

Cervical Cancer Screening Patterns Among HIV-positive Women in Estonia: A Population Based Retrospective Cohort Study

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Abstract

Introduction

The World Health Organisation (WHO) calls for the elimination of cervical cancer (CC) as a public health issue. To achieve elimination, efforts must be aligned and accelerated. Women living with HIV (WLWH) have excess risk for developing and dying from CC over the general population. Estimates of cervical cancer screening (CCS) program coverage in Eastern European countries that have experienced HIV epidemics since early 2000s are scarce.

Methods

This population-based retrospective study uses healthcare administrative database and follows cohorts of all WLWH and in a ratio 1:3 randomly matched (age, region) HIV negative women from 2009-2018. Annual and longitudinal (over the whole study period) coverage for CCS (opportunistic, organised, HIV specific) and adjusted odds ratios (AORs) for longitudinal screening coverage predictors were estimated from 2009-2018.

Results

Among WLWH and HIV negative women, the mean annual coverage with opportunistic screening was 61.45%, and 65.59%; organised screening 20.4%, and 28.7%, respectively (both: $p < 0.00001$). 19.01% (95% CI 18.05-19.97) HIV negative and 13.9% (95% CI 12.35-15.45) WLWH were longitudinally covered with organised CCS. Among WLWH, the mean annual HIV specific CCS coverage was 49.4% and 24.3% were longitudinally covered. Longitudinal coverage with HIV specific CCS was inversely associated with age, HCV co-infection AOR 0.754 (95% CI 0.619, 0.916), not having insurance AOR 0.331 (95% CI 0.264, 0.412), drug abuse (AOR 0.459, 95% CI 0.336, 0.618) and higher among those retained in HIV care AOR 1.972 (95% CI 1.615, 2.410). Among HIV negative women, longitudinal coverage with organised CCS was inversely associated with residence region and higher among older women.

Conclusions

Our results highlight unacceptably low coverage of WLWH with cervical cancer screening in Estonia. There is a need for a dedicated cervical cancer screening efforts for WLWH considering the high cancer risk and rate in the study population.

Background

Globally, 570 000 cancer cases (8.6%) per year in women are attributable to human papillomavirus (HPV). Cervical cancer (CC) is the fourth most common cancer in women.[1] Yet, in 2020, cervical cancer persists as the leading cause of cancer-related deaths among women in 42 countries. Elimination of this cancer will only be possible if the global community and governments will advance an evidence-based, gendered approach to cancer risk and cancer control.

For people living with HIV (PLWH), cancer is now one of the leading causes of death [2] HPV infection is a necessary cause for cervical cancer.[3] HIV is known to have an unfavourable impact on HPV natural history, associated with increased acquisition and persistence of HPV infection, as well as with increased risk of invasive CC.[2] In the results multi-cohort prospective study the CC incidence in women living with HIV (WLWH) was four times higher than that in HIV negative women (incidence rate of 26 and 6 per 100 000 respectively).[4] The incidence of CC among WLWH has not declined since the introduction of antiretroviral therapy (ART).[2] Globally, 1 to 2% of HIV negative women develop pre-cancerous conditions annually whilst WLWH are five times more prone to developing CIN stages 2/3 (10% annual incidence).[5] The natural history of HPV infection has a slow progression however, WLWH progress more frequently and quickly to pre-cancer and cancer.[6] As a consequence, international guidelines recommend more frequent cervical cancer screening (CCS) in WLWH.[7]

Organised screening programmes have been remarkably successful in reducing the incidence and mortality of CC, while opportunistic screening varies in its effectiveness.[8] Failure to undergo recommended routine screening has been identified as the most significant risk for the development of CC, both in WLWH and in the general population (in countries where routine CCS programs are in place).[9] There is a knowledge gap on CCS coverage in European countries experiencing HIV epidemics among high-risk women (such as WLWH). Multiple risk factors for deficient cervical cancer screening in women without HIV have been identified. Risk factors for deficient screening in the HIV-infected population are less well-known.

The aim of the study was to assess the CCS coverage among WLWH and in the general population of women in Estonia and to identify risk factors associated with low coverage in WLWH in order to guide HIV specific CCS strategies if needed.

The CC incidence in Estonia is high, comparable to the very high incidence (per 100 000 population) observed in Central European countries in 2018 (Romania 19.5, Bulgaria 20.3 and 21.4 in the Republic of Moldova), and over two times higher than in neighbouring Northern European/Scandinavian countries (Sweden 9.0, Finland 4.7).[10] Furthermore, in Estonia, CC incidence is increasing (2012 19.6 and 2018 22.5 per 100 000), while mortality is not declining (2012 5.52 and 2018 4.3 per 100 000), and stage distribution has shifted towards later stages.[11] A organised CC screening program (using conventional cytology, Papanicolaou (Pap) test) has been in place in Estonia since 2006. Organised screening targets women in age range 30–55 years, with a screening interval 5 years across the whole period.[12] The failure of CC screening has been attributed to the low screening uptake (less than 50% in 2016) and insufficient quality of the Pap test based program.[10] Vaccination of girls against HPV was introduced in 2018.

In 2018, Estonia had the third highest rate of newly diagnosed HIV cases in the EU (Estonia 14.4/100 000 compared to an EU average of 5.1).[13] The large burden is also reflected in HIV/AIDS mortality rate which was 2.77 per 100 000 in Estonia in 2017 – that is very high in comparison to neighbouring

countries it (Finland 0ž1 and Sweden 0ž2).[14]

Based on the Estonian HIV cohort data, about 36% of people infected with HIV in Estonia are women, and at the time of HIV care entry 53% of patients are late presenters (CD4 count below 350 cells/ml at enrolment to cohort/HIV care).[15] Cancer related deaths comprise close to one tenth (7ž1%) among PLWH infected in Estonia.[16]

General population coverage with CCS in Estonia has been extensively studied.[17] We are not aware of CCS studies among WLWH from Estonia or from other Eastern European countries that have experienced HIV epidemics since the early 2000s.

Methods

Overview

In this population-based retrospective cohort study, data on CCS among HIV infected women and randomly selected age-matched women from the controls with no known history of HIV infection prior to the index date (defined below) were evaluated.

Sources of data

Data were obtained from the Estonian Health Insurance Fund (EHIF), which maintains a complete record of health care services provided in the country. The EHIF health claims database contains personal (e.g. gender, date of birth, and region), health care utilization (e.g. date of service, primary and other diagnoses, services/procedures/tests provided) information, and the date of death.

As of 31 December 2018, the EHIF had 1 251 617 individuals covered by insurance (95% of the Estonian population). HIV medical care is free to everyone in need and HIV health care utilization is captured in the EHIF database, irrespective of an individuals' health insurance status.

Identification of women living with HIV

Health care utilization data for WLWH between 1st January 2009 and 30th June 2018 were included. The case definition of living with HIV was based on the HIV care specific diagnosis codes (International Classification of Diseases, Tenth Revision (ICD-10): B23.0; B23.1, Z21; F02.4, B20-B24) on any of the EHIF claims over the period of observation. The index date of diagnosis was defined as the first day of care indicated in the first claim with the HIV identifying diagnosis code.

Identification of general population women

The sample frame included all insured individuals, including those with no record of receiving health care services. The WLWH were randomly matched by region and age (year of birth) in a 1:3 ratio to the general population women. By definition, general population subjects were alive and without evidence of HIV infection prior to the case patient's index date of HIV diagnosis.

For study purposes, study subjects were assigned a unique identifier decoupled from personal identification information to enable longitudinal tracking of care and mortality while maintaining patient privacy. Data on women younger than 16 years at the start of the study and women with a history of CC were excluded.

Identification of cervical cancer screening

We identified episodes of CCS on the basis of Pap test code and a CC screening indicative ICD-10 diagnosis code recorded on the health care service claim. In the context of opportunistic screening, Pap test code (codes 66807, 66809, 66811) are recorded on healthcare claim.[18] In the context of organised screening, ICD-10 diagnosis code Z12.4 (encounter for screening for malignant neoplasm of cervix) is used. As both (Pap testing, healthcare claim with the Z12.4 diagnosis code) were recurring outcomes, women could experience multiple screening episodes during the observation period.

Follow up and identification of outcome

We followed all study subjects (belonging to the WLWH and general population group) until the study end (30th June 2018), diagnosis date of CC or date of death.

To assess the population coverage with CC we used definitions presented below. Annual and longitudinal coverage estimates are presented by the type of screening (opportunistic, organised, HIV specific) and population group (WLWH and general population group).

Annual coverage

(1) An opportunistic CC screening episode was defined as a Pap test on a healthcare claim without ICD-10 code Z12.4 independent of age (16+), and the tested woman was considered to be 'covered by the opportunistic screening' for the next five years starting from the date, when the test was done.

(2) WLWH were considered to be covered by HIV specific CC screening, for the next two years starting from the date, when the test was done independently of age (16+). There is no special CC screening program for WLWH in Estonia, but the Estonian Society of Infectious Diseases recommends WLWH should be screened every second year.[19]

(3) Study subjects (WLWH, general population group), aged 30–55 years were considered covered by the organised CC screening, for five years after a health care claim of ICD-10 Z12.4 was filed (Fig. 1).

Longitudinal coverage

We also analysed factors associated with organised CCS coverage over nine years of the study follow up period (longitudinal coverage) among WLWH and general population women and with the HIV specific CCS among WLWH (Table 2).

The primary outcome of interest for this study, namely longitudinal coverage with organised CCS, was defined using a binary variable indicating whether a person has been screened longitudinally (yes or no).

WLWH and general population women aged 30–55 years were considered longitudinally covered by the organised CCS if a Pap test (Z12.4) was done once every five years (with a minimum of two times over the observation period).

WLWH (aged 16 + years) were considered longitudinally covered by HIV specific screening if a Pap test was done once every two years (at minimum two times over five-year period of observation) (Table 2).

Other variables (screening predictors)

For all women: age (at the time of cohort inclusion), place of residence - regions of Estonia (capital, north-east and other) were ascertained. For WLWH: HIV stage at index visit based on the ICD-10 code (acute – B23.0; clinical latency - B23.1, Z21; AIDS F02.4, B20-B24; and unknown), AIDS diagnosis at any time of follow up (defined in occurrence of and healthcare claim with the ICD-10 codes F02.4, or B20-B24), retention in HIV care (defined by at least two HIV related physician visits within a 12-months period continuously across the whole period of observation, [20] comorbidities as drug use (based on ICD-10 diagnoses: F10-F19, T40, Y12) and HCV infection (ICD 10 diagnoses. B17.1, or B18.2).

Statistical analysis

Descriptive statistics (i.e. proportions, means, standard deviations and medians) for length of follow-up time, number of Pap tests and population based annual and longitudinal screening coverages (opportunistic, organised, HIV-specific) are presented. In addition, we characterise the WLWH cohort using HIV stage at index date, AIDS diagnosis at any time of follow up, drug abuse and infection rates for HCV co-morbidities. The ORs and AORs with 95% confidence intervals (CI) for predictors of longitudinal coverage were estimated in univariate and multivariate logistic regression analyses (adjusted for region and age at entry to the study and insurance status). All analyses were performed in R (version 3.5.1, 2018).

Results

Study population

We identified 2614 women from the EHIF database who had received HIV related health care services between 2009 and 2018. From these WLWH, we excluded 112 who were under 16 years old, 9 due to previous CC diagnosis and 47 non-citizens.

In all, 2448 WLWH and 7558 general population women were followed for 17 210 and 70 990 person-years, respectively (Table 1).

Table 1. Characteristics of women living with HIV (WLWH) and general population women in Estonia, 2009-2018

Characteristics	WLWH	General population group
N	2448	7558
Age, mean (SD)	31.2 (11.3)	29.9 (10.9)
Age groups n,(%)		
16-19	114 (4.7)	612 (8.1)
20-29	1335 (54.5)	4196 (55.5)
30-39	563 (23.0)	1587 (21.0)
40-49	222 (9.1)	647 (8.6)
50-55	98 (4.0)	252 (3.3)
56+	116 (4.7)	264 (3.5)
Follow-up, years mean (SD)	7.03 (3.0)	9.39 (0.8)
Follow-up time total, person years	17 210.5	70 990.3
Region (n,%)		
Capital	1009 (41.2)	3104 (41.1)
North-East	1214 (49.6)	3822 (50.5)
Other	225 (9.2)	632 (8.4)
Time to the 1st Pap test after the index date (months) (range, mean, SD; median)	0.1315-120.7; 34.2; 24.8; 25.8	0.0657-119.9; 28.2; 24.5; 21.0
Uninsured (ever during the follow up) (%)	744 (30.4)	13 (0.2)
Drug abuse (%)	360 (14.7)	9 (0.1)
HCV (%)	916 (37.4)	20 (0.3)

The mean age of WLWH at the beginning of follow up was 30.6 (SD 11.8) years and most (over 90%) were from the capital and North-eastern regions of Estonia. The majority of WLWH (79.8%) were in the 'clinical latency' stage at the start of follow up, and 31% were considered retained in care over the entire follow up. One fifth (19.7%) of the WLWH developed AIDS during the study period, 14.7% (n=360) had diagnoses codes indicating drug abuse and 37.4% (n=916) had concomitant HCV infection.

During the whole follow-up period, 53 women from the general population group were diagnosed with HIV (incidence 0.75 cases per 1000 population).

Cervical cancer screening

A total of 7304 Pap tests (opportunistic and organised) were linked to 2448 WLWH and 25 078 to 7558 general population women. Overall, 587 (24%) of WLWH and 1269 (16.8%) of general population women had no record of any Pap testing during 2009–2018. 30.4% of WLWH and 0.2% of women in the general population were not insured. 314 (12.8%) WLWH and 914 (12.1%) of general population women (difference in proportions: $p=0.336$) had only one Pap test done during the whole follow up period. The maximum number of Pap tests per woman during the study period was 20. Mean time between two consecutive Pap tests was 21.0 (median 17.1, SD 13.7, range 0.1-116) and 22.9 (median 19.5, SD 14.6, range 0.1-100.3) months in WLWH and general population women respectively $p=0.00002$.

Opportunistic screening

The mean annual opportunistic screening coverage was 61.45% among WLWH and 65.59% among comparator group ($p<0.00001$) (Figure 1).

The mean annual opportunistic screening coverage among WLWH meeting HIV specific screening target (repeated testing every second year) was 49.4% (Figure 1). One quarter (n=595, 24.3%) of WLWH were covered longitudinally by HIV-specific CCS.

Organised screening

The mean annual coverage with organised screening was 20.4% and 28.7% among WLWH and general population respectively ($p < 0.00001$) (Figure 1).

The proportion of women in the general population group and WLWH longitudinally covered by organised screening was 19.01% (95% CI 18.05-19.97) and 13.9% (95% CI 12.35-15.45) respectively.

Factors associated with CCS longitudinal coverage

Longitudinal coverage with HIV-specific CCS was inversely associated with age. The oldest WLWH (aged over 56 years) had the lowest odds for coverage AOR 0.136 (95% CI 0.060, 0.281), as had the HCV co-infected AOR 0.754 (95% CI 0.619, 0.916), uninsured AOR 0.331 (95% CI 0.264, 0.412) and those abusing drugs AOR 0.459 (95% CI 0.336, 0.618). WLWH retained in HIV care AOR 1.972 (95% CI 1.615, 2.410) had higher odds of being covered (Table 2).

Table 2. Predictors of cervical cancer screening program period coverage in Estonia, 2009-2018.

	WLWH: HIV specific screening (595/2448) 24.31%			WLWH: organized screening (266/1914) 13.90%			General population women: organized screening (1210/6365) 19.01%		
	N (% covered)	OR (95% CI)	AOR (95% CI)	N (% covered)	OR (95% CI)	AOR (95% CI)	N (% covered)	OR (95% CI)	AOR (95% CI)
Region									
Capital	1009 (31.32)	1	1	788 (13.71)	1	1	2618 (20.02)	1	1
North-East		0.704 (0.581,0.851)	0.705 (0.581,0.855)	970 (14.85)	0.999 (0.759,1.317)	1.007 (0.764,1.330)	3273 (18.70)	0.920 (0.808,1.048)	0.918 (0.806,1.046)
Else	1214 (27.76)	0.662 (0.473,0.915)	0.767 (0.544,1.071)	156 (8.97)	0.560 (0.298,0.978)	0.610 (0.324,1.070)	474 (15.61)	0.739 (0.563,0.959)	0.732 (0.557,0.951)
Age groups									
16-19	114 (34.21)	1	1						
20-29	1335 (32.96)	0.937 (0.622,1.424)	0.930 (0.618,1.419)	1031 (16.39)	1	1	3879 (18.72)	1	1
30-39		0.691 (0.448,1.078)	0.686 (0.444,1.071)	563 (11.19)	0.617 (0.449,0.838)	0.621 (0.452,0.843)	1587 (17.77)	0.939 (0.805,1.091)	0.948 (0.813,1.103)
40-49	563 (28.42)	0.523 (0.315,0.868)	0.521 (0.314,0.866)	222 (10.36)	0.554 (0.340,0.865)	0.565 (0.347,0.883)	647 (23.65)	1.344 (1.099,1.635)	1.364 (1.115,1.660)
50-55	222 (23.87)	0.204 (0.095,0.411)	0.206 (0.096,0.416)	98 (11.22)	0.563 (0.278,1.038)	0.586 (0.289,1.083)	252 (19.44)	1.047 (0.751,1.433)	1.083 (0.776,1.484)
56+	98 (12.25)	0.136 (0.060,0.281)	0.135 (0.060,0.281)						
116 (8.62)									
Insured (uninsured if it occurs ever during the follow up) (baseline is insured)									
	1704 (34.04)	1	1	1339 (15.53)	1	1	6355 (19.02)	1	1
	744 (18.01)	0.426 (0.343,0.525)	0.331 (0.264,0.412)	575 (10.09)	0.610 (0.444,0.826)	0.545 (0.394,0.745)	10 (10.00)	0.4729 (0.026,2.520)	0.477 (0.026,2.545)
stage at index visit (n %)									
clinical latency	1955 (29.67)	1	1	1548 (13.44)	1	1			
acute	87 (39.08)	1.340 (0.851,2.085)	1.444 (0.908,2.271)	69 (23.19)	1.794 (0.974,3.136)	1.993 (1.073,3.523)			
AIDS	382 (24.35)	0.689 (0.531,0.887)	0.874 (0.666,1.138)	278 (14.03)	1.005 (0.686,1.441)	1.198 (0.811,1.734)			
unknown	24 (29.17)	0.885 (0.338,2.085)	1.069 (0.399,2.602)	19 (15.79)	1.178 (0.272,3.586)	1.331 (0.304,4.131)			
AIDS dgn at any time of follow up (baseline is AIDS not diagnosed)									
	1383 (31.67)	1	1	1066 (14.92)	1	1			
	483 (27.54)	0.874 (0.690,1.102)	0.879 (0.691,1.114)	400 (10.75)	0.708 (0.489,1.006)	0.678 (0.466,0.966)			
HIV care retention (yes: n %) (baseline is not retained)									
	1691 (25.43)	1	1	1324 (14.50)	1	1			
	757 (37.52)	1.751 (1.453,2.108)	1.972 (1.615,2.410)	590 (12.54)	0.824 (0.614,1.095)	0.939 (0.688,1.273)			
Drug abuse (yes: n, %)									
		1	1		1	1		1	1

(baseline is no drug abuse)	2088 (31.37)	0.517 (0.380,0.693)	0.459 (0.336,0.618)	1624 (14.84)	0.600 (0.379,0.914)	0.543 (0.342,0.830)	6360 (19.03)	0 (-)	0 (-)
	360 (16.39)			290 (8.62)			5 (0.00)		
HCV infection (yes: n %)	1532 (31.27)	1	1	1164 (14.26)	1	1	6355 (18.98)	1	1
baseline is no HCV	916 (25.66)	0.868 (0.718,1.048)	0.754 (0.619,0.916)	750 (13.33)	0.998 (0.759,1.307)	0.844 (0.637,1.115)	10 (40.00)	3.450 (0.845,13.217)	3.500 (0.856,13.418)
Drug abuse or HCV co infection	1448 (32.46)	1	1	1092 (15.11)	1	1	6353 (18.98)	1	1
	1000 (24.40)	0.780 (0.646,0.940)	0.683 (0.562,0.828)	822 (12.28)	0.856 (0.651,1.122)	0.732 (0.552,0.965)	12 (33.33)	2.703 (0.682,9.567)	2.751 (0.693,9.751)

In WLWH, organised CCS program uptake was inversely associated with age 30-39 years old AOR 0.621 (95% CI 0.452, 0.843), 40-49 years old AOR 0.565 (95% CI 0.347, 0.883), drug abuse AOR 0.543 (95% CI 0.342, 0.830) and not having insurance AOR 0.545 (95% CI 0.394, 0.745). Those in the 'acute HIV' stage were more likely to be screened AOR 1.993 (95% CI 1.073, 3.523).

In general population women, longitudinal coverage with organised screening was inversely associated with living in a region other than the capital and north-east AOR 0.732 (95% CI 0.557, 0.951). 40-49 years old were more likely to be covered AOR 1.364 (95% CI 1.115, 1.660).

Discussion

This study provides CCS coverage data and correlates of CCS among HIV-infected women and the general population in Estonia.

To our knowledge, this is the first population based study assessing CCS among WLWH in an Eastern European country with a characteristic HIV epidemic. Our results highlight an unacceptably low coverage of WLWH with CCS.

The annual screening coverage found in the present study is lower than that found in previous studies of HIV CCS program coverage (France 76.5%[21] and Italy 61%[22]). These findings suggest that a substantial proportion of HIV infected women in Estonia are under-screened, which is in line with the findings from Danish study [23]. However, the difference might also reflect the methodologies used to measure coverage. Studies based on self-reported data are more likely to overestimate screening.

There is an increasing need of evidence whether targeted preventive and treatment guidelines are necessary for the management of HIV-infected patients. We choose to include data on general population women in to this analysis, to determine barriers that WLWH face in excess of what would be expected. This data is essential to minimize vulnerability to HIV, eliminate inequities in the HIV cervical cancer care cascade, reduce vulnerabilities to poor outcomes, and improve health and well-being. We found that almost a quarter (24.0%) of WLWH in contact with healthcare services had no Pap testing undertaken in comparison to less than one fifth in the general population women. For the whole study period, quarter of WLWH (24.3%) were covered with the opportunistic Pap testing that met meeting HIV specific CCS target. Longitudinal coverage of WLWH with the organised screening was two times lower (13.9%). While exceedingly few women in general population were uninsured, one third (30.4%) of the WLWH lacked health insurance over the study period. It is of importance to note, that while HIV care in Estonia is free for those in need, this does not extend to all health care and prevention services. For example, the only women covered with health insurance are invited to the organised CCS. CCS coverage among WLWH in Estonia is unacceptably low and significantly lower than that in general population in our study.

Unlike in general population women, coverage with organized screening tended to decrease with age among WLWH, and was highly affected by insurance status and concomitant drug use (or HCV infection). One exception: WLWH co-infected with HCV had significantly lower odds of being covered than those without HCV.

In the present study, younger age was a predictor for screening attendance in WLWH, which is in line with a study from Canada by Burchell et al.[24] This may reflect differences in health behaviour and awareness of the importance of screening programs. WLWH retained in HIV care were more likely to be screened, a finding also documented in the UK [25]. This may be explained by health beliefs and behaviour of women, and by the opportunity to engage women in HIV care into preventive services. Our findings highlight barriers to cervical cancer screening in WLWH. Consistent with previous studies we found that drug abuse [26] and lack of access (is not having insurance) [27] are the main barriers. In line with Elfström et al [29] we found that organised screening uptake by the general population women in Estonia was low (< 20%) in parallel with the relatively high (65%) uptake of opportunistic screening. Our findings support the worrisome fact that women are more likely to be Pap tested opportunistically, which has been shown to provide no additional benefit on preventing cancer. [29]

Given our findings, there is a clear need to improve CCS attendance among women in Estonia. We did not assess the performance of Pap test in our study, but there are indirect indications of significant under-detection/diagnosis of CIN2+ in Estonia. [30] However, we support the idea of seeking and testing new innovative interventions to improve program uptake through interventions like self-sampling and electronic [30] reminders as well as changing CC test for screening to HPV DNA.

The strength of our analysis lies in the use of population-based data free of individual recall / social desirability bias. We had a sufficient sample size to derive credible and precise estimates over the long follow-up period. With these data we were able to assess continuous coverage with screening, that allowed us to evaluate the screening behavior longitudinally in WLWH and in the general population for 10 years. It is important to have longitudinal life-course perspective in CCS.

Our study had some limitations. Using administrative health insurance data has drawbacks. While HIV care is free for all in need, CCS is only provided for those who are insured. This could potentially lead to overestimation of all coverage rates in the study. But it is likely, that this does not significantly affect the interpretation of our results, given that being uninsured had the strongest effect on CCS non-adherence – both among WLWH and in general population. Ignoring the impact of pregnancy, dysplasia and CIN treatment in coverage estimation our results are prone for overestimation of coverage. Furthermore, there might be some misclassification of the use of ICD diagnosis code for organized CCS. However, we are not aware of any data helping to quantify this effect. We were not able to control for potential (known) confounders (income, education, occupation, ART treatment) for both the coverage estimates and measures of coverage association, as this data is not available in the EHIF database. Our study started from 2009, and some subjects who underwent a Pap test prior to study might have been misclassified resulting in a slight underestimation of coverage in the first study years. However, such potential limitations seem unlikely to account for the clear patterns observed in this study, and we believe that our study provides informative results allowing inferences for other populations of European WLWH.

Conclusion

In conclusion, our findings provide new evidence to address barriers to CCS in WLWH. The CCS coverage among WLWH in Estonia is unacceptably low. Being uninsured has the strongest effect, both among WLWH and in the general population. This barrier needs urgent attention. Given the efficacy of antiretroviral treatment, the increased risk of CC among WLWH, and the low coverage screening in several countries with high HIV prevalence, integrating CCS with HIV healthcare services is needed. WLWH with concomitant comorbidities need further attention to assure state of the art health care and cancer prevention.

Declarations

Ethics approval

Ethical approval was obtained from the *Ethics Review Board* of the University of Tartu. Study was approved 15th November 2018 (nr 2018 286/T-6).

Competing interests

The authors declare that they have no competing interests.

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Authors contributions

AT and AU conceptualized and designed the study. AT collected the data, interpreted the analyses, drafted the initial manuscripts and critically revised it.

SEO carried out the statistical analyses, reviewed and critically revised the manuscript.

PV and PS contributed to the interpretation of the results, reviewed and critically revised the manuscript.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects for the work.

Conflicts of interest

There are no conflicts of interests

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Figures

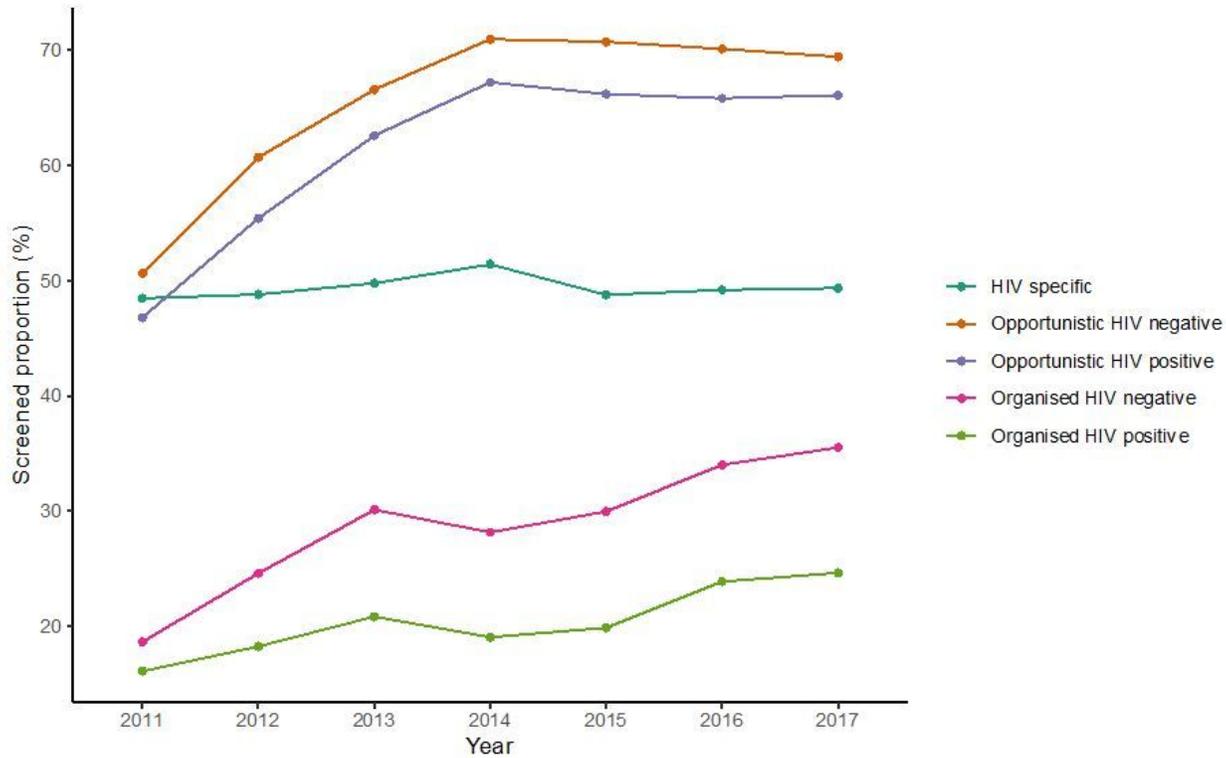


Figure 1

The proportion of women covered annually with the cervical cancer screening program in Estonia, 2011-2017. WLWH and general population group were divided into five categories: 1) WLWH, studied according to the HIV screening program (HIV specific); 2) General population women, studied outside the organised (opportunistic) screening program (Opportunistic HIV negative); 3) WLWH, studied outside the organised screening program (Opportunistic HIV positive); 4) General population women, studied according to general population organised screening program (Organised HIV negative); 5) WLWH, studied according to general population organised screening program (Organised HIV positive)