over 46,000 (126,127). These people are immigrating from East Africa, where cervical cancer incidence is the highest globally (25), routine screening is unavailable, and cultural taboos surrounding genital health are common (16,26). As reported in Chapter One of this dissertation, cervical cancer screening adherence among East African Immigrants with access to primary healthcare was 63%, much lower than the national average of over 80% (7,128). This estimate is expected to be much lower among the general East African immigrant community, which may comprise a non-ignorable number of people who do not have regular healthcare access (12–14). Addressing the screening disparities among these populations may require implementing new interventions that tackle potential barriers (10,30).

In recent years, HPV self-sampling, where patients take their sample instead of undergoing pelvic examination by clinicians, has received greater attention. Several clinical trials have shown that self-sampling has potential to improve screening uptake among underserved populations (129–133). Implementing self-sampling as a screening strategy may alleviate barriers related to genital examination and the time and place of screening (15,19,134–138). In addition, multiple studies have shown that patient-collected samples for HPV testing have comparable accuracy to provider-collected samples for HPV testing for detecting cervical precancers (139,140). As a result, there has been an increasing inclination towards the self-sampling strategy to expand screening coverage among underserved people (139,141,142). Several countries have included

self-sampling as part of their routine screening programs, but it has not yet been approved by the US Food and Drug Administration (FDA) (143).

The success of screening requires that patients with abnormal screening results complete follow-up testing and treatment as recommended. Although self-sampling may increase uptake of screening, data suggest that the need for additional clinic visits for patients who test HPV-positive for high-risk genotypes via self-collection may have lower follow-up for colposcopy and treatment (144–146), which may reduce the effectiveness of HPV self-sampling as a cervical cancer screening strategy (143–145).

Empirical studies are typically clinical trials that run for a maximum of a few years, and they inherently lack the potential to show the long-term impact of implementing self-sampling on the subsequent burden of cervical cancer among underserved populations (133,147,148). To fill this knowledge gap, using decision analysis modeling, we predicted the impact of self-sampling compared to the standard of care on cervical cancer incidence and mortality among East African immigrant women, and tested various scenarios of possible implementation targets.

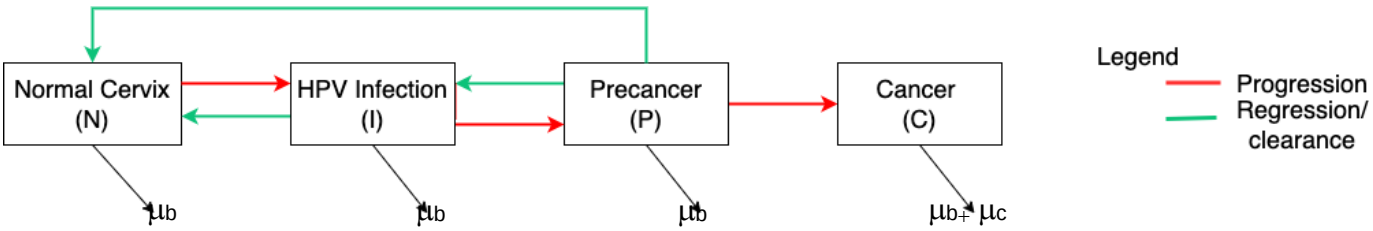
Methods

Study design and population

We fitted a Markov cohort state-transition model to simulate the natural history of high-risk (hr) HPV and estimate the effect of primary HPV screening by self-sampling relative to standard of care clinician-collected sampling on cervical cancer incidence and mortality among East African immigrant women living in Washington state. Our model simulated a hypothetical cohort of 10,000 women aged 25 years and followed them until 80 years of age – the average life expectancy of women in the US (149).

Model Structure

The model defines four mutually exclusive health states: normal (N), hr-HPV infection (I), precancer (P), and cancer (C). Individuals with a normal cervix may transition to the hr-HPV infection compartment. Hr-HPV-infected individuals either recover to the normal state or progress to the precancer state. From precancer, people may either transition to the final compartment, invasive cancer (Ca), or regress to the normal or hr-HPV infection states. The cohort was divided into 11 age groups with a five-year interval. Age-specific background mortality rates apply to all people at all compartments, and in addition to that, people in the cervical cancer compartment experience excess cervical cancer-specific mortality. The model runs in 6-month cycles, with transition probabilities defined accordingly. We made a simplifying assumption that recovery or treatment from precancer would not influence subsequent infection or cervical dysplasia risk (Figure 3.1).



μ_b= Background mortality; μ_c = Cervical cancer-specific mortality

Figure 3. 1. Model diagram for the natural history of cervical cancer

The primary outcomes of the model were cervical cancer incidence and cervical cancer-specific mortality. The new strategy was primary HPV testing using self-sampled specimens, and the

comparator was standard of care primary HPV testing on clinician-collected specimens (*Supplemental Table 3.1*). We compared primary HPV testing by self-sampling every five years to the standard-of-care primary HPV testing every five years. All screening modalities were assumed to start at the age of 25, and routine screening continues until the age of 65 regularly (33,124). There was no screening for individuals aged 65 to 80.

Out of the standard-of-care screening strategies, the primary HPV test was chosen because it is the closest to self-sampling and has become the preferred screening approach (124,150,151). In clinical practice, patients who are positive for HPV 16 & 18 are referred directly to diagnostic colposcopy in both self-sampling and the standard of care strategies. However, for patients who test positive for other hr-HPV types (not HPV 16 & 18), colposcopy is indicated only when reflex cytology is abnormal. With clinician sampling, reflex cytology is done using the original sample, but in the case of self-sampling, patients require an additional in-clinic visit for cytology (135,152). This is because self-collected samples are inadequate for cervical cytological testing (153). As a result, the need for an additional clinic visit can be a barrier to completing follow-up. When indicated, follow-up for colposcopy is also suggested to be lower after self-sampling relative to standard of care strategies.

Model parameters

Model parameters were defined using published data, with modifications to reflect the dynamics of cervical cancer among East African immigrants. As presented below, HPV incidence and natural history parameters were calibrated to match the age-specific prevalence of HPV among Black or African American women in the US (154). Prior values for parameters for the natural course of cervical cancer (i.e., progression, clearance, invasion, and regression) were taken from a prior modeling study that estimated duration-specific probabilities for high-risk HPV infection

using data from a series of cohort studies and clinical trials (155). We transformed the duration-specific probabilities to age-specific probabilities to align with the approaches we applied in our model (*Supplemental Table 3.2*). While there is evidence that natural history parameters are duration-dependent (156), using a Markov model with memoryless transitions limited our ability to define and apply duration-specific transitions. As such, we used age as a proxy for duration, in line with other models (157,158).

Mortality estimates were derived by combining estimates from US Black/African populations and East Africa. We assume that neither population represented East African immigrants specifically. Despite better evidence for African Americans, most studies have overrepresented US-born African Americans. On the other hand, studies done in sub-Saharan Africa may reflect risk factors that East African immigrants may carry to the new context, but we expect mortality to be lower for these women in the US due to better healthcare access. As a result, we took a weighted average of the estimates from Black or African American women in the US and women in East Africa, with a ratio of 70% and 30%, respectively. Mortality data for Black or African American women were taken from the Centers for Disease Control (CDC) for background mortality and from Surveillance for Epidemiologic Evaluation and Research (SEER) for cervical cancer-specific mortality (159,160). World Health Organization (WHO) data was taken for background and cervical cancer-specific mortalities for East African women (*Supplemental Table 3.3*) (161).

We retrieved estimates for the test sensitivity and specificity of both self-sampling and the standard of care from high-quality US-representative meta-analyses. Test performances for self-sampling and the standard of care were similar - sensitivity 93% vs. 94% and specificity 85% vs. 87%, respectively (*Supplemental Table 3.1*) (162,163). For a base case screening coverage in the standard of care, we used estimates from Chapter One, where 63% of East African Immigrants living in Washington state with access to primary healthcare adhered to screening (128). We

estimated the base case scenario coverage for self-sampling using evidence from the STEP trial, a pragmatic trial done in Kaiser Permanente Washington in Washington State evaluating mailed self-sampling for increasing cervical cancer screening (164). The study reported that mailing self-sampling kits to individuals overdue for cervical cancer screening increased screening completion by 17% over 6-month follow-up compared with standard of care reminders to attend in-clinic screening (148). We assumed that people adherent to the standard of care remain adherent to the self-sampling strategy and apply the 17% increase for only the remaining 37% - making the baseline self-sampling screening coverage about 70%. In addition, we compared differences by incrementally increasing self-sampling screening coverage up to 100%. We used estimates for colposcopy and treatment adherence from the HOME HPV self-sampling clinical trial that was also done among screening overdue participants at Kaiser Permanente Washington in Washington State (135). The trial reported that 83% vs. 67% of eligible participants were colposcopy adherent in the standard of care and self-sampling, respectively (133). Treatment adherence was reported as almost 100% in both cases, but we have also considered a treatment adherence of 85% to account for uncertainties. In both strategies, we assumed patients positive for hr-HPV should receive colposcopy. However, as noted above, in the self-sampling strategy, only HPV16/18 positive patients are referred directly for colposcopy, whereas those who are positive for other hr-HPV types need a clinic visit to undergo reflex Pap testing from a provider-collected sample before potential colposcopy referral. To discount the loss to follow-up due to additional visits, we incorporated probabilities for adherence to follow-up Pap screening for about half of the HPV-positive patients in the self-sampling strategy who were estimated to be positive for other hr-HPV genotypes (133,165). To explore the sensitivity of model results to these variables, we compared scenarios varying the level of screening coverage and colposcopy adherence for the standard of care and self-sampling strategies. Treatment adherence was not varied between both approaches (*Supplemental Table 3.*4).

As sensitivity analyses, we fitted separate models using background mortality and cervical cancer-specific mortalities for East African women specifically and for Black or African American women without adjustment, and we evaluated differences across models (*Supplemental Table 3.*3) (149,160,161).

Model simulation and calibration

We simulated the natural history of high-risk HPV with and without screening using 6-month Markov cycles. Individuals move to a different disease state at each cycle or remain in the same state. The prevalence of HPV infection and precancer at age 25 was considered to initiate the model. Individuals in infected and precancer states upon model initiation were dispersed to each infection and precancer compartment based on the chance of possible duration of infection and precancer at age 25-29. An HPV infection prevalence of 24.1% and a precancer prevalence of 3.2% were used to initiate the model (154).

There is substantial uncertainty in the natural history of cervical cancer, so most models of HPV calibrate these parameters to match cervical cancer incidence and of HPV prevalence data. Due to a lack of prior evidence on the burden of HPV and cervical cancer among East African immigrants, we calibrated the model for the prevalence of HPV and incidence of cervical cancer among Black or African American women in the US. The SEER 2015-2019 age-specific incidence of cervical cancer for Black or African American women was used as a calibration target of cancer incidence, and Clarke's (2021) study on the age-specific prevalence of HPV among Black or African American in the Mississippi Delta was considered for the prevalence calibration target (154,160).

We used values from Campos et al. to define prior ranges (155) , and we defined age-specific ranges for each disease transition probability (*Supplemental Table 3.*2). Using Latin Hypercube sampling, we generated 10,000 parameter combinations. We calculated and standardized the

mean square distance between the observed and predicted estimates for both HPV prevalence and cervical cancer incidence. Then, we summed the standardized mean square distance values of HPV prevalence and cervical cancer incidence and selected the best-fitting model parameters as the parameters corresponding to the minimum summed standardized mean square distance (*Supplemental Table 3.*2). Since cytology has been the primary screening method used in the period corresponding to the calibration target of cervical cancer incidence in 2015-2019, the comparison was made between SEER estimates and the predicted incidence of cervical cancer using cytology's performance characteristics as a primary screening strategy. The model parameters were calibrated to fit empirical data on HPV prevalence and cervical cancer incidence (Figure 3.2). As a sensitivity analysis, since we don't have data on the HPV prevalence among East African immigrants, we re-ran scenarios in a model that adjusted HPV incidence to match the HPV prevalence in East Africa (27).

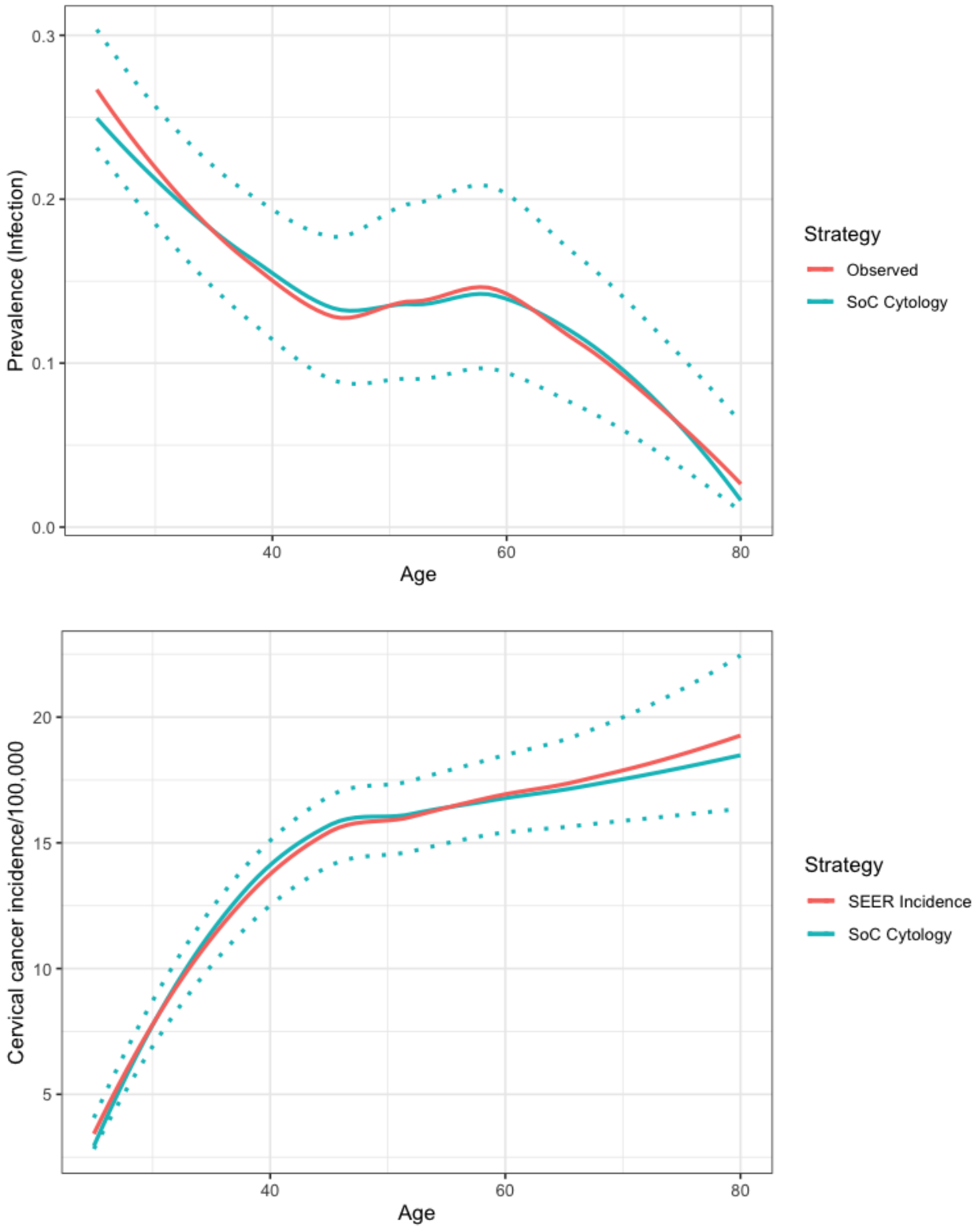


Figure 3. 2. Model calibration of age-specific HPV prevalence and cervical cancer incidence.

The dotted lines are the 95% confidence intervals of the observed estimates.

Model scenarios

For the base case analysis, we assumed a screening coverage of 63% for the standard of care and 70% for self-sampling, and a colposcopy adherence of 83% in the standard of care and 67% for self-sampling (128,133). We considered 85% of individuals from both groups to adhere to the treatment of precancer in the primary analysis, and we also did a separate analysis considering 100% treatment adherence for both groups. The additional scenarios considered were increasing screening coverage for self-sampling to 80%, 90%, and 100%, keeping colposcopy adherence at base case levels; concurrently increasing the colposcopy adherence for self-sampling to match to the standard of care; and making screening adherence for self-sampling 100% with a colposcopy and treatment adherence of 100% for both strategies. We have included multiple other scenarios with varying estimates for both strategies as part of the sensitivity analysis (*Supplemental Table 3.4*). We used a Poisson regression model to compare differences in incidence and mortality rates across screening strategies, including comparisons with no screening.

Results

Cervical cancer incidence

Both the standard of care and self-sampling strategies are estimated to significantly reduce the incidence of cervical cancer compared to no screening. Out of 10,000 individuals, 85 people are estimated to develop cervical cancer in their lifetime in the unscreened category, and it ranges from 60-74 in the screened category. The lowest number of cases is seen in the self-sampling strategy when screening coverage, adherence to colposcopy, and treatment probability are all 100% (Table 3.1).

Table 3. 1. Cumulative number of predicted cervical cancer cases comparing unscreened, the standard of care and self-sampling.

		Precancer (CIN2+)				
		Unscreened	SoC HPV[a]	Self-sampling[b]	Unscreened	S
Colposcopy 83% (SoC) vs 67% (SS)	Screening 63% vs 70%	3782	3755	3762	85	
	Screening 63% vs 80%	3782	3755	3760	85	
	Screening 63% vs 90%	3782	3755	3757	85	
	Screening 63% vs 100%	3782	3755	3754	85	
Colposcopy both 83%	Screening 63% vs 70%	3782	3755	3752	85	
	Screening 63% vs 80%	3782	3755	3747	85	
	Screening 63% vs 90%	3782	3755	3743	85	
	Screening 63% vs 100%	3782	3755	3739	85	
Colposcopy both 100%	Screening 63% vs 100%	3782	3750	3730	85	

a: Standard of care primary HPV test after provider-collected sample; SoC- Standard of care
b: Primary HPV test after patient self-collected sample; SS- Self-sampling

Age-specific incidence of cervical cancer was very similar across screening strategies in the base case scenario. Keeping colposcopy adherence at 83% (SoC) vs. 67% (self-sampling), the standard of care has lower incidence of cervical cancer until the screening coverage of self-sampling increases up to 80%. At 90% screening coverage, both have equal incidence of cervical cancer, but when the self-sampling screening coverage is 100%, the incidence in the self-sampling strategy is lower than the standard of care. When the follow-up to colposcopy after self-sampling reaches up to the level of the standard of care, the incidence of cervical cancer is in the self-sampling strategy becomes always lower than the standard of care - the level of reduction increases together with the screening coverage (Figure 3.3).

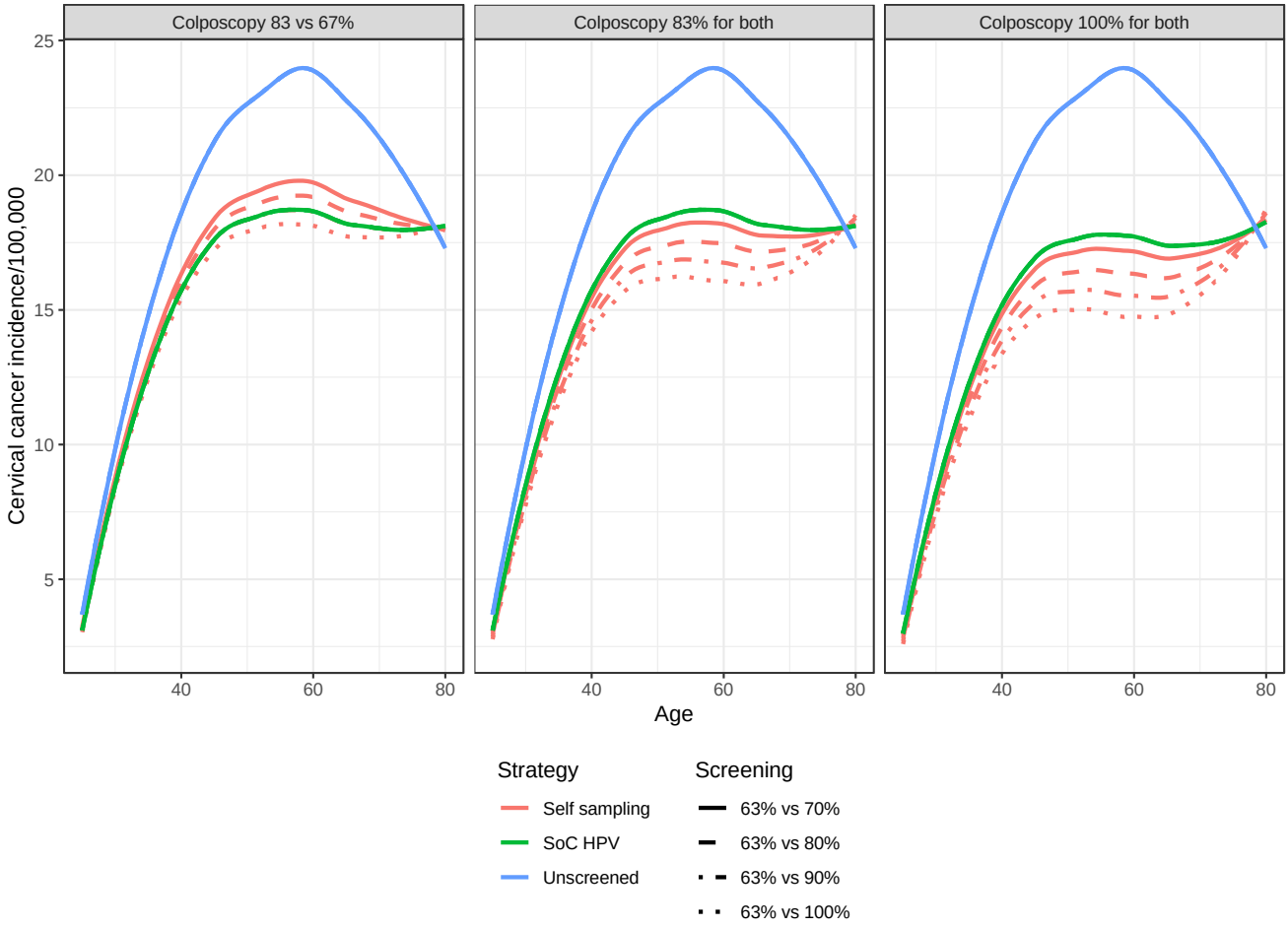


Figure 3. 3. Age-specific incidence of cervical cancer across model scenarios and screening strategies

Compared to being unscreened, screening in either strategy decreases cervical cancer incidence by at least 13% (range - 13%- 28%). The standard of care had 4% lower incidence than self-sampling in the base case scenario and a 2% lower incidence when self-sampling screening increase to 80%. Both have equal cervical cancer incidence when the base case level coloscopy adherence and self-sampling screening coverage are 90%. Compared to the standard of care screening strategy, a 7% reduction in the incidence was observed when screening by self-sampling is 90% with a colposcopy adherence equal to the standard of care. With equal

adherence for colposcopy in both strategies, an increase in screening coverage by self-sampling to 100% decreases incidence by 10%. In a different scenario, when treatment for precancer cases was assumed to be 100% in addition to the latter case, the incidence of cervical cancer in the self-sampling strategy becomes 12% lower than the standard of care (Table 3.2)

Table 3. 2. Comparison of the incidence rate of cervical cancer across screening strategies

	Colposcopy: 83% Standard of care and 67% self-sampling				
	Screening 63% (SOC) vs 70% (SS)*	Screening 63% vs 80%	Screening 63% vs 90%	Screening 63% vs 100%	
Characteristic	IRR	IRR	IRR	IRR	
Strategy					
Unscreened	ref.	ref.	ref.	ref.	
SoC HPV	0.84	0.84	0.84	0.84	
Self-sampling	0.87	0.86	0.84	0.82	
Strategy					
SoC HPV	ref.	ref.	ref.	ref.	
Self-sampling	1.04	1.02	1.00	0.98	
	Colposcopy both 83%				**Colposcopy both 100%**
	Screening 63% (SOC) vs 70% (SS)	Screening 63% vs 80%	Screening 63% vs 90%	Screening 63% vs 100%	Screening 63% vs 100%
	IRR	IRR	IRR	IRR	IRR
Strategy					
Unscreened	ref.	ref.	ref.	ref.	ref.
SoC HPV	0.84	0.84	0.84	0.84	0.81
Self-sampling	0.82	0.80	0.78	0.76	0.72
Strategy					
SoC HPV	ref.	ref.	ref.	ref.	ref.
Self-sampling	0.98	0.96	0.93	0.90	0.88

1IRR = Incidence Rate Ratio, CI = Confidence Interval

**SOC- Standard of care primary HPV-testing; SS- Self-sampling HPV-testing*

Cervical cancer specific mortality

Out of 10,000 women aged 25 and followed until age 80, the total number of cervical-cancer-specific deaths among the unscreened people was 44. The estimated number of deaths in the screened people ranged from 30 to 38 – the lowest being among those in the perfect self-sampling

scenario where screening coverage and adherence to colposcopy and treatment were 100% (Table 3.3).

Table 3. 3. Cumulative number of predicted cervical cancer deaths.

		Cancer-specific mortality		
		Unscreened	SoC HPV[a]	Self-sampling[b]
Colposcopy 83% (SoC) vs 67% (SS)	Screening 63% vs 70%	44	36	38
	Screening 63% vs 80%	44	36	37
	Screening 63% vs 90%	44	36	36
	Screening 63% vs 100%	44	36	36
Colposcopy both 83%	Screening 63% vs 70%	44	36	36
	Screening 63% vs 80%	44	36	35
	Screening 63% vs 90%	44	36	34
	Screening 63% vs 100%	44	36	32
Colposcopy both 100%	Screening 63% vs 100%	44	35	30

a: Standard of care primary HPV test after provider-collected sample; SOC- Standard of care
b: Primary HPV test after patient self-collected sample; SS- Self-sampling

Mortality due to cervical cancer exponentially increases with age. The highest mortality rate was observed among the unscreened population, and the lowest was observed in the self-sampling strategy with the perfect screening scenario (Figure 3.4).

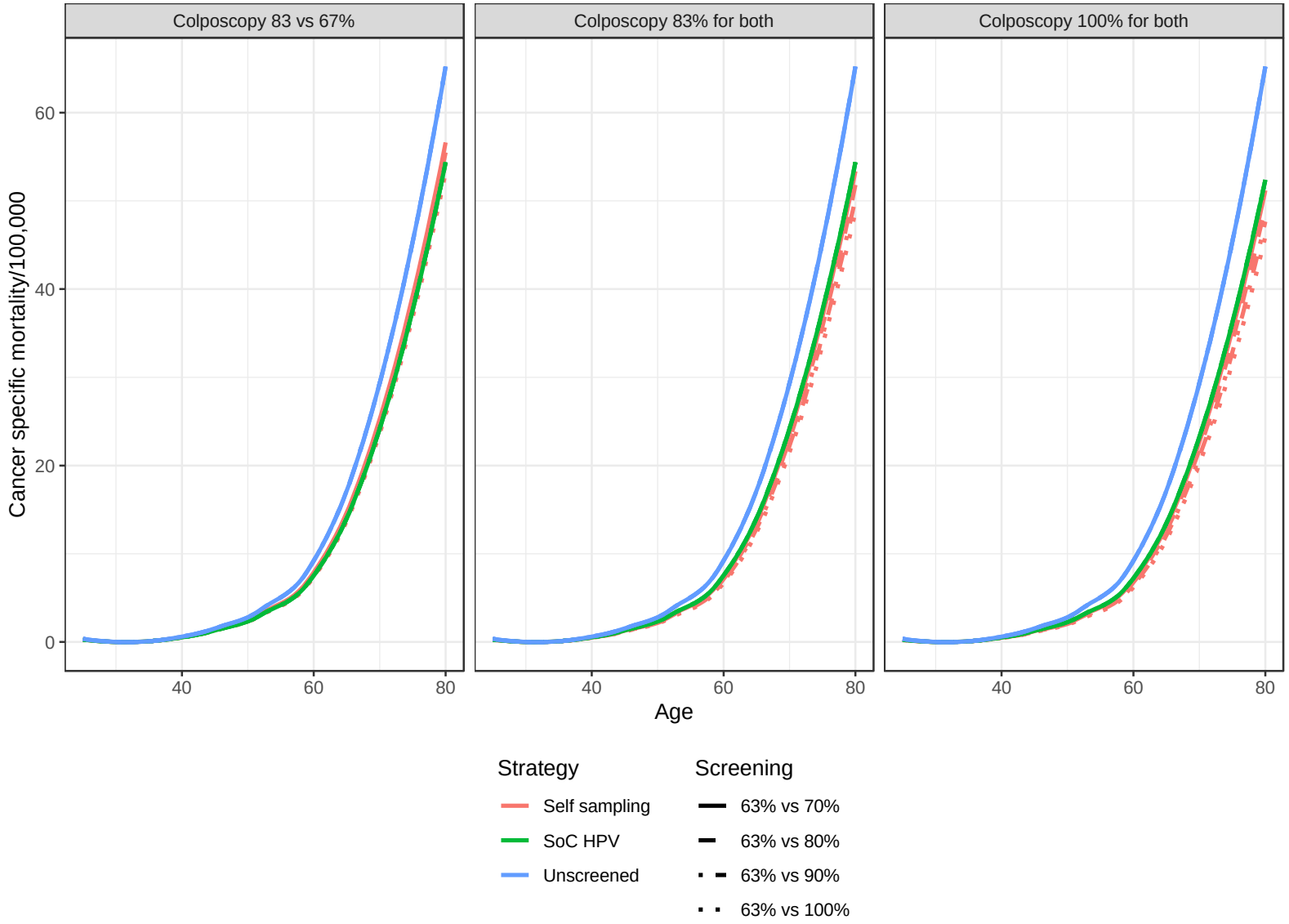


Figure 3. 4. Age-specific cervical cancer mortality comparing various screening strategies and scenarios.

The mortality rate ratio of cervical cancer for all screening strategies was significantly lower than not screening. However, as with the incidence, the standard of care had lower mortality in the base case scenario and when self-sampling screening coverage is 80%. This ratio reverts when self-sampling screening coverage is increased to 100%, keeping colposcopy adherence the base case level. Self-sampling has a lower cervical cancer-specific mortality rate than the standard of care screening strategies when both have an equal colposcopy adherence. An 8% reduction in mortality was observed with an equal colposcopy adherence and a self-sampling screening coverage of 90% and 11% reduction with a self-sampling screening coverage of 100% (as compared to 63% in the standard of care). In the perfect scenario where treatment and colposcopy adherence are 100% and screening coverage by self-sampling is also 100%, mortality in the self-sampling strategy is 13% lower than the standard of care (Table 3.4).

Table 3. 4. Cervical-cancer-specific mortality comparing screening strategies across different scenarios.

Colposcopy 83% Standard of care and 67% self-sampling					
	Screening 63% (SOC) vs 70% (SS)*	Screening 63% vs 80%	Screening 63% vs 90%	Screening 63% vs 100%	
Characteristic	IRR	IRR	IRR	IRR	
Strategy					
Unscreened	ref.	ref.	ref.	ref.	
SoC HPV	0.83	0.83	0.83	0.83	
Self-sampling	0.86	0.84	0.83	0.81	
Strategy					
SoC HPV	ref.	ref.	ref.	ref.	
Self-sampling	1.04	1.02	1	0.98	
	Colposcopy both 83%				**Colposcopy both 100%**
	Screening 63% (SOC) vs 70% (SS)*	Screening 63% vs 80%	Screening 63% vs 90%	Screening 63% vs 100%	Screening 63% vs 100%
	IRR	IRR	IRR	IRR	IRR

Strategy					
Unscreened	ref.	ref.	ref.	ref.	ref.
SoC HPV	0.83	0.83	0.83	0.83	0.8
Self-sampling	0.81	0.79	0.76	0.74	0.69
Strategy					
SoC HPV	ref.	ref.	ref.	ref.	ref.
Self-sampling	0.98	0.95	0.92	0.89	0.87

1IRR = Incidence Rate Ratio, CI = Confidence Interval

**SOC- Standard of care primary HPV-testing; SS- Self-sampling HPV-testing*

Sensitivity analyses

The base case scenario estimates were used to compare predictions for East African immigrants, US Black or African American Women, and women living in East Africa. The estimate for cervical cancer incidence is strikingly higher than the model estimated when the incidence of HPV in the model was fitted for the prevalence HPV in East Africa (Figure 3.5).

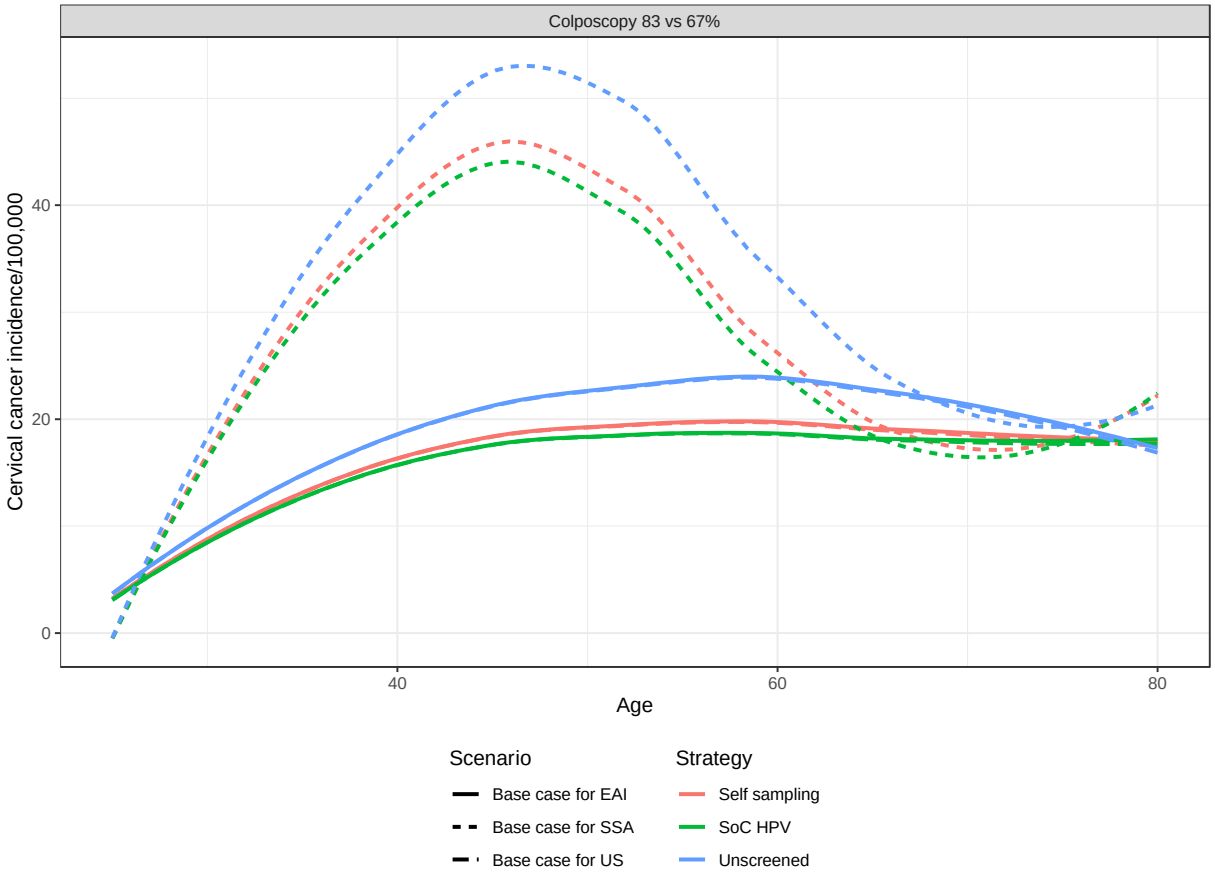


Figure 3. 5. Cervical cancer incidence estimates comparing predictions based on the prevalence of HPV for Black or African American and East African women.

For cervical cancer-specific mortality, we fitted the model with estimates of background mortality, cervical cancer-specific mortality, and HPV prevalence specific to East African immigrants, Black or African American women, and women living in East Africa. Since we did not have specific estimates for East African immigrants, the mortality data for East African immigrants was the weighted average of the other two, as mentioned in the methods, and the HPV prevalence data for East African immigrant women was the same as for Black or African American women. The predicted cervical-cancer-specific mortality when estimates from East Africa were taken is strikingly higher than the other two estimates, and the estimate for East African immigrants lies between the other two (Figure 3.6)

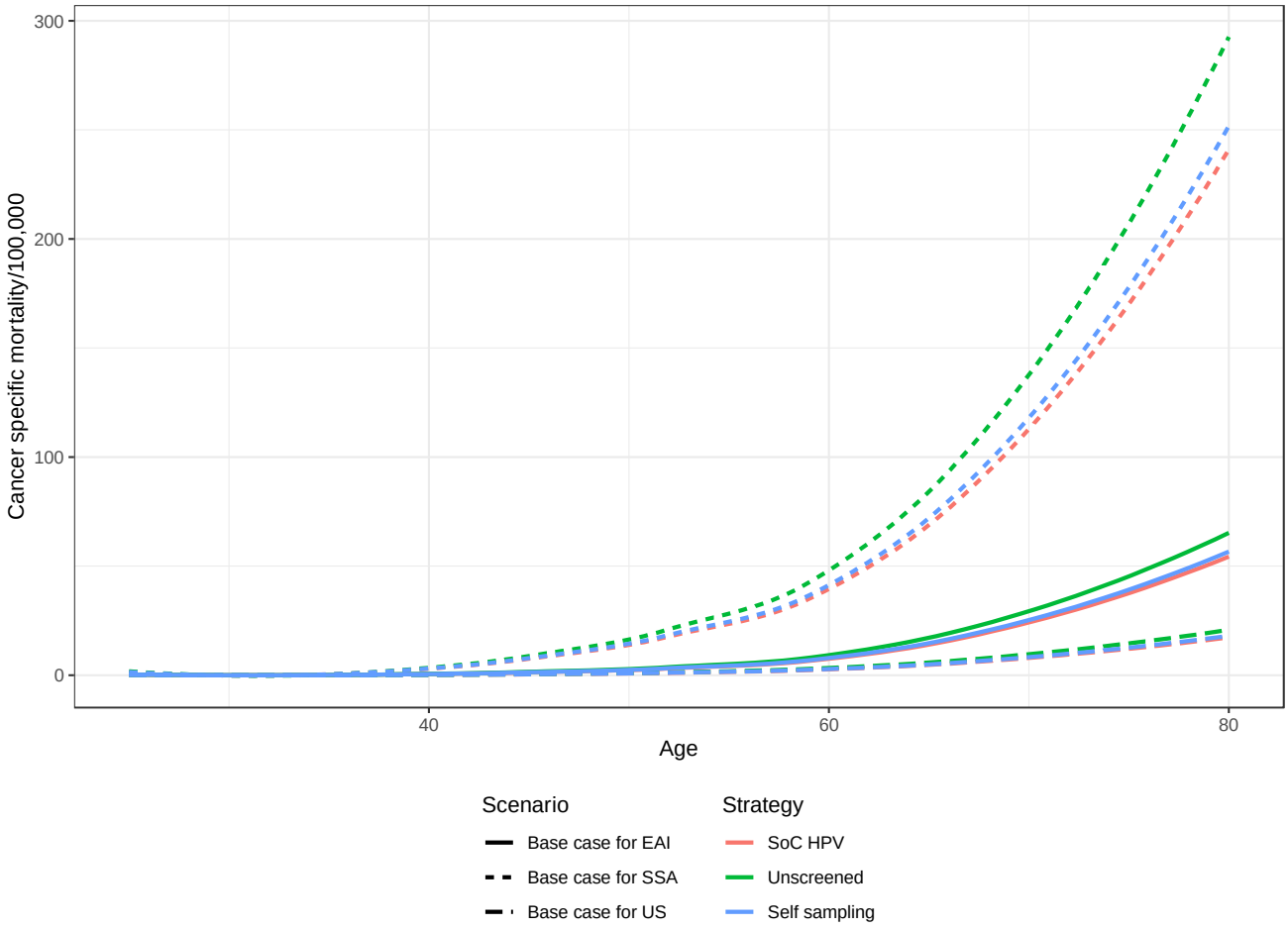


Figure 3. 6. Cervical cancer-specific mortality estimates comparing predictions based on mortality and HPV prevalence data specific to East African immigrants, East African, Black or African American women.

NB: Base case is screening coverage 63%(SoC) vs. 70% (SS) and colposcopy adherence 83%(SoC) and 67%(SS).

We also did a sensitivity analysis comparing 14 scenarios with varying screening and colposcopy adherence coverages. The estimates from the sensitivity analysis were like what we have observed in the scenarios discussed above. Keeping colposcopy adherence for self-sampling lower than the standard of care, increasing only screening coverage may lead to a statistically significant decrease in the incidence of cervical cancer if the screening coverage of self-sampling

is 30 to 35% higher than he standard of care. Otherwise, an increase in screening coverage becomes more evident in minimizing the burden of cervical cancer when the follow-up for colposcopy for self-sampling is equal to the standard of care (*Supplemental tables 3.5 & 3.6, Supplemental figures 3.1&3.2*)

Discussion

This study compared the impact of cervical cancer screening with primary HPV testing by standard-of-care clinician-collected sampling versus self-sampling on cervical cancer incidence and mortality. We found that a 30-40% increase in screening coverage only or an improved colposcopy adherence up to the level of the standard of care coupled with increase in screening coverage is required for the self-sampling strategy to yield a better reduction in the incidence and mortality of cervical cancer. Using self-sampling could result in up to 11%-13% reduction in cervical cancer incidence and mortality when screening coverage and adherence to colposcopy and treatment are maximized. Increased adherence to colposcopy is the key driver of the impact of self-sampling. An increase in screening coverage by self-sampling, assuming lower follow-up adherence compared with standard of care approaches, in line with empirical data (133), can only lower mortality and incidence of cervical cancer when it reaches about 100%.

For underserved populations like East African immigrants, self-sampling has the potential to improve screening uptake, but its impact may heavily depend on the implementation approach. Self-sampling can be implemented at health facilities with the assistance of clinicians, using mailed test kits, and by deploying community health workers. Despite consistently reported increases in screening coverage, the magnitude of the increase and adherence to follow-up testing is variable across strategies (130,132,136,145,166). Based on a meta-analysis conducted by Arbyn et al, self-sampling may increase screening uptake by 3%-40% depending on the

implementation strategy (162). The highest increase in screening uptake has been achieved by delivering testing kits door-to-door, followed by mailing-to-all, community campaigns, and opt-in strategies (162,167). Even using the high end of the range for increasing screening, the impact on screening coverage in some underserved populations might not be sufficient. Therefore, additional strategies to increase uptake of self-sampling, especially for priority populations like East African immigrants, may need to be considered.

Our model predicted the impact of self-sampling with various levels of screening coverage that were all higher than the standard of care. Although we used results from a study that utilized direct mailing of HPV self-sampling kits to estimate the base case scenario of a 7% increase in screening coverage compared with standard of care (148), we would like to emphasize the rate of increase required to achieve a significant decline in incidence and mortality in the target population. For example, self-sampling decreases incidence and mortality relative to the standard of care when it has an equal level of colposcopy adherence or when the screening uptake is at least 30 to 40% higher than the standard of care. However, a mere increase in screening coverage lower than 30% did not decrease incidence and mortality. Follow-up compliance after self-sampling is lower than the standard of care (133,162,168). This partly happens due to the need for an additional clinic visit for other hr-HPV-positive cases in self-sampling (146,152,167). As a result, decision-makers may need to choose an implementation strategy or combination of strategies that potentially boost screening coverage and colposcopy adherence. Furthermore, additional resources or tailored approaches may be needed for priority populations.

Screening by self-sampling can help people facing barriers related to pelvic examinations and busy work schedules (169). However, other barriers cannot be addressed only by offering self-sampling. For example, many avoid screening for fear of positive findings and related anxiety (170,171). As our model foretells, self-sampling strategies will be more effective in decreasing the

burden of cervical cancer if it both increases screening coverage for a large proportion of the population and brings them to the health facility for further follow-up and investigation, when indicated. Unless self-sampling implementation strategies are comprehensive enough to address the other barriers and provide sufficient improvement in screening coverage, it may fail to achieve the desired outcome of decreasing incidence and mortality from cervical cancer. For instance, barriers related to awareness and beliefs associated with screening may need tailored education (172,173). Understanding East African immigrants' level of acculturation and interaction with the US health system could be a critical initiative to tailor screening strategies. As reported in Chapter One, more than half of East African immigrant women who have access to primary healthcare use a language interpreter service (128), highlighting the importance of making self-sampling instructions and educational materials available in the native languages of the target populations. Similarly, designing materials and delivering culturally tailored health education is critically important (174).

This study has several strengths. It highlights the role of self-sampling among a specific under-served population and provides evidence that may inform policy and programmatic decisions. We also tested various scenarios as a sensitivity analysis and compared the impacts of the interventions in a broader context. However, some limitations need to be considered. Firstly, we did not have sufficient estimates from studies done among East African immigrants, and most of the parameters were extracted from other populations. Although we made several sensitivity analyses to address the uncertainties, the results may need to be cautiously interpreted. When we applied mortality estimates and HPV incidence fitting the age-specific HPV prevalence of East Africa, both cervical cancer incidence and mortality substantially increased. Therefore, not knowing the exact estimates of East African immigrants and fitting the model using parameters from various sources might have impacted the results. Similarly, we modeled for high-risk HPV due to a lack of reliable evidence on the genotype distribution of HPV among the targeted

population and not considering that might impact the real-world applicability of the findings. Thirdly, we did not consider the effect of hysterectomy in our model; however, people who undergo hysterectomy should not be at risk of cervical cancer. Even though it might not have a substantial impact, not excluding them in the denominator might have led to an overestimation of the incidence of cervical cancer (175). Thirdly, based on the current guideline, we assumed people to be regularly screened every three to five years up to age 65 (124). Specifically, as a Markov model, we do not track individual screening history, with screening intervals and procedures differing by previous screening results. Unlike the real-world screening adherence of individuals, assuming a consistently regular screening adherence might have underestimated the burden of cervical cancer. Finally, this study represents the screening strategies as either/or, but in reality, there will probably be a mix of strategies between individuals and within an individual over a lifetime of screening.

Conclusion

An increase in screening coverage by self-sampling alone is not predicted to substantially impact cervical cancer incidence and mortality compared to the standard of care. The critical opportunity with implementing self-sampling is addressing underserved people who are more likely than the general population to be never screened or overdue for screening. Even with a lower follow-up rate, self-sampling can be as beneficial as the standard of care, and it should be considered an option for people who could not get screened by the standard of care. Nevertheless, the impact of a self-collection strategy is optimized if the loss to follow-up can be minimized, and the value increases if screening reaches more people than the standard of care. Therefore, strategies with high patient follow-up and treatment adherence should be concurrently implemented to consider self-sampling as a better screening alternative. Although we did not do a cost-effectiveness analysis, strategies to increase screening coverage and colposcopy adherence may require significant resources. As a result, decision-makers may need to thoroughly investigate available

evidence and conduct additional studies to evaluate the feasibility and cost-effectiveness of implementing such interventions.

Appendix

Supplemental Table 3.1. Model Parameters for screening test-related characteristics

Variable	Baseline value
Screening age	25-65
Screening interval (124)	
HPV test (SoC and self-sampling)	Every 5 years
Treatment failure (176)	6%
Test sensitivity/specificity for precancer	
HPV test by clinician sampling (163)	94%/85%
HPV test by self-sampling (162,163)	93%/85%
Colposcopy (177)	92%/51%

Supplemental Table 3.2. The range of simulated bi-annual probabilities for the natural history of cervical cancer used to choose the best-fitting model (155).

Age	HPV incidence			Clearance from precancer			Progression to precancer			Regression from precancer			Invasion (Progression to cancer)		
	Fitted	Range simulated		Fitted	Range simulated		Fitted	Range simulated		Fitted	Range simulated		Fitted	Range simulated	
25-29	0.0602	0.0550	0.0650	0.2065	0.1724	0.3103	0.0166	0.0146	0.0244	0.2543	0.1149	0.2553	0.0013	0.0012	0.0014
30-34	0.0556	0.0495	0.0683	0.1760	0.1379	0.2793	0.0213	0.0146	0.0317	0.2301	0.1034	0.2425	0.0033	0.0022	0.0036
35-39	0.0314	0.0248	0.0512	0.1592	0.1103	0.2653	0.0276	0.0146	0.0413	0.2030	0.0827	0.2182	0.0034	0.0022	0.0040
40-44	0.0241	0.0161	0.0435	0.1399	0.0883	0.2520	0.0322	0.0146	0.0536	0.1797	0.0662	0.1964	0.0046	0.0027	0.0055
45-49	0.0200	0.0129	0.0413	0.1354	0.0706	0.2520	0.0324	0.0146	0.0644	0.1457	0.0529	0.1768	0.0041	0.0023	0.0053
50-54	0.0290	0.0167	0.0703	0.1243	0.0565	0.2520	0.0332	0.0146	0.0676	0.1440	0.0503	0.1750	0.0040	0.0020	0.0058
55-59	0.0277	0.0159	0.0773	0.1480	0.0508	0.3025	0.0302	0.0132	0.0710	0.1420	0.0478	0.1733	0.0038	0.0019	0.0061
60-64	0.0300	0.0159	0.0850	0.1758	0.0458	0.3629	0.0319	0.0112	0.0780	0.1354	0.0454	0.1715	0.0039	0.0019	0.0067
65-69	0.0211	0.0111	0.0680	0.1593	0.0389	0.3629	0.0318	0.0090	0.0780	0.1294	0.0431	0.1698	0.0037	0.0017	0.0064
70-74	0.0106	0.0050	0.0408	0.1577	0.0381	0.3992	0.0338	0.0090	0.0859	0.1239	0.0410	0.1681	0.0034	0.0016	0.0060
75-80	0.0050	0.0023	0.0245	0.1582	0.0374	0.4392	0.0338	0.0090	0.0859	0.1093	0.0328	0.1513	0.0050	0.0023	0.0090

Method of estimating transition probabilities

The estimates from Campos et al paper were duration specific monthly probabilities for all high-risk HPV genotypes (155). Initially, we converted monthly transition probabilities to bi-annual probabilities to align with our model transition cycle. Then, we selected three estimates. The first one was the minimum of all the transition probabilities presented for each genotype, the second was the maximum probability, and the third was the average of all the transition probabilities. The transition probabilities for HPV infection progression and clearance were presented on monthly bases for a maximum of 64+ months duration, and the probabilities for precancer progression and clearance were presented on years based for a maximum of 50+ years. We initiated our model with the average transition probability we expected to have at the age of 25 (the first category of probabilities) and applied multipliers that provide estimates within the range of expected transition probabilities (*Supplemental Table 3.3.1 & 3.3.2*)

Supplemental Table 3.3.1. Duration-specific transition probabilities for hr-HPV infection progression and clearance (155).

Progression from hr-HPV infection of precancer				Clearance from hr-HPV infection		
Duration	**Minimum**	**Average**	**Maximum**	**Minimum**	**Average**	**Maximum**
1-15 Months	0.00000000	0.016446155622	0.01644616	0.22642568	0.344782226704	0.40716871
16-27 Months	0.00000000	0.020674514208	0.02067451	0.18654995	0.262143415831	0.33882686
28-39 Months	0.00141636	0.036486503244	0.0364865	0.18654995	0.233713360975	0.28315878
40-51 Months	0.01461312	0.056646751324	0.05664675	0.11749200	0.182554547424	0.26132335
52-64 Months	0.01461312	0.114276929985	0.11427693	0.03017535	0.130318719006	0.21393414
64+ Months	0.01461312	0.114276929985	0.11427693	0.03017535	0.130318719006	0.21393414

Supplemental Table 3.3.2. Duration-specific transition probabilities for precancer invasion and regression (155).

	Probabilities for progression to cancer (invasion)			Probabilities for regression from precancer		
	Minimum	Average	Maximum	Minimum	Average	Maximum
Months 1-60 (years 1-5)	0.00013175	0.000513753989	0.00098779	0.12763025	0.195593334798	0.26490811
Months 61-120 (years 6-10)	0.00014255	0.000555831228	0.00106872	0.10325508	0.159269448530	0.21724221
Months 121-240 (years 11-20)	0.00342231	0.013291862358	0.02543028	0.07831496	0.121588856808	0.167028
Months 241-348 (years 21-29)	0.00998064	0.038456270166	0.0728527	0.00538786	0.008519598436	0.01194016
Months 349-408 (years 30-34)	0.01987813	0.075672156401	0.1412277	0.00269696	0.004267392386	0.00598502
Months 409-468 (years 35-39)	0.02151967	0.081756482509	0.15220399	0.00269696	0.004267392386	0.00598502
Months 469-528 (years 40-44)	0.04586914	0.169093414667	0.30333887	0.00134924	0.002135597193	0.00299625
Months 529-588 (years 45-49)	0.04907724	0.180196510442	0.32167394	0.00134924	0.002135597193	0.00299625
Months 589+ (years 50+)	0.04907724	0.310179535825	0.37360195	0.00134924	0.002135597193	0.00299625

Supplemental Table 3.3. Parameters for bi-annual background and cervical cancer specific mortalities (159–161)

	Background mortality			Cervical cancer specific mortality		
Age	SSA	US	Weighted average (US -0.7,SSA -0.3)	SSA	US	weighted average (US -0.7,SSA -0.3)
25	0.01	0.000831	0.0035817	0.000047	0.000042	0.0000455
26	0.01	0.000844	0.0035908	0.000047	0.000042	0.0000455
27	0.01	0.000876	0.0036132	0.000047	0.000042	0.0000455
28	0.01	0.000938	0.0036566	0.000047	0.000042	0.0000455
29	0.01	0.001028	0.0037196	0.000047	0.000042	0.0000455
30	0.015	0.001134	0.0052938	0.000087	0.000097	0.000090
31	0.015	0.001245	0.0053715	0.000087	0.000097	0.000090
32	0.015	0.001360	0.005452	0.000087	0.000097	0.000090
33	0.015	0.001469	0.0055283	0.000087	0.000097	0.000090
34	0.015	0.001572	0.0056004	0.000087	0.000097	0.000090
35	0.019	0.001682	0.0068774	0.000123	0.000194	0.0001443
36	0.019	0.001803	0.0069621	0.000123	0.000194	0.0001443
37	0.019	0.001921	0.0070447	0.000123	0.000194	0.0001443
38	0.019	0.002037	0.0071259	0.000123	0.000194	0.0001443
39	0.019	0.002156	0.0072092	0.000123	0.000194	0.0001443
40	0.025	0.002289	0.0091023	0.000159	0.000342	0.0002139
41	0.025	0.00244	0.009208	0.000159	0.000342	0.0002139
42	0.025	0.002606	0.0093242	0.000159	0.000342	0.0002139
43	0.025	0.002781	0.0094467	0.000159	0.000342	0.0002139
44	0.025	0.002967	0.0095769	0.000159	0.000342	0.0002139
45	0.032	0.003167	0.0118169	0.000146	0.000537	0.0002633
46	0.032	0.003389	0.0119723	0.000146	0.000537	0.0002633
47	0.032	0.003636	0.0121452	0.000146	0.000537	0.0002633
48	0.032	0.003918	0.0123426	0.000146	0.000537	0.0002633

49	0.032	0.004241	0.0125687	0.000146	0.000537	0.0002633
50	0.043	0.004592	0.0161144	0.000157	0.000776	0.0003427
51	0.043	0.004979	0.0163853	0.000157	0.000776	0.0003427
52	0.043	0.005424	0.0166968	0.000157	0.000776	0.0003427
53	0.043	0.005925	0.0170475	0.000157	0.000776	0.0003427
54	0.043	0.006460	0.017422	0.000157	0.000776	0.0003427
55	0.057	0.006987	0.0219909	0.000165	0.001023	0.0004224
56	0.057	0.007524	0.0223668	0.000165	0.001023	0.0004224
57	0.057	0.008125	0.0227875	0.000165	0.001023	0.0004224
58	0.057	0.008824	0.0232768	0.000165	0.001023	0.0004224
59	0.057	0.009611	0.0238277	0.000165	0.001023	0.0004224
60	0.084	0.010462	0.0325234	0.000168	0.001210	0.0004806
61	0.084	0.011322	0.0331254	0.000168	0.001210	0.0004806
62	0.084	0.012163	0.0337141	0.000168	0.001210	0.0004806
63	0.084	0.012959	0.0342713	0.000168	0.001210	0.0004806
64	0.084	0.013738	0.0348166	0.000168	0.001210	0.0004806
65	0.12	0.014575	0.0462025	0.000178	0.001305	0.0005161
66	0.12	0.015481	0.0468367	0.000178	0.001305	0.0005161
67	0.12	0.016471	0.0475297	0.000178	0.001305	0.0005161
68	0.12	0.017483	0.0482381	0.000178	0.001305	0.0005161
69	0.12	0.018599	0.0490193	0.000178	0.001305	0.0005161
70	0.19	0.019878	0.0709146	0.000168	0.001284	0.0005028
71	0.19	0.02130	0.071910	0.000168	0.001284	0.0005028
72	0.19	0.022739	0.0729173	0.000168	0.001284	0.0005028
73	0.19	0.024996	0.0744972	0.000168	0.001284	0.0005028
74	0.19	0.026821	0.0757747	0.000168	0.001284	0.0005028
75	0.27	0.029371	0.1015597	0.000188	0.001236	0.0005024
76	0.27	0.032051	0.1034357	0.000188	0.001236	0.0005024
77	0.27	0.035073	0.1055511	0.000188	0.001236	0.0005024

78	0.27	0.038198	0.1077386	0.000188	0.001236	0.0005024
79	0.27	0.041634	0.1101438	0.000188	0.001236	0.0005024
80	0.4	0.046739	0.1527173	0.000201	0.001184	0.0004959

Supplemental Table 3.4. Model scenarios

Current screening	Screening coverage		Colposcopy adherence	
	Standard of care (SOC)	Self-sampling (SS)	Standard of care (SOC)	Self-sampling (SS)
Base case	63%	70%	83%	67%
Scenario 1	63%	80%	83%	67%
Scenario 2	63%	90%	83%	67%
Scenario 3	63%	100%	83%	67%
Scenario 4	63%	70%	83%	83%
Scenario 5	63%	80%	83%	83%
Scenario 6	63%	90%	83%	83%
Scenario 7	63%	100%	83%	83%
Scenario 8	63%	100%	100%	100%
Sensitivity analysis				
Sens 1	40	50	70	50
Sens 2	40	75	70	50
Sens 3	40	100	70	50
Sens 4	40	50	70	70
Sens 5	40	75	70	70
Sens 6	40	100	70	70
Sens 7	40	100	100	100
Sens 8	50	60	70	50
Sens 9	50	80	70	50
Sens 10	50	100	70	50
Sens 11	50	60	70	70
Sens 12	50	80	70	70
Sens 13	50	100	70	70
Sens 14	50	100	100	100

Supplemental Table 3.5. Incidence of cervical cancer from the sensitivity analysis

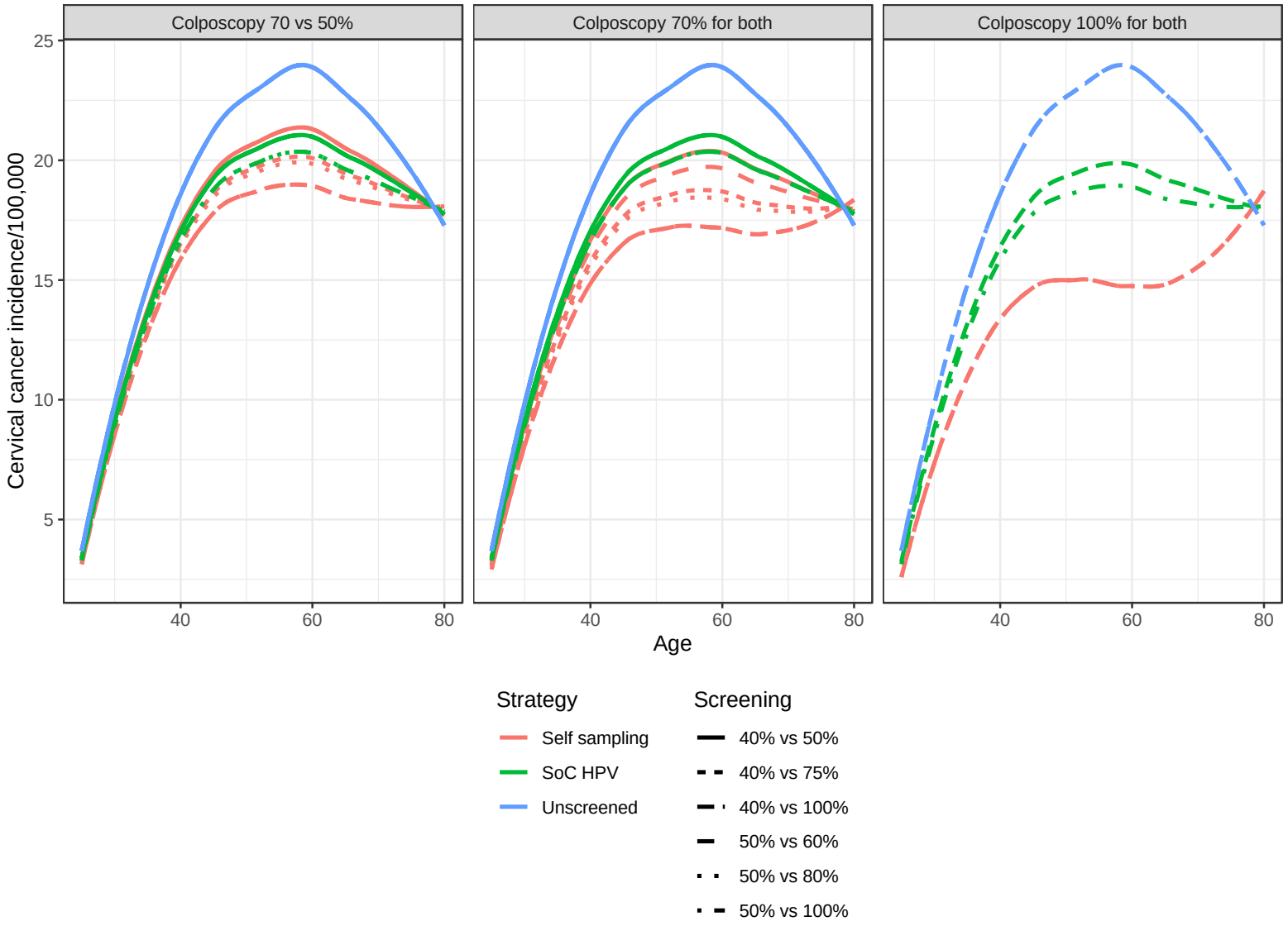
	Colposcopy 70% vs 50%			Colposcopy 70% both			Colposcopy 100% both
Screening	**40% vs 50%**	**40% vs 75%**	**40% vs 100%**	**40% vs 50%**	**40% vs 75%**	**40% vs 100%**	**40% vs 100%**
Characteristic	**IRR**	**IRR**	**IRR**	**IRR**	**IRR**	**IRR**	**IRR**
Strategy							
Unscreened	ref.	ref.	ref.	ref.	ref.	ref.	ref.
SoC HPV	0.91	0.91	0.91	0.91	0.91	0.91	0.88
Self-sampling	0.92	0.88	0.85	0.89	0.84	0.79	0.72
Strategy							
SoC HPV	ref.	ref.	ref.	ref.	ref.	ref.	—
Self-sampling	1.01	0.97	0.93	0.98	0.92	0.87	0.82
	Colposcopy 70% vs 50%			**Colposcopy 70% both**			**Colposcopy 100% both**
Screening	**50% vs 60%**	**50% vs 80%**	**50% vs 100%**	**50% vs 60%**	**50% vs 80%**	**50% vs 100%**	**50% vs 100%**
Characteristic	**IRR**	**IRR**	**IRR**	**IRR**	**IRR**	**IRR**	**IRR**
Strategy							
Unscreened	—	—	—	—	—	—	—
SoC HPV	0.91	0.89	0.89	0.89	0.89	0.89	0.85
Self-sampling	0.92	0.88	0.85	0.87	0.83	0.79	0.72
Strategy							
SoC HPV	—	—	—	—	—	—	—
Self-sampling	1.01	0.98	0.95	0.98	0.93	0.89	0.85

1IRR = Incidence Rate Ratio, CI = Confidence Interval

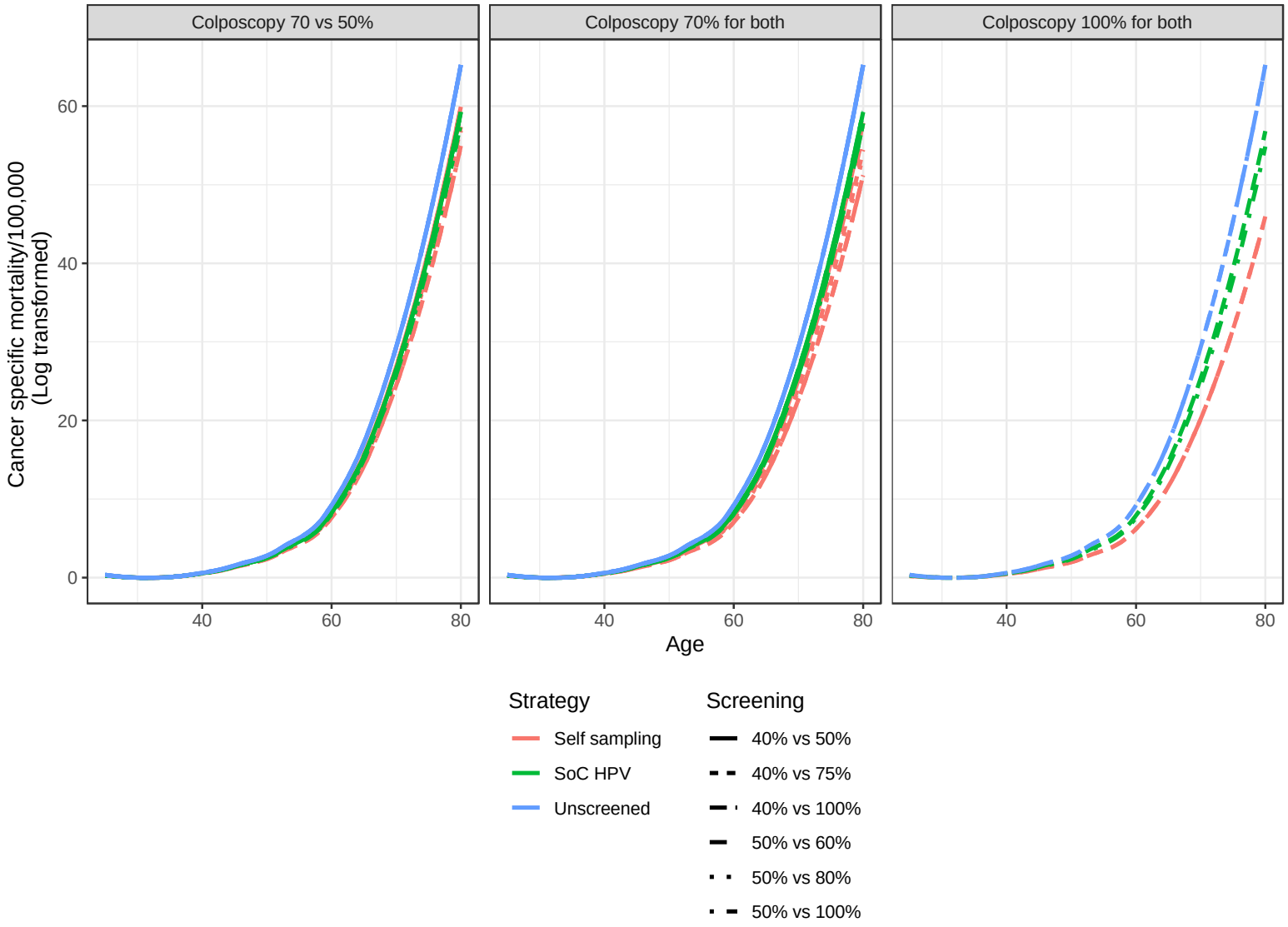
Supplemental Table 3.6. Cervical cancer specific mortality from the sensitivity analysis

	Colposcopy 70% vs 50%			Colposcopy 70% both			Colposcopy 100% both
Screening	**40% vs 50%**	**40% vs 75%**	**40% vs 100%**	**40% vs 50%**	**40% vs 75%**	**40% vs 100%**	**40% vs 100%**
Characteristic	**IRR**	**IRR**	**IRR**	**IRR**	**IRR**	**IRR**	**IRR**
Strategy							
Unscreened	—	—	—	—	—	—	—
SoC HPV	0.9	0.9	0.9	0.9	0.9	0.9	0.87
Self-sampling	0.92	0.88	0.84	0.88	0.83	0.78	0.69
Strategy							
SoC HPV	—	—	—	—	—	—	—
Self-sampling	1.01	0.97	0.92	0.98	0.92	0.86	0.8
	Colposcopy 70% vs 50%			**Colposcopy 70% both**			**Colposcopy 100% both**
Screening	**50% vs 60%**	**50% vs 80%**	**50% vs 100%**	**50% vs 60%**	**50% vs 80%**	**50% vs 100%**	**50% vs 100%**
Characteristic	**IRR**	**IRR**	**IRR**	**IRR**	**IRR**	**IRR**	**IRR**
Strategy							
Unscreened	—	—	—	—	—	—	—
SoC HPV	0.9	0.88	0.88	0.88	0.88	0.88	0.83
Self-sampling	0.92	0.87	0.84	0.86	0.82	0.78	0.69
Strategy							
SoC HPV	—	—	—	—	—	—	—
Self-sampling	1.01	0.98	0.95	0.98	0.93	0.88	0.83

1IRR = Incidence Rate Ratio, CI = Confidence Interval



Supplemental figure 3.1. Cervical cancer incidence curves based on the sensitivity analysis.



Supplemental figure 3.2. Cervical cancer mortality curves based on the sensitivity analysis.

Bibliography

1. Wingo PA, Cardinez CJ, Landis SH, Greenlee RT, Ries LAG, Anderson RN, et al. Long-term trends in cancer mortality in the United States, 1930-1998. Cancer. 2003;97(12 SUPPL.):3133–275.
2. Preventive Medicine. A world without cervical cancer is within our reach. Prev Med (Baltim). 2021;144.
3. Office of Disease Prevention and Health Promotion. (n.d.). U.S. Department of Health and Human Services. Healthy People 2030.
4. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention and National Cancer Institute. U.S. Cancer Statistics Working Group. U.S. Cancer Statistics Data Visualizations Tool, based on 2021 submission data (1999-2019). 2022.
5. Centers for Disease Control and Prevention. United States Cancer Statistics: Data Visualizations. US Cancer Statistics [Internet]. 2016;(CDC):6–8. Available from: https://gis.cdc.gov/Cancer/USCS/DataViz.html
6. Murray KE, Mohamed AS, Ndunduyenge G. Health and prevention among east African women in the U.S. J Health Care Poor Underserved. 2013;24(1):233–46.
7. Sabatino SA, Thompson TD, White MC, Shapiro JA, de Moor J, Doria-Rose VP, et al. Cancer Screening Test Receipt — United States, 2018. MMWR Morb Mortal Wkly Rep. 2021;70(2):29–35.
8. Endeshaw M, Clarke T, Senkomago V, Saraiya M. Cervical cancer screening among women by birthplace and percent of lifetime living in the United States. J Low Genit Tract Dis. 2018;22(4):280–7.

9. Amuta-Jimenez AO, Smith GPA, Brown KK. Patterns and Correlates of Cervical Cancer Prevention Among Black Immigrant and African American Women in the USA: the Role of Ethnicity and Culture. Journal of Cancer Education. 2020;
10. Abdi HI, Hoover E, Fagan SE, Adsul P. Cervical Cancer Screening Among Immigrant and Refugee Women: Scoping-Review and Directions for Future Research. J Immigr Minor Health. 2020;22(6):1304–19.
11. Samuel PS, Pringle JP, James NW 4th, Fielding SJ, Fairfield KM. Breast, cervical, and colorectal cancer screening rates amongst female Cambodian, Somali, and Vietnamese immigrants in the USA. Int J Equity Health. 2009 Aug;8:30.
12. Morrison T Ben, Wieland ML, Cha SS, Rahman AS, Chaudhry R. Disparities in Preventive Health Services Among Somali Immigrants and Refugees. J Immigrant Minority Health. 2012;14:968–974.
13. Morrison T Ben, Flynn PM, Weaver AL, Wieland ML. Cervical cancer screening adherence among Somali immigrants and refugees to the United States. Health Care Women Int. 2013;34(11):980–8.
14. Harcourt N, Ghebre RG, Whembolua GL, Zhang Y, Osman SW, Okuyemi KS. Factors associated with breast and cervical cancer screening behavior among African immigrant women in Minnesota. J Immigr Minor Health. 2014;16(3):450–6.
15. Ghebre RG, Sewali B, Osman S, Joseph A. Cervical Cancer : Barriers to Screening in the Somali Community in Minnesota. J Immigr Minor Health [Internet]. 2015;722–8. Available from: http://dx.doi.org/10.1007/s10903-014-0080-1
16. Elmore CE, Keim-Malpass J, Mitchell EMK. Health Inequity in Cervical Cancer Control among Refugee Women in the United States by Country of Origin. Health Equity. 2021;5(1):119–23.

17. Omenka OI, Watson DP, Hendrie HC. Understanding the healthcare experiences and needs of African immigrants in the United States: A scoping review. BMC Public Health. 2020;20(1):1–13.

18. Lefevere E, Hens N, Theeten H, Van Den Bosch K, Beutels P, De Smet F, et al. Like mother, like daughter? Mother's history of cervical cancer screening and daughter's Human Papillomavirus vaccine uptake in Flanders (Belgium). Vaccine. 2011;29(46).

19. Adunlin G, Cyrus JW, Asare M, Sabik LM. Barriers and Facilitators to Breast and Cervical Cancer Screening Among Immigrants in the United States. J Immigr Minor Health [Internet]. 2019;21(3):606–58. Available from: http://dx.doi.org/10.1007/s10903-018-0794-6

20. Johnson CE, Mues KE, Mayne SL, Kiblawi AN. Immigrants and Ethnic Minorities: Health Belief Model. J Low Genit Tract Dis. 2008;12:232–41.

21. Lee F, Paszat LF, Sutradhar R. Immigration and Adherence to Cervical Cancer Screening: A Provincewide Longitudinal Matched Cohort Study Using Multistate Transitional Models. Journal of Obstetrics and Gynaecology Canada. 2019;41(6):813–23.

22. Kuniyuki A, Fischer M, Yasui Y, Thompson B, Schwartz SM, Jackson JC, et al. Cervical cancer screening among Cambodian-American women. Cancer Epidemiology Biomarkers and Prevention [Internet]. 1999;8(6):541–6. Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed6&NEWS=N&AN=29270339

23. Ndukwe EG, Williams KP, Sheppard V. Knowledge and perspectives of breast and cervical cancer screening among female African immigrants in the Washington D.C. metropolitan area. Journal of Cancer Education. 2013;28(4):748–54.

24. Markides KS, Rote S. The Healthy Immigrant Effect and Aging in the United States and Other Western Countries. Gerontologist. 2019 Mar 14;59(2):205–14.

25. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68(6):394–424.

26. Anaman-torgbor JA, King J, Correa-velez I. Barriers and facilitators of cervical cancer screening practices among African immigrant women living in Brisbane , Australia. European Journal of Oncology Nursing. 2017;31:22–9.

27. Human Papillomavirus and Related Diseases Report AFRICA [Internet]. 2021. Available from: www.hpvcentre.net

28. McDermott S, Desmeules M, Lewis R, Gold J, Payne J, Lafrance B, et al. Cancer incidence among Canadian immigrants, 1980-1998: Results from a national cohort study. J Immigr Minor Health. 2011 Feb;13(1):15–26.

29. McDonald JT, Farnworth M, Liu Z. Cancer and the healthy immigrant effect: a statistical analysis of cancer diagnosis using a linked Census-cancer registry administrative database. BMC Public Health. 2017 Apr 5;17(1).

30. Benard VB, Watson M, Saraiya M, Harewood R, Townsend JS, Stroup AM, et al. Cervical cancer survival in the United States by race and stage (2001-2009): Findings from the CONCORD-2 study. Cancer. 2017;123(i):5119–37.

31. UW Medicine. Fact Book 2021 [Internet]. 2021. Available from: https://www.uwmedicine.org/sites/stevie/files/2021-04/Fact-Book-03-20201.pdf

32. Saslow D, Solomon D, Lawson HW, Killackey M, Kulasingam SL, Cain J, et al. American Cancer Society, American Society for Colposcopy and Cervical Pathology, and American Society for Clinical Pathology screening guidelines for the prevention and early detection of cervical cancer. CA Cancer J Clin. 2012;62(3):147–72.

33. Curry SJ, Krist AH, Owens DK, Barry MJ, Caughey AB, Davidson KW, et al. Screening for Cervical Cancer US Preventive Services Task Force Recommendation Statement. JAMA - Journal of the American Medical Association. 2018 Aug 21;320(7):674–86.

34. CDC SVI 2018 Documentation [Internet]. Available from: https://www.census.gov/programs-surveys/acs/technical-

35. Charlson ME, Charlson RE, Peterson JC, Marinopoulos SS, Briggs WM, Hollenberg JP. The Charlson comorbidity index is adapted to predict costs of chronic disease in primary care patients. J Clin Epidemiol [Internet]. 2008;61(12):1234–40. Available from: http://dx.doi.org/10.1016/j.jclinepi.2008.01.006

36. Davidson KW, Barry MJ, Mangione CM, Cabana M, Caughey AB, Davis EM, et al. Screening for Colorectal Cancer: US Preventive Services Task Force Recommendation Statement. Vol. 325, JAMA - Journal of the American Medical Association. American Medical Association; 2021. p. 1965–77.

37. Siu AL. Screening for breast cancer: U.S. Preventive services task force recommendation statement. Vol. 164, Annals of Internal Medicine. American College of Physicians; 2016. p. 279–96.

38. Azur MJ, Stuart EA, Frangakis C, Leaf PJ. Multiple imputation by chained equations: What is it and how does it work? Int J Methods Psychiatr Res. 2011 Mar;20(1):40–9.

39. Echeverria SE, Carrasquillo O. The Roles of Citizenship Status, Acculturation, and Health Insurance in Breast and Cervical Cancer Screening Among Immigrant Women. Med Care. 2006;44(8):788–92.

40. Ko LK, Taylor VM, Mohamed FB, Do HH, Gebeyaw FA, Ibrahim A, et al. “We brought our culture here with us”: A qualitative study of perceptions of HPV vaccine and vaccine uptake among East African immigrant mothers. Papillomavirus Research. 2019;7(October 2018):21–5.

41. Pratt R, Njau SW, Ndagire C, Chaisson N, Toor S, Ahmed N, et al. “We are Muslims and these diseases don’t happen to us”: A qualitative study of the views of young Somali men and women concerning HPV immunization. Vaccine. 2019 Apr;37(15):2043–50.

42. Atlas SJ, Grant RW, Ferris TG, Chang Y, Barry MJ. Patient-Physician Connectedness and Quality of Primary Care [Internet]. 2009. Available from: https://annals.org
43. Plantinga LC, Jaar BG, Fink NE, Sadler JH, Levin NW, Coresh J, et al. Frequency of patient-physician contact in chronic kidney disease care and achievement of clinical performance targets. International Journal for Quality in Health Care. 2005 Apr;17(2):115–21.
44. Graugaard PK, Holgersen K, Eide H, Finset A. Changes in physician-patient communication from initial to return visits: A prospective study in a haematology outpatient clinic. Patient Educ Couns. 2005;57(1):22–9.
45. Labeit AM, Peinemann F. Determinants of a GP visit and cervical cancer screening examination in Great Britain. PLoS One. 2017 Apr 1;12(4).
46. Millar MM, Edwards SL, Herget KA, Orleans B, Ofori-Atta BS, Kirchhoff AC, et al. Adherence to Guideline-Recommended cancer screening among Utah cancer survivors. Cancer Med. 2022 Feb 1;3543–54.
47. Van Til L, MacQuarrie C, Herbert R. Understanding the barriers to cervical cancer screening among older women. Qual Health Res. 2003;13(8):1116–31.
48. Almeida CM, Rodriguez MA, Skootsky S, Pregler J, Steers N, Wenger NS. Cervical Cancer Screening Overuse and underuse: Patient and Physician Factors [Internet]. Vol. 19, Am J Manag Care. 2013. Available from: www.ajmc.com
49. Ishii K, Tabuchi T, Iso H. Combined patterns of participation in cervical, breast, and colorectal cancer screenings and factors for non-participation in each screening among women in Japan. Prev Med (Baltim). 2021 Sep 1;150.
50. Kregting LM, Olthof EMG, Breekveldt ECH, Aitken CA, Heijnsdijk EAM, Toes-Zoutendijk E, et al. Concurrent participation in breast, cervical, and colorectal cancer screening in the Netherlands. Eur J Cancer. 2022 Nov 1;175:180–6.

51. Malone C, Buist DSM, Tiro J, Barlow W, Gao H, Lin J, et al. Out of reach? Correlates of cervical cancer underscreening in women with varying levels of healthcare interactions in a United States integrated delivery system. Prev Med (Baltim). 2021 Apr 1;145.

52. Damiani G, Basso D, Acampora A, Bianchi CBNA, Silvestrini G, Frisicale EM, et al. The impact of level of education on adherence to breast and cervical cancer screening: Evidence from a systematic review and meta-analysis. Vol. 81, Preventive Medicine. Academic Press Inc.; 2015. p. 281–9.

53. Razuka-Ebela D, Zile I, Tzivian L, Ebela I, Polaka I, Parshutin S, et al. Does Family History of Cancer Influence Undergoing Screening and Gastrointestinal Investigations? J Gastrointestin Liver Dis. 2020 Oct 27;29(4):523–8.

54. Deguara M, Calleja N, England K. Cervical cancer and screening: Knowledge, awareness and attitudes of women in Malta. J Prev Med Hyg. 2021 Jan 14;61(4):E584–92.

55. Terret C, Castel-Kremer E, Albrand G, Droz JP. Effects of comorbidity on screening and early diagnosis of cancer in elderly people. Vol. 10, The Lancet Oncology. 2009. p. 80–7.

56. Desimpel F, Declercq S, Makar A. Cervical cancer screening and outcomes for women under 25 years of age in Belgium: a 10-year nationwide study. European Journal of Cancer Prevention. 2023;32:163–70.

57. Castañón A, Landy R, Cuzick J, Sasieni P. Cervical Screening at Age 50-64 Years and the Risk of Cervical Cancer at Age 65 Years and Older: Population-Based Case Control Study. PLoS Med. 2014 Jan;11(1).

58. Bravington A, Chen H, Dyson J, Jones L, Dalgliesh C, Bryan A, et al. Challenges and opportunities for cervical screening in women over the age of 50 years: a qualitative study. British Journal of General Practice. 2022 Dec 1;72(725):E873–81.

59. Bates CK, Carroll N, Potter J. The challenging pelvic examination. J Gen Intern Med. 2011 Jun;26(6):651–7.

60. Samman E, Mkuu R, Zhang X, Scummings S, Burdine J. Body Mass Index and Breast and Cervical Cancer Screening. Women's Health Reports. 2022 May 1;3(1):508–14.
61. Gnade CM, Hill EK, Botkin HE, Hefel AR, Hansen HE, Sheets KA, et al. Effect of Obesity on Cervical Cancer Screening and Outcomes. J Low Genit Tract Dis. 2020 Oct 1;24(4):358–62.
62. Urbute A, Kjaer SK, Kesmodel US, Frederiksen K, Thomsen LT. Women with obesity participate less in cervical cancer screening and are more likely to have unsatisfactory smears: Results from a nationwide Danish cohort study. Prev Med (Baltim). 2022 Jun 1;159.
63. Charkhchi P, Schabath MB, Carlos RC. Breast, Cervical, and Colorectal Cancer Screening Adherence: Effect of Low Body Mass Index in Women. J Womens Health. 2020 Jul 1;29(7):996–1006.
64. Golubnitschaja O, Liskova A, Koklesova L, Samec M, Biringer K, Büsselberg D, et al. Caution, "normal" BMI: health risks associated with potentially masked individual underweight—EPMA Position Paper 2021. EPMA Journal. 2021 Sep 1;12(3):243–64.
65. Cristancho S, Peters K, Garces M. Preferencias de los inmigrantes hispanos/latinos en el Medio Oeste rural de los Estados Unidos de America, en relación con la información sanitaria. Glob Health Promot. 2014;21(1):40–9.
66. Cha AE, Cohen RA. Demographic Variation in Health Insurance Coverage: United States, 2021 [Internet]. Vol. 177, National Health Statistics Reports Number. 2021. Available from: https://www.cdc.gov/nchs/products/index.htm.
67. Fletcher JM, Frisvold DE. Higher education and health investments: Does more schooling affect preventive health care use? J Hum Cap. 2009 Jun;3(2):144–76.
68. Health Resources and Services Administration, Office of Women's Health, The Federal Cervical Cancer Collaborative Opportunities Report. Maryland: 2023.

69. Bogani G, Serati M, Maggiore ULR, Ditto A, Gardella B, Ferrero S, et al. Cervical intraepithelial neoplasia in women who had vaccination against HPV. International Journal of Gynecology and Obstetrics. 2019;147(2):233–7.

70. Chen ST, Huybrechts KF, Bateman BT, Hernández-Díaz S. Trends in Human Papillomavirus Vaccination in Commercially Insured Children in the United States. Pediatrics. 2020;146(4):e20193557.

71. Smith RA, Andrews KS, Brooks D, Fedewa SA, Manassaram-Baptiste D, Saslow D, et al. Cancer screening in the United States, 2019: A review of current American Cancer Society guidelines and current issues in cancer screening. CA Cancer J Clin. 2019;69(3):184–210.

72. Rosenblum HG, Lewis RM, Gargano JW, Querec TD, Unger ER, Markowitz LE. Morbidity and Mortality Weekly Report Declines in Prevalence of Human Papillomavirus Vaccine-Type Infection Among Females after Introduction of Vaccine-United States, 2003-2018 [Internet]. 2021. Available from: https://www.cdc.gov/rdc/index.htm

73. Centers for Disease Control and Prevention. Cancers Associated with Human Papillomavirus, United States, 2013-2017. USCS Data Brief, no 18 Atlanta, GA: Centers for Disease Control and Prevention, US Department of Health and Human Services [Internet]. 2020;1–2. Available from: https://www.cdc.gov/cancer/uscs/about/data-briefs/no18-hpv-assoc-cancers-UnitedStates-2013-2017.htm%0Ahttps://www.cdc.gov/cancer/hpv/

74. Centers for Disease Control and Prevention. Vaccines and Preventable Diseases: Administering HPV Vaccine. 2020;1–2.

75. Senkomago V, Henley ; S Jane, Thomas CC, Mix JM, Markowitz LE, Saraiya M. Morbidity and Mortality Weekly Report Human Papillomavirus-Attributable Cancers-United States, 2012-2016 [Internet]. Available from: https://www.cdc.gov/cancer/uscs.

76. World Health Organisation. Global strategy to accelerate the elimination of cervical cancer as a public health problem and its associated goals and targets for the period 2020 – 2030. Vol. 2, United Nations General Assembly. 2020. 1–3 p.

77. Harper DM, DeMars LR. HPV vaccines – A review of the first decade. Gynecol Oncol. 2017;146(1):196–204.

78. Markowitz LE, Gee J, Chesson H, Stokley S. Ten Years of Human Papillomavirus Vaccination in the United States. Acad Pediatr. 2018;18(2):S3–10.

79. Pingali C, Yankey D, Elam-Evans LD, Markowitz LE, Valier MR, Fredua B, et al. Morbidity and Mortality Weekly Report National Vaccination Coverage Among Adolescents Aged 13-17 Years-National Immunization Survey-Teen, United States, 2021 [Internet]. 2021. Available from: https://www.

80. Walker TY, Elam-Evans LD, Williams CL, Fredua B, Yankey D, Markowitz LE, et al. Trends in human papillomavirus (HPV) vaccination initiation among adolescents aged 13–17 by metropolitan statistical area (MSA) status, National Immunization Survey–Teen, 2013–2017. Hum Vaccin Immunother. 2020;16(3):554–61.

81. Agrawal S, Morain SR. Who calls the shots? the ethics of adolescent self-consent for HPV vaccination. J Med Ethics. 2018 Aug 1;44(8):531–5.

82. Nguyen KH, Santibanez TA, Stokley S, Lindley MC, Fisher A, Kim D, et al. Parental vaccine hesitancy and its association with adolescent HPV vaccination. Vaccine. 2021 Apr 22;39(17):2416–23.

83. Markovitz AR, Song JY, Paustian ML, El Reda DK. Association between maternal preventive care utilization and adolescent vaccination: It's not just about pap testing. J Pediatr Adolesc Gynecol [Internet]. 2014;27(1):29–36. Available from: http://dx.doi.org/10.1016/j.jpag.2013.08.012

84. Chao C, Slezak JM, Coleman KJ, Jacobsen SJ. Papanicolaou screening behavior in mothers and human papillomavirus vaccine uptake in adolescent girls. Am J Public Health. 2009;99(6):1137–42.

85. Lutringer-Magnin D, Cropet C, Barone G, Canat G, Kalecinski J, Leocmach Y, et al. HPV vaccination among French girls and women aged 14-23 years and the relationship with their mothers' uptake of Pap smear screening: A study in general practice. Vaccine [Internet]. 2013;31(45):5243–9. Available from: http://dx.doi.org/10.1016/j.vaccine.2013.08.068

86. Sander BB, Vázquez Prada M, Rebolj M, Lynge E, Valentiner Branth P. Mothers' and their daughters' use of preventive measures against cervical cancer. Scand J Public Health. 2015;43(4):415–22.

87. Markovitz AR, Song JY, Paustian ML, El Reda DK. Association between maternal preventive care utilization and adolescent vaccination: It's not just about pap testing. J Pediatr Adolesc Gynecol [Internet]. 2014;27(1):29–36. Available from: http://dx.doi.org/10.1016/j.jpag.2013.08.012

88. Berenson AB, Brown VG, Fuchs EL, Hirth JM, Chang M. Relationship between maternal experiences and adolescent HPV vaccination. Hum Vaccin Immunother [Internet]. 2017;13(9):2150–4. Available from: https://doi.org/10.1080/21645515.2017.1332551

89. Spencer AM, Brabin L, Verma A, Roberts SA. Mothers' screening histories influence daughters' vaccination uptake: An analysis of linked cervical screening and human papillomavirus vaccination records in the North West of England. Eur J Cancer. 2013;49(6):1264–72.

90. Lutringer-Magnin D, Cropet C, Barone G, Canat G, Kalecinski J, Leocmach Y, et al. HPV vaccination among French girls and women aged 14-23 years and the relationship with their mothers' uptake of Pap smear screening: A study in general practice. Vaccine

[Internet]. 2013;31(45):5243–9. Available from: http://dx.doi.org/10.1016/j.vaccine.2013.08.068

91. Hechter RC, Chao C, Sy LS, Ackerson BK, Slezak JM, Sidell MA, et al. Quadrivalent human papillomavirus vaccine uptake in adolescent boys and maternal utilization of preventive care and history of sexually transmitted infections. Am J Public Health. 2013;103(9):63–8.
92. Preventive US, Task S, Cancer A. Breast Cancer Screening Guidelines for Women Some organizations release different breast cancer screening guidelines for women who are considered to be at high risk of developing breast cancer . Different. :2–4.
93. Venturelli F, Baldacchini F, Campari C, Perilli C, Pascucci MG, Finarelli AC, et al. Association between mothers ' screening uptake and daughters ' HPV vaccination : a quasi-experimental study on the effect of an active invitation campaign. 2017;
94. Smith PJ, Stokley S, Bednarczyk RA, Orenstein WA, Omer SB. HPV vaccination coverage of teen girls: The influence of health care providers. Vaccine. 2016 Mar 18;34(13):1604–10.
95. Tinsley BJ. Multiple Influences on the Acquisition and Socialization of Children's Health Attitudes and Behavior: An Integrative Review. Vol. 63. 1992.
96. Bowung A. Implications of Preventive Health Behaviour for Cervical and Breast Cancer Screening Programmes: A Review [Internet]. Vol. 6. 1389. Available from: https://academic.oup.com/fampra/article/6/3/224/426954
97. Beran MS, Craft C. Medicare Annual Wellness Visits Understanding the Patient and Physician Perspective. Vol. 38, Clinical AND Health Affairs. 2015.
98. wellness-improved-utilization-of-preventive-services-among-patients-following-team-based-annual-wellness-visits.

99. Tong ST, Webel BK, Donahue EE, Richards A, Sabo RT, Brooks EM, et al. Understanding the Value of the Wellness Visit: A Descriptive Study. Am J Prev Med. 2021 Oct 1;61(4):591–5.

100. McMurry TL, Lobo JM, Kang H, Kim S, Balkrishnan R, Anderson R, et al. Annual wellness visits are associated with increased use of preventive services in patients with diabetes living in the Diabetes Belt. Diabetes Epidemiology and Management. 2022 Jul;7:100094.

101. Lindley MC, Jeyarajah J, Yankey D, Curtis CR, Markowitz LE, Stokley S. Comparing human papillomavirus vaccine knowledge and intentions among parents of boys and girls. Hum Vaccin Immunother. 2016 Jun 2;12(6):1519–27.

102. Kempe A, O'Leary ST, Markowitz LE, Crane LA, Hurley LP, Brtnikova M, et al. HPV vaccine delivery practices by primary care physicians. Pediatrics. 2019;144(4).

103. Lindsay AC, Delgado D, Valdez MJ, Restrepo E, Guzman YM. "I don't Think He Needs the HPV Vaccine Cause Boys Can't Have Cervical Cancer": a Qualitative Study of Latina Mothers' (Mis) Understandings About Human Papillomavirus Transmission, Associated Cancers, and the Vaccine. Journal of Cancer Education. 2022 Apr 1;37(2):370–8.

104. Monnat SM, Wallington SF. Is there an association between maternal pap test use and adolescent human papillomavirus vaccination? Journal of Adolescent Health. 2013;52(2):212–8.

105. McCauley L, Phillips RL, Meisnere M, Robinson SK. Implementing high-quality primary care: Rebuilding the foundation of health care (2021). Implementing High-Quality Primary Care. National Academies Press; 2021. 1–428 p.

106. Cataldi JR, O'Leary ST, Markowitz LE, Allison MA, Crane LA, Hurley LP, et al. Changes in Strength of Recommendation and Perceived Barriers to Human Papillomavirus Vaccination: Longitudinal Analysis of Primary Care Physicians, 2008-2018. Journal of Pediatrics. 2021 Jul 1;234:149-157.e3.

107. Allgood KL, Rauscher GH, Whitman S, Vasquez-Jones G, Shah AM. Validating self-reported mammography use in vulnerable communities: Findings and recommendations. Cancer Epidemiology Biomarkers and Prevention. 2014;23(8):1649–58.

108. Smulian EA, Mitchell KR, Stokley S. Interventions to increase HPV vaccination coverage: A systematic review. Vol. 12, Human Vaccines and Immunotherapeutics. Taylor and Francis Inc.; 2016. p. 1566–88.

109. Sara Heath. Patient Engagement HIT. 2018. Challenges Impacting Patient Access to Healthcare.

110. Kreimer AR, Cernuschi T, Rees H, Brotherton JML, Porras C, Schiller J. Public health opportunities resulting from sufficient HPV vaccine supply and a single-dose vaccination schedule. J Natl Cancer Inst. 2023 Mar 9;115(3):246–9.

111. Bumatay S, Dickinson C, Larsen R, Stock I, Day MR, Hatch B, et al. A comparison of electronic health records and the Oregon state immunization registry for human papilloma virus vaccine delivery (2005–2022). Vaccine [Internet]. 2023 Aug; Available from: https://linkinghub.elsevier.com/retrieve/pii/S0264410X23009490

112. Taylor VM, Burke NJ, Ko LK, Sos C, Liu Q, Do HH, et al. Understanding HPV Vaccine Uptake Among Cambodian American Girls. J Community Health. 2014;39(5):857–62.

113. Markovitz AR, Song JY, Paustian ML, El Reda DK. Association between maternal preventive care utilization and adolescent vaccination: It's not just about pap testing. J Pediatr Adolesc Gynecol. 2014;27(1):29–36.

114. Steens A, Wielders CCH, Bogaards JA, Boshuizen HC, De Greeff SC, De Melker HE. Association between human papillomavirus vaccine uptake and cervical cancer screening in the Netherlands: Implications for future impact on prevention. Int J Cancer. 2012;132(4):932–43.

115. Hansen BT, Campbell S, Burger E, Nygård M. Correlates of HPV vaccine uptake in school-based routine vaccination of preadolescent girls in Norway: A register-based study of 90,000 girls and their parents. Prev Med (Baltim). 2015;77:4–10.

116. Moody CA, Laimins LA. Human papillomavirus oncoproteins: Pathways to transformation. Nat Rev Cancer. 2010;10(8):550–60.

117. de Sanjosé S, Brotons M, Pavón MA. The natural history of human papillomavirus infection. Best Pract Res Clin Obstet Gynaecol. 2018;47:2–13.

118. Gravitt PE, Winer RL. Natural history of HPV infection across the lifespan: Role of viral latency. Vol. 9, Viruses. MDPI AG; 2017.

119. Demarco M, Hyun N, Carter-Pokras O, Raine-Bennett TR, Cheung L, Chen X, et al. A study of type-specific HPV natural history and implications for contemporary cervical cancer screening programs. EClinicalMedicine. 2020 May 1;22.

120. Bosch FX, Lorincz A, Muñoz N, Meijer LM. The causal relation between human papillomavirus and cervical cancer [Internet]. Vol. 55, J Clin Pathol. 2002. Available from: http://www.ipvsoc.org

121. Miller M, Unger E. The Topic Is Cancer Teal and White Yesterday and Today: The Evolution of Cervical Cancer Screening [Internet]. Available from: https://blogs.cdc.gov/cancer/2020/01/30/

122. Saraiya M, Steben M, Watson M, Markowitz L. Evolution of cervical cancer screening and prevention in united states and canada: Implications for public health practitioners and clinicians. Prev Med (Baltim). 2013 Nov;57(5):426–33.

123. Monsonego J, Autillo-Touati A, Bergeron C, Dachez R, Liaras J, Saurel J, et al. Liquid-based cytology for primary cervical cancer screening: A multi-centre study. Br J Cancer. 2001;84(3):360–6.

124. Fontham ETH, Wolf AMD, Church TR, Etzioni R, Flowers CR, Herzig A, et al. Cervical cancer screening for individuals at average risk: 2020 guideline update from the American Cancer Society. CA Cancer J Clin. 2020;70(5):321–46.

125. Morrison T Ben, Flynn PM, Weaver AL, Wieland ML. Cervical Cancer Screening Adherence Among Somali Immigrants and Refugees to the United States. Health Care Women Int. 2013;34(11):980–8.

126. Colby SL, Ortman JM. Projections of the Size and Composition of the U.S. Population: 2014 to 2060. Program. 2014;1–13.

127. Zong J, Batalova J. Frequently Requested Statistics on Immigrants and Immigration in the United States. Migration Policy Institute. 2015;1–55.

128. Tsegaye AT, Lin J, Cole AM, Szpiro AA, Rao DW, Walson JL, et al. Adherence and correlates of cervical cancer screening among East African Immigrants in Washington State. Vol. 5, Pediatrics and Epidemiology.

129. Howard M, Lytwyn A, Lohfeld L, Redwood-Campbell L, Fowler N, Karwalajtys T. Barriers to acceptance of self-sampling for human papillomavirus across ethnolinguistic groups of women. Can J Public Health. 2009;100(5):365–9.

130. Kobetz E, Seay J, Koru-Sengul T, Bispo JB, Trevil D, Gonzalez M, et al. A randomized trial of mailed HPV self-sampling for cervical cancer screening among ethnic minority women in South Florida. Cancer Causes & Control [Internet]. 2018;29:793–801. Available from: https://doi.org/10.1007/s10552-018-1055-7

131. Jalili F, O'Conaill C, Templeton K, Lotocki R, Fischer G, Manning L, et al. Assessing the impact of mailing self-sampling kits for human papillomavirus testing to unscreened non-responder women in Manitoba. Current Oncology. 2019;26(3):167–72.

132. Gizaw M, Teka B, Ruddies F, Abebe T, Kaufmann AM, Worku A, et al. Uptake of Cervical Cancer Screening in Ethiopia by Self-Sampling HPV DNA Compared to Visual Inspection with Acetic Acid: A Cluster Randomized Trial. 2019; Available from: www.aacrjournals.org

133. Winer RL, Lin J, Tiro JA, Miglioretti DL, Beatty T, Gao H, et al. Effect of Mailed Human Papillomavirus Test Kits vs Usual Care Reminders on Cervical Cancer Screening Uptake, Precancer Detection, and Treatment: A Randomized Clinical Trial. JAMA Netw Open. 2019;2(11):1–14.

134. Musa J, Achenbach CJ, Dwyer LCO, Evans CT, Mchugh M, Hou L, et al. Effect of cervical cancer education and provider recommendation for screening on screening rates : A systematic review and meta-analysis. 2017;1–28.

135. Winer RL, Tiro JA, Miglioretti DL, Thayer C, Beatty T, Lin J, et al. Rationale and design of the HOME trial : A pragmatic randomized controlled trial of home-based human papillomavirus (HPV) self-sampling for increasing cervical cancer screening uptake and effectiveness in a U.S. healthcare system. Contemp Clin Trials [Internet]. 2018;64(November 2017):77–87. Available from: https://doi.org/10.1016/j.cct.2017.11.004

136. Arrossi S, Thouyaret L, Herrero R, Campanera A, Magdaleno A, Cuberli M, et al. Effect of self-collection of HPV DNA off ered by community health workers at home visits on uptake of screening for cervical cancer (the EMA study): a population-based cluster-randomised trial. Lancet Glob Health [Internet]. 2015;3(2):e85–94. Available from: http://dx.doi.org/10.1016/S2214-109X(14)70354-7

137. Burger EA, Smith MA, Killen J, Sy S, Simms KT, Canfell K, et al. Projected time to elimination of cervical cancer in the USA: a comparative modelling study. Lancet Public Health. 2020 Apr 1;5(4):e213–22.

138. Huhmann K. Barriers and Facilitators to Breast and Cervical Cancer Screening in Somali Immigrant Women: An Integrative Review. Oncol Nurs Forum. 2020 Mar;47(2):177–86.

139. Moscicki AB, Widdice L, Ma Y, Farhat S, Miller-Benningfield S, Jonte J, et al. Comparison of natural histories of human papillomavirus detected by clinician-and self-sampling. Int J Cancer. 2010;127(8):1882–92.

140. Sellors JW, Lorincz AT, Mahony JB, Mielzynska I, Lytwyn A, Roth P, et al. Comparison of self-collected vaginal, vulvar and urine samples with physician-collected cervical samples for human papillomavirus testing to detect high-grade squamous intraepithelial lesions. Journal of Canadian Medical Association. 2000;163(5):513–8.

141. Malone C, Barnabas R V., Buist DSM, Tiro JA, Winer RL. Cost-effectiveness studies of HPV self-sampling: A systematic review. Prev Med (Baltim) [Internet]. 2020;132(July 2019):105953. Available from: https://doi.org/10.1016/j.ypmed.2019.105953

142. Reques L, Rolland C, Lallemand A, Lahmidi N, Aranda-Fernández E, Lazzarino A, et al. Comparison of cervical cancer screening by self-sampling papillomavirus test versus pap-smear in underprivileged women in France. 2020; Available from: https://doi.org/10.1186/s12905-021-01356-8

143. Serrano B, Ibáñez R, Robles C, Peremiquel-Trillas P, de Sanjosé S, Bruni L. Worldwide use of HPV self-sampling for cervical cancer screening. Prev Med (Baltim). 2022 Jan 1;154.

144. Hariprasad R, John A, Abdulkader RS. CANCER PREVENTION AND CONTROL review articles Challenges in the Implementation of Human Papillomavirus Self-Sampling for Cervical Cancer Screening in India: A Systematic Review. 2023; Available from: https://ascopubs.org/go/authors/open-access

145. Daponte N, Valasoulis G, Michail G, Magaliou I, Daponte AI, Garas A, et al. HPV-Based Self-Sampling in Cervical Cancer Screening: An Updated Review of the Current Evidence in the Literature. Cancers (Basel). 2023 Mar 8;15(6):1669.

146. Nishimura H, Yeh PT, Oguntade H, Kennedy CE, Narasimhan M. HPV self-sampling for cervical cancer screening: A systematic review of values and preferences. BMJ Glob Health. 2021 May 19;6(5).

147. Sewali B, Okuyemi KS, Askhir A, Belinson J, Vogel RI, Joseph A, et al. Cervical cancer screening with clinic-based Pap test versus home HPV test among Somali immigrant women in Minnesota: a pilot randomized controlled trial. Cancer Med. 2015 Apr;4(4):620–31.

148. Winer R, Lin J, Tiro J, Anderson M, Hansen K, Gao H, et al. Effectiveness of Approaches for Offering HPV Self-Sampling to Increase Cervical Cancer Screening in Previously-adherent, Overdue, and Unknown Screening History Populations: U.S.-based STEP trial results. In: International Papillomavirus Conference. 2023.

149. Arias E, Tejada-Vera B, Kochanek KD, Ahmad FB. Vital Statistics Rapid Release Provisional Life Expectancy Estimates for 2021 [Internet]. 2021. Available from: https://www.cdc.gov/nchs/products/index.htm.

150. Franco EL. The time has come to implement primary human papillomavirus screening for cervical cancer in the United States. Cancer. John Wiley and Sons Inc; 2023.

151. Nayar R. Cervical cancer prevention in the United States—where we've been and where we're going: The American Cancer Society Primary HPV Screening Initiative. Cancer Cytopathology. John Wiley and Sons Inc; 2023.

152. Perkins RB, Guido RS, Castle PE, Chelmow D, Einstein MH, Garcia F, et al. 2019 ASCCP Risk-Based Management Consensus Guidelines for Abnormal Cervical Cancer Screening Tests and Cancer Precursors. J Low Genit Tract Dis. 2020 Apr 1;24(2):102–31.

153. Gibert MJ, Sánchez-Contador C, Artigues G. Validity and acceptance of self vs conventional sampling for the analysis of human papillomavirus and Pap smear. Sci Rep. 2023 Dec 1;13(1).

154. Clarke MA, Risley C, Stewart MW, Geisinger KR, Hiser LM, Morgan JC, et al. Age-specific prevalence of human papillomavirus and abnormal cytology at baseline in a diverse statewide prospective cohort of individuals undergoing cervical cancer screening in Mississippi. Cancer Med. 2021 Dec 1;10(23):8641–50.

155. Campos NG, Burger EA, Sy S, Sharma M, Schiffman M, Rodriguez AC, et al. Practice of Epidemiology An Updated Natural History Model of Cervical Cancer: Derivation of Model Parameters. Am J Epidemiol [Internet]. 2014;180(5):545–55. Available from: http://aje.oxfordjournals.

156. Campos NG, Demarco M, Bruni L, Desai KT, Gage JC, Adebamowo SN, et al. A Proposed New Generation of Evidence-Based State-Transition Models to Inform Global Control of Cervical Cancer. Prev Med (Baltim) [Internet]. 2021;144:106438. Available from: https://doi.org/10.1016/j.ypmed.2021.106438

157. Liu G, Mugo NR, Bayer C, Rao DW, Onono M, Mgodi NM, et al. Impact of catch-up human papillomavirus vaccination on cervical cancer incidence in Kenya: A mathematical modeling evaluation of HPV vaccination strategies in the context of moderate HIV prevalence. Available from: https://doi.org/10.1016/j.

158. Rao DW, Bayer CJ, Liu G, Chikandiwa A, Sharma M, Hathaway CL, et al. Modelling cervical cancer elimination using single-visit screening and treatment strategies in the context of high HIV prevalence: estimates for KwaZulu-Natal, South Africa. J Int AIDS Soc [Internet]. 2022;2022:26021. Available from: http://onlinelibrary.wiley.com/doi/10.1002/jia2.26021/full|https://doi.org/10.1002/jia2.26021

159. Arias E, Xu J, Tejada-Vera B, Murphy SL, Bastian B. National Vital Statistics Reports Volume 71, Number 2 August 23, 2022 [Internet]. Vol. 71, National Vital Statistics Reports. 2020. Available from: https://www.cdc.gov/nchs/products/index.htm.

160. SEER*Explorer. Surveillance Research Program, National Cancer Institute; [cited 2023 Jan 18]. Available from: https://seer.cancer.gov/statistics-network/explorer/. 2023. An interactive website for SEER cancer statistics [Internet]. .

161. WHO. Available at: https://www.who.int/data/gho/data/themes/topics/topic-details/GHO/healthy-life-expectancy-(hale). 2022. World Health Statistics. Global Health Estimates: Life expectancy and leading causes of death and disability.

162. Arbyn M, Smith SB, Temin S, Sultana F, Castle P. Detecting cervical precancer and reaching underscreened women by using HPV testing on self samples: Updated meta-analyses. BMJ (Online). 2018;363.

163. Terasawa T, Hosono S, Sasaki S, Hoshi K, Hamashima Y, Katayama T, et al. Comparative accuracy of cervical cancer screening strategies in healthy asymptomatic women: a systematic review and network meta-analysis. Sci Rep. 2022 Dec 1;12(1).

164. Winer RL, Lin J, Anderson ML, Tiro JA, Meenan RT, Hansen K, et al. Design of a pragmatic randomized controlled trial of home-based human papillomavirus (HPV) self-sampling for increasing cervical cancer screening uptake in a U.S. healthcare system: The STEP trial. Contemp Clin Trials. 2022 Nov 1;122.

165. Dartell M, Rasch V, Kahesa C, Mwaiselage J, Ngoma T, Junge J, et al. Human papillomavirus prevalence and type distribution in 3603 HIV-positive and HIV-Negative Women in the General Population of Tanzania: The PROTECT study. Sex Transm Dis. 2012 Mar;39(3):201–8.

166. Shin HY, Lee B, Hwang SH, Lee DO, Sung NY, Park JY, et al. Evaluation of satisfaction with three different cervical cancer screening modalities: Clinician-collected pap test vs. HPV test by self-sampling vs. HPV test by urine sampling. J Gynecol Oncol. 2019;30(5):1–10.

167. Yeh PT, Kennedy CE, De Vuyst H, Narasimhan M. Self-sampling for human papillomavirus (HPV) testing: A systematic review and meta-Analysis. Vol. 4, BMJ Global Health. BMJ Publishing Group; 2019.

168. Martinez-Gutierrez J, Chima S, Boyd L, Sherwani A, Drosdowsky A, Karnchanachari N, et al. Failure to follow up abnormal test results associated with cervical cancer in primary and ambulatory care: a systematic review. BMC Cancer. 2023 Dec 1;23(1):653.

169. Ghebre RG, Sewali B, Osman S, Adawe A, Nguyen HT, Okuyemi KS, et al. Cervical cancer: barriers to screening in the Somali community in Minnesota. J Immigr Minor Health. 2015 Jun;17(3):722–8.

170. Anaman-Torgbor JA, King J, Correa-Velez I. Barriers and facilitators of cervical cancer screening practices among African immigrant women living in Brisbane, Australia. Eur J Oncol Nurs. 2017 Dec;31:22–9.

171. Idehen EE, Pietilä AM, Kangasniemi M. Barriers and Facilitators to Cervical Screening among Migrant Women of African Origin: A Qualitative Study in Finland. Int J Environ Res Public Health [Internet]. 2020 Oct 14;17(20):7473. Available from: https://www.mdpi.com/1660-4601/17/20/7473

172. Sumiaty S, Hasnawati H. Health Education with Media Leaflet Against Women's Knowledge of Cervical Cancer Screening. Napande: Jurnal Bidan. 2022 Apr 25;1(1):15–22.

173. Abu SH, Woldehanna BT, Nida ET, Tilahun AW, Gebremariam MY, Sisay MM. The role of health education on cervical cancer screening uptake at selected health centers in Addis Ababa. PLoS One. 2020 Oct 1;15(10 October).

174. Seo JY, Park SH, Choi SE, Lee M, Strauss SM. Development and Modification of a Culturally Tailored Education Program to Prevent Breast Cancer in Korean Immigrant Women in New York City. Journal of Cancer Education. 2022 Jun 1;

175. Campos NG, Scarinci IC, Tucker L, Peral S, Li Y, Regan MC, et al. Cost-effectiveness of offering cervical cancer screening with HPV self-sampling among african-American women in the mississippi delta. Cancer Epidemiology Biomarkers and Prevention. 2021 Jun 1;30(6):1114–21.

176. Arbyn M, Redman CWE, Verdoodt F, Kyrgiou M, Tzafetas M, Ghaem-Maghami S, et al. Incomplete excision of cervical precancer as a predictor of treatment failure: a systematic review and meta-analysis. Lancet Oncol. 2017 Dec 1;18(12):1665–79.

177. Qin D, Bai A, Xue P, Seery S, Wang J, Mendez MJG, et al. Colposcopic accuracy in diagnosing squamous intraepithelial lesions: a systematic review and meta-analysis of the International Federation of Cervical Pathology and Colposcopy 2011 terminology. BMC Cancer. 2023 Dec 1;23(1).