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Understanding the high-risk human papillomavirus prevalence and associated factors in the European country with a high incidence of cervical cancer

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Background: High-risk human papillomavirus (HR-HPV) is a known cause of cervical cancer (CC). Latvia has a high incidence of CC compared with the average incidence in the European Union. This study aims to fill the data gap on the HR-HPV burden in Latvia, providing information on its prevalence and associated factors. **Methods:** The cross-sectional study was conducted from February 2021 to April 2022. Participants 25–70 years old visiting a general practitioner (general population) or those referred to a colposcopy clinic with changes in their cervical cytology (colposcopy population) collected vaginal self-sample and completed a paper-based questionnaire. Samples were analyzed with Cobas 6800 System (Roche) for HPV16, HPV18 and other HR-HPV (HPV31/33/35/39/45/51/52/56/58/59/66/68). Descriptive statistics for categorical variables were performed. The Chi-square test was used to determine for the statistical significance of differences in the proportions of the dependent variable between subgroups of the independent variable. Univariate and multivariate binary logistic regression were used to identify factors associated with positive HR-HPV status. Results were considered statistically significant at $P < 0.05$. **Results:** A total of 1274 participants provided a valid sample. The prevalence of any HR-HPV infection was 66.8% in the colposcopy group and 11.0% in the general population. Factors associated with positive HR-HPV status were marital status single/divorced/widowed (vs. married/cohabiting) [adjusted OR (aOR) 2.6; $P = 0.003$], higher number of lifetime sex partners [aOR 5.1 ($P < 0.001$) and 4.0 ($P = 0.001$)] for six or more and three to five partners in the general population; in the colposcopy group, the statistical significance remained only for Latvian ethnicity (vs. other) (aOR 1.8; $P = 0.008$) and current smoking (vs. never) (aOR 1.9; $P = 0.01$). **Conclusion:** We documented a comparison to European Union HR-HPV infection burden in Latvia. Any HR-HPV positivity was significantly associated with sexual and other health behavior.

Introduction

Human papillomavirus (HPV) is the most common sexually transmitted infection globally. HPV viruses are divided into high-risk HPV (HR-HPV), an important cause of oropharyngeal and anogenital cancers, and low-risk HPV (LR-HPV), responsible for cutaneous and anogenital warts. Cancer of the cervix uteri is the most well-known malignant HR-HPV-related disease worldwide.[1–3] HPV-associated burden and overall epidemiological distribution differ considerably worldwide. The worldwide prevalence of high-risk HPV infection is 11.7%, which can be as high as 35.4% in some developing countries.[3,4]

The factors associated with HR-HPV prevalence include geographical, socioeconomic, cultural, HPV genotype and age/health state.[3–5]

The World Health Organization has developed a global strategy for eliminating cervical cancer (CC) as a public health problem. HR-HPV-focused CC prevention programs have been established in many countries. HR-HPV primary screening strategies have replaced screening methods based on cervical cytology. Vaccination, screening programs and post-screening treatment have decreased CC morbidity and mortality in many European countries.[6–9]

In 2020, Latvia had a high age-standardized incidence of CC (18.4 per 100 000 women) compared with the average incidence in the European Union (12.8 per 100 000), with an accompanying trend in mortality at 6.8 per 100 000 compared with the average incidence in the European Union (5.3 per 100 000).[4] In 2010, a bivalent vaccine against HPV was introduced in the Latvian vaccination calendar for girls aged 12–14. Later, in 2020, it was replaced with a nonavalent vaccine, and the vaccination age for girls was extended to 12–18 years. In 2022, the vaccination of boys aged 12–18 commenced in Latvia. By implementing successful and informative campaigns nationwide, targeting healthcare professionals and patients, the vaccination coverage among girls reached 72.3% and that of boys reached 51.8% in 2022. In 2009, an organized CC screening program was introduced in Latvia among women aged 25–70 years, and it was based on cervical cytology. Until 2022, Leishman cytology staining was used, the accuracy of which was not clear; it was later changed to liquid-based cytology. Since July 2022, HR-HPV primary screening has been implanted in the 30–70 age group. The participation rate in the screening program until 2016 was low, reaching only about 25%, but it has been increasing from 2017 onwards, reaching 46.7% in 2022. One of the main

disadvantages of the Latvian screening system is the low participation rate, minor involvement of general practitioners (GPs) in screening test sampling, and the lack of program surveillance and quality control.[10–13]

This study aims to fill the data gap on the HR-HPV burden in our country, providing crucial information on its prevalence and associated factors. The findings will aid in developing tailored primary and secondary CC prevention (creating innovative approaches to CC screening intensification and health literacy) in the HR-HPV prevalence groups.

Methods

Data source and study sample

A cross-sectional study was carried out from February 2021 to April 2022. Two target populations were defined for the study—25- to 70-year-old women from the general population and those referred for colposcopy because of changes in their PAP smear (colposcopy population). Thus, the sampling was carried out in the mentioned strata:

(1) as per the general population—all eligible women attending ten GP were invited to participate until the required sample per GP practice was reached. GPs were selected based on convenience so that at least two practices represented each of the five Latvian regions. GPs were invited to contribute to conducting the study during professional conferences about CC prevention in 2020;
(2) as per the colposcopy population—all women who visited the Riga East University Hospital colposcopy unit because of an abnormal cytological smear were consecutively invited to participate in the study.

The study's exclusion criteria were previous treatment for cervical precancerous lesions with excision or ablation methods, age under 25 or above 70, and refusal to participate.

The sample size was estimated based on the expected prevalence of specifically HR-HPV, at least 207 in the general population group (taking into account that the size of the target population—women aged 25–70 years in Latvia at the beginning of 2021 is 603 801[14] and that the expected HR-HPV prevalence in the general population as per the literature is 16.5%[4,15]) (the chosen limit for α error is 5%) and at least 296 in colposcopy population (taking into account that the size of the target population—average number per year of women aged 25–70 in Latvia who participated at the CC screening during 2016 and 2020 and had positive result is 3166[16] and that the expected HR-HPV prevalence in colposcopy population as per the literature is from 25.8 up to 51.9% in high-grade squamous intraepithelial lesion (HSIL) and up to 69.4% in CC[4,17] and the chosen limit for α error is 5%).

Participants visiting a healthcare facility (such as a GP practice or colposcopy clinic) completed a paper-based questionnaire, gathering demographic, socioeconomic, health status and health behavior data. Additionally, a self-collection kit with graphic and written instructions was provided for participants to collect a vaginal smear for HR-HPV testing.

The Riga Stradiņš University Ethics Committee approved the study (number of approval 6-1/07/33). Financial support was provided by the 'EEA Financial Mechanism Baltic Research Program 2014-2022'.

Specimen collection and laboratory methods

Cervicovaginal samples were collected with a self-sample device and a dry cotton swab (FLOQSwabs™, COPAN, Brescia, Italy). They were shipped by parcel machine service to the National Microbiology Reference Laboratory, Riga East University Hospital, within 7 days after sampling. All samples were recorded in the laboratory hospital system 'ĀrstuBirojs' and then sent to the molecular diagnostic department. Upon arrival at the laboratory department, cervicovaginal sample swabs were placed into the ThinPrep liquid medium (Hologic, Marlborough, MA, USA) and stored for 1–2 weeks at 2–8°C.

The cervicovaginal samples were analyzed with *the Cobas 6800 System* (Roche Molecular Diagnostics, Pleasanton, CA, USA) *using* the standard protocol.

Statistical analysis

Prevalence of any (of the 14) HR-HPV types and of the following subgroups: HPV 16, HPV 1 and HPV other was assessed. Prevalence proportions, together with corresponding 95% confidence intervals (CI), have been calculated using the one-sample test for binomial proportion, normal-theory (Wilson) method.[18]

Descriptive statistics, such as proportions for categorical variables, were performed. The Chi-square test was used to determine the statistical significance of differences in the proportions of the dependent variable between subgroups of the independent variable. Univariate and multivariate binary logistic regression were used to identify factors associated with positive HR-HPV status. A multivariate model was constructed, adjusting for all independent variables statistically significantly associated with the outcome in univariate analysis. Results were considered statistically significant at $P < 0.05$.

Data were processed using IBM SPSS Statistics (Statistical Package for the Social Sciences) version 26.0.

Results

A total of 1413 women were invited to participate in the study (800 from GP practices and 613 from the colposcopy unit). The refusal rate (proportion of women invited to participate in the study but declined) was 11.1% in the general population group and 4.0% in the colposcopy group. The main reasons for refusal were the same in both groups: reluctance to take a sample by themselves (47.1%), lack of time (20.6%) and the opinion that such a test was not needed because the gynecologist had already performed a regular examination (14.7%).

There were 545 participants recruited in the colposcopy group and 768 in the general population group, and a valid sample was obtained for HR-HPV testing.

The demographic and socioeconomic characteristics of women are presented in table 1. The colposcopy group had a younger population pattern ($P < 0.001$), lower education ($P < 0.001$), higher diversity in ethnicity ($P = 0.04$) and a higher proportion of economically inactive and unemployed women ($P = 0.01$). No significant differences were observed by marital status, income and self-assessed financial status.

Three percent of all samples were invalid. The prevalence of any HR-HPV infection was 66.8% (60.1–74.0) in the colposcopy group and 11.0% (8.8–13.6) in the general population group. In the colposcopy group ($n = 530$), HPV type 16 was present in 34.2% (30.2–38.3), HPV type 18 in 4.0% (2.6–6) and other pooled high-risk types were present in 42.0% (37.8–46.2) of women. In the general population group ($n = 744$), HPV 16 was present in 3.5% (2.4–5.1), type 18 in 1.2% (0.6–2.3), and other high-risk types in 7.5% (5.9–9.67) of cases. Data are displayed in figure 1.

A single HR-HPV infection was more common, and multiple-type HR-HPV infection was low in both participant groups.

Age-stratified prevalence of any HR-HPV for the colposcopy group was the highest for respondents up to 29 years of age at 78.2%, after which the HR-HPV prevalence decreased slowly, reaching the second peak at 75.0% in the age group 60+. For the general population, the highest age-stratified prevalence of any HR-HPV was in respondents aged 30–39 at 17.2% and below 29 at 15.2%. The results are displayed in figure 2.

In univariate logistic regression in the general population group (table 2), any HR-HPV positivity was associated with sociodemographic factors like age 30–39 [odds ratio (OR) 2.6; $P = 0.04$], single/divorced/widowed marital status (vs. married/cohabiting) (OR 2.6; $P < 0.001$), participants overall health status—the presence of chronic diseases (vs. absence) (OR 0.6; $P = 0.03$), body mass index (BMI) <18.5 (vs. BMI 25+) (OR 3.3; $P = 0.049$), casual smoking (vs. never) (OR 2.2; $P = 0.047$) and sexual and reproductive health behavior like six or more and three to five lifetime sex partners [vs. 1–2 partners (none of the study participants had no sexual experience)] [(OR 5.7 ($P < 0.001$) and 3.9 ($P < 0.001$), respectively], and also with the last visit to a gynecologist 3–5 years ago (vs. ≤3 years ago) (OR 2.1; $P = 0.003$). The number of pregnancies also played a role in higher HR-HPV prevalence—no pregnancies vs. four and more (OR 3.4; $P = 0.02$) and also HPV vaccination status (OR 0.3; $P = 0.01$). After adjustment for all factors found to be significant in univariate analysis, the statistical significance remained for single/divorced/widowed marital status (vs. married/cohabiting) [adjusted OR (aOR) 2.6; $P = 0.003$] and the higher number of lifetime sex partners [aOR 5.1 ($P < 0.001$) and 4.0 ($P = 0.001$)] for women with six or more and three to five partners, respectively.

In the colposcopy group in univariate binary logistic regression, any HR-HPV positivity was associated with sociodemographic factors like Latvian ethnicity (vs. other) (OR 1.7; $P = 0.008$), participants' health behavior like current smoking (vs. never) (OR 2.0; $P = 0.007$), and higher number of lifetime sex partners [OR 1.8 ($P = 0.03$) and 1.8 ($P = 0.03$) for women with six or more and three to five partners, respectively, vs. 1–2 partners]. After adjustment for all factors found to be significant in univariate analysis, the statistical significance remained for Latvian ethnicity (vs. other) (aOR 1.8; $P = 0.008$) and current smoking (vs. never) (aOR 1.9; $P = 0.01$).

Table 1 Demographic and socioeconomic characteristics of women recruited from GP practices and women recruited from colposcopy clinic in Latvia in 2020

Variable	Colposcopy group		General population group		*P*
	n	%	*n*	%	
Age (years)					
25–29	124	23.5	99	13.4	<0.001
30–39	245	46.5	233	31.4	
40–49	100	19.0	187	25.2	
50–59	42	8.0	141	19.0	
60+	16	3.0	81	10.9	
Ethnicity					
Latvian	381	72.0	572	77.0	0.04
other	148	28.0	171	23.0	
Marital status					
Single, divorced, widow	168	31.6	215	28.9	0.30
Married, cohabiting	363	68.4	528	71.1	
Education					
Primary	39	7.4	20	2.7	<0.001
Secondary	243	45.8	293	39.4	
University	248	46.8	430	57.9	
Employment					
Economically inactive	76	15.0	81	11.3	0.01
Unemployed	46	9.1	43	6.0	
Employed	386	76.0	549	82.7	
Income					
Missing	69	13.0	93	12.5	0.31
≤500 EUR	127	23.9	178	23.9	
501–700	96	18.1	159	21.4	
701–1000	161	30.3	191	25.7	
1001+	78	14.7	123	16.5	
Self-assessed financial status					
Bad/very bad	99	18.8	113	15.5	0.13
Very good/good	427	81.2	614	84.5	

Discussion

The current study provides essential insights into HR-HPV prevalence in Latvia among the population and contributing risk factors for each group (colposcopy—a high-risk group—and general population—a low-risk group). Overall HR-HPV prevalence in the general population group was 11% (95% CI 8.8–13.6). There are geographical varieties in the low-risk (general) population prevalence of HR-HPV worldwide. European data show that HR-HPV prevalence fluctuates among countries; in Eastern Europe, it is as high as 21.4%, and in Western Europe, it is on average at 9.0%, ranging from 2% in Spain to approximately 12% in France and Belgium. Current study data are comparable to Western Europe HR-HPV prevalence data but are lower than in neighboring countries like Poland (14.4%; 95% CI 12.1–17.0), Czech Republic (25.6%; 95% CI 23.3–28.0) or Lithuania (24.2%; 95% CI 19.5–29.6).[4] These

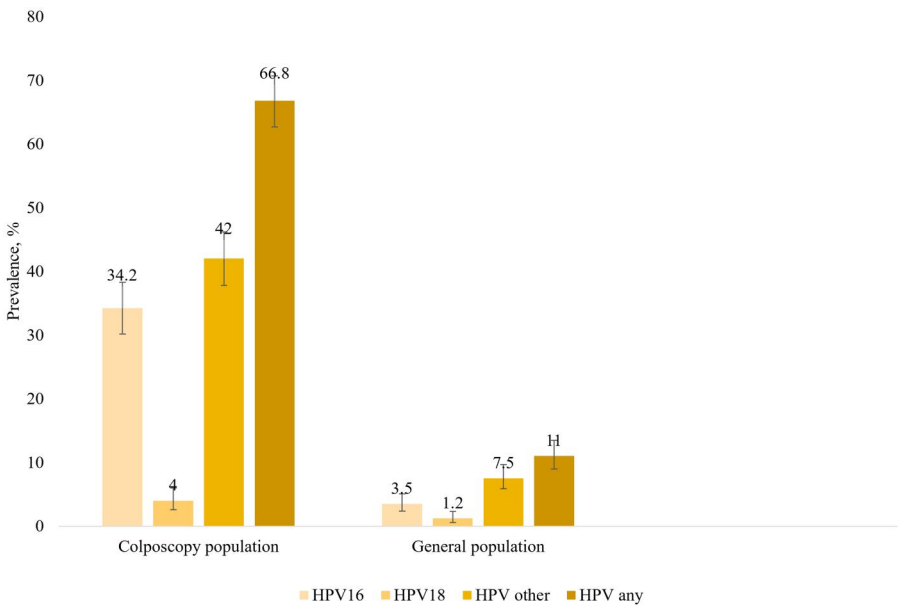

Figure 1 The prevalence of HR-HPV in two study groups: women recruited from GP practices and women recruited from a colposcopy clinic in Latvia in 2020

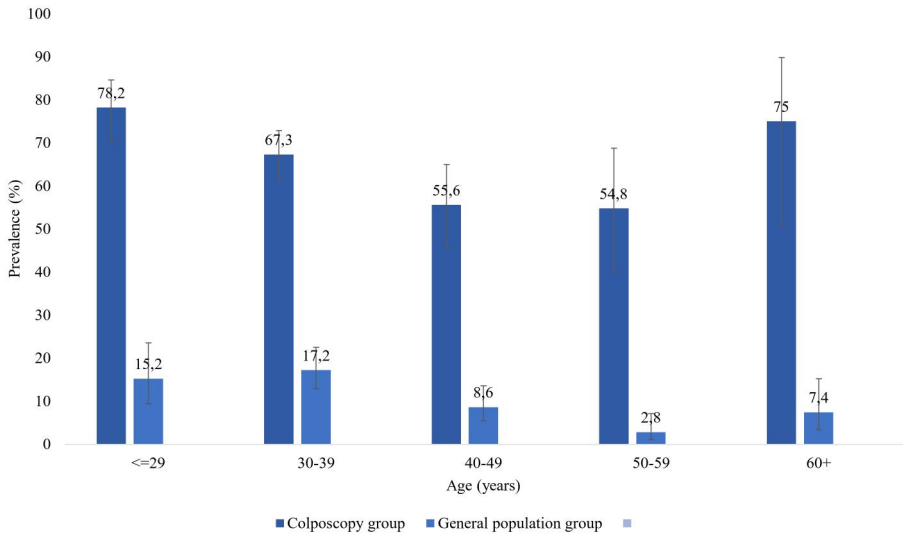

Figure 2 Prevalence of HR-HPV among the study groups

Table 2 Any HR-HPV associated factors in the study groups in univariate analysis (results of multivariate analysis are described in the text)

Variable	General population group					Colposcopy group				
	Any HPV		OR	95% CI	*P*	Any HPV		OR	95% CI	*P*
	n	%				*n*	%			
Sociodemographics										
Age (years)										
25–29	15	15.2	2.2	0.8–6.0	0.11	97	78.2	1.2	0.4–4.0	0.77
30–39	40	17.2	2.6	1.1–6.4	0.04	165	67.3	0.7	0.2–2.2	0.53
40–49	16	8.6	1.2	0.4–3.1	0.75	55	55.6	0.4	0.1–1.4	0.15
50–59	4	2.8	0.4	0.1–1.3	0.13	23	54.8	0.4	0.1–1.5	0.17
60+	6	7.4	1			12	75.0	1		
Ethnicity										
LV	62	10.8	0.9	0.6–1.7	0.92	267	70.3	1.7	1.1–2.5	0.008
Other	19	11.1	1			86	58.1	1		
Marital status										
Single, divorced, widow	42	19.5	3.0	1.9–4.9	<0.001	113	67.3	1.03	0.7–1.5	0.88
Married, cohabiting	39	7.4	1			241	66.6	1		
Education										
Primary	2	10.0	0.8	0.2–3.7	0.82	30	76.9	2.0	0.9–4.5	0.08
Secondary	29	9.9	0.8	0.5–1.4	0.47	170	70.0	1.4	0.9–2.1	0.06
University	50	11.6	1			153	61.9	1		
Employment										
Economically inactive	7	8.6	0.7	0.3–1.7	0.45	53	69.7	1.2	0.7–2.1	0.42
Unemployed	3	7.0	0.6	0.2–1.9	0.37	34	73.9	1.5	0.8–3.1	0.23
Employed	68	11.4	1			250	64.9	1		
Income										
Missing	10	10.8	0.7	0.3–1.6	0.40	48	69.6	1.4	0.7–2.7	0.39
≤500 EUR	15	8.4	0.5	0.3–1.1	0.09	86	67.7	1.2	0.7–2.2	0.47
501–700	13	8.2	0.5	0.2–1.1	0.09	65	67.7	1.2	0.7–2.3	0.50
701–1000	26	13.6	0.9	0.5–1.8	0.80	106	66.3	1.2	0.7–2.0	0.60
1001+	18	14.6	1			49	62.8	1		
Self-assessed financial status										
Bad/very bad	14	12.4	1.2	0.6–2.2	0.61	63	64.3	0.9	0.6–1.4	0.61
Very good/good	66	10.7	1			286	67.0	1		
Overall health										
Self-rated health										
Very good, good	58	13.1	1.1	0.3–3.7	0.93	229	68.4	1.9	0.6–5.6	0.3
Average	19	7.0	0.5	0.1–1.9	0.33	117	64.4	1.6	0.5–4.9	0.4
Bad, very bad	3	12.5	1			7	53.8	1		
Chronic diseases										
Yes	21	7.5	0.6	0.3–0.9	0.03	88	64.2	0.8	0.5–1.2	0.35
No	57	12.8	1			258	68.6	1		
BMI										
<18.5	4	23.5	3.3	1.01–10.7	0.049	18	66.7	1.0	0.4–2.3	0.99
18.5–<25	43	12.4	1.5	0.9–2.5	0.10	196	67.1	1.01	0.7–1.5	0.95
25+	31	8.6	1			137	66.8	1		

(continued)

Table 2 Continued

Variable	General population group					Colposcopy group				
	Any HPV		OR	95% CI	*P*	Any HPV		OR	95% CI	*P*
	n	%				*n*	%			
Smoking										
Current	14	13.9	1.8	0.9–3.4	0.09	98	74.8	2.0	1.2–3.2	0.007
Casual	9	17.0	2.2	1.01–5.0	0.047	28	60.9	1.02	0.5–2.0	0.94
Stopped	20	13.3	1.7	0.9–3.0	0.08	104	70.3	1.6	0.9–2.4	0.054
Never	36	8.4	1			123	60.3	1		
Binge drinking										
Once per week or more	7	16.3	1.4	0.6–3.4	0.42	27	75.0	1.8	0.8–4.0	0.17
Rarely	35	10.2	0.8	0.5–1.4	0.48	193	67.0	1.2	0.8–1.8	0.37
Never	38	11.9	1			103	62.8	1		
Sexual and reproductive health										
Current sexual activity										
Yes	67	11.5	1.2	0.7–2.3	0.49	306	68.6	1.6	0.9–2.5	0.08
No	13	9.4	1			48	58.5	1		
No of lifetime sex partners										
6+	34	18.5	5.7	2.7–11.9	<0.001	137	69.2	1.8	1.1–3.0	0.03
3–5	34	13.4	3.9	1.9–8.1	<0.001	149	69.0	1.8	1.04–2.9	0.03
1–2	10	3.8	1			47	56.0	1		
Last visit to gynecologist										
Never	2	20.0	2.1	0.4–10.3	0.34	22	73.3	1.4	0.6–3.2	0.41
5+ years ago	3	13.0	1.3	0.4–4.4	0.69	5	71.4	1.3	0.2–6.7	0.76
3–5 years ago	9	20.9	2.3	1.04–4.9	0.04	6	85.7	3.1	0.6–2.0	0.30
≤3 years ago	67	10.4	1			303	66.0	1		
Hormonal contraceptives lifetime use										
No	28	13.1	1.3	0.8–2.2	0.25	105	70.9	1.3	0.8–1.9	0.24
Yes	52	10.1	1			246	65.6	1		
No of pregnancies										
0	25	22.9	3.4	1.6–7.5	0.002	61	63.5	0.9	0.5–1.6	0.62
1	20	16.1	2.2	0.9–4.9	0.053	84	71.2	1.2	0.7–2.3	0.55
2	15	6.8	0.8	0.4–1.9	0.69	104	67.5	1.02	0.6–1.8	0.95
3	10	7.1	0.9	0.4–2.2	0.78	52	62.7	0.8	0.4–1.6	0.56
4+	10	8.0	1			51	67.1	1		
Self-assessed STI (sexually transmitted disease) risk										
Risk, high risk	9	12.0	1.1	0.5–2.3	0.82	72	72.0	1.3	0.8–2.2	0.24
No, minimal	72	11.1	1			273	65.8	1		
STI in anamnesis										
Yes	19	12.3	1.1	0.7–2.0	0.63	79	61.7	0.8	0.5–1.1	0.17
No	61	10.9	1			264	68.4	1		
Knowledge on screening										
No, don't know	15	12.6	1.2	0.7–2.2	0.51	77	70.0	1.2	0.8–1.9	0.39
Yes	65	10.6	1			273	65.6	1		
HPV vaccination status										
No	75	10.6	0.3	0.1–0.7	0.01	337	67.3	1.6	0.6–4.2	0.30
Yes	6	30.0	1			10	55.6	1		
Family anamnesis of any cancer										
Yes	28	11.4	1.1	0.7–1.7	0.80	111	61.7	0.7	0.5–1.04	0.08
No, don't know	53	10.8	1			239	69.3	1		

LV: Latvian ethnicity.

data may conform to previous studies that the main reason for high CC incidence in Latvia is the shortcomings of Latvia's national screening program, like low participation in CC screening and lack of proper surveillance, and not the high HR-HPV infection burden.[10–13]

Worldwide data show that HR-HPV prevalence in cervicovaginal specimens with abnormal cytology overall varies; for example, in ASCUS (atypical squamous cells of undetermined significance), the prevalence is 37–52%; in low-grade squamous intraepithelial lesion (LSIL), 76–79%; and in HSIL, 85%.[4,17] This finding correlates with the present study data, where HR-HPV prevalence accounted for 66.8% (95% CI 60.1–74.0) in the colposcopy group with abnormal cytology smears. This also shows a slightly lower HR-HPV burden and may contribute to cervical screening system flaws.[10–13]

It is well-known that HR-HPV genotyping helps to predict CC risk. Many authors have also contributed that a high load of HPV DNA increases the progression of cervical intraepithelial lesion and the chances of malignancy. Not all HR-HPV types have the same high-risk oncogenic potential. The highest risk for cancer progression is identified for HPV 16 or 18 infections and co-infection with various HR-HPV types.[3,19–22] The present study had a low prevalence of HR-HPV co-infection in both study populations. The worldwide data show the prevalence of HPV 16 or 18 and other HR-HPV at approximately 0.06%, HPV16 and HPV18 co-infection at 0.03% and HPV 16 and other HR-HPV co-infection at 0.8%.[23,24] One of the most important predictor factors of CC is HPV 16 prevalence.[20] The current study data show that HPV 16 prevalence is 3.5%, HPV18 prevalence is 1.2% and other high-risk HPV types prevalence is 7.5% in the general population. The most common HR-HPV type is HPV16, and its prevalence is around 2.5% in women with normal cytology.[3,4,15] By European data, overall HPV16 prevalence was 2.8%, from 5.6% (95% CI 4.3–7.3) in Belgium and 10.6% (95% CI 7.6–14.6) in France to 1.0% (95% CI 0.9–1.1) in the Netherlands and 1.3 (95% CI 1.0–1.7) in Norway, which corresponds with the current study finding. This is the same pattern we can find in the literature about HPV18 prevalence in

Europe (1%) and other high-risk types (7.8%) in patients with normal cytology that is similar to the current study finding. The current study data showed HPV16 prevalence in the colposcopy population as high as 34.2%, HPV18 at 4.0% and other pooled high-risk types at 42.0%. The European data are similar and show 20.7% HPV16 prevalence in LSIL and 47.4% prevalence in HSIL, but HPV18 prevalence in European data tends to be higher in LSIL at 6.4% and 7.1% in HSIL, which may be explained by geographical varieties of HPV-type prevalence and may be different study methodologies.[3,4,15]

The HR-HPV prevalence tendencies among age groups are important. Other studies demonstrate that most HR-HPV infections tend to happen upon sexual debut and at a younger age. Still, persistence above the age of 30 and older is a consecutive risk factor for CC.[8,14] The current study found that the colposcopy group prevalence of HR-HPV was the highest in the age group under 30 years (78.2%), then declined and peaked again in the age group 60+ (75.0%). The general population reached the highest age-stratified prevalence of any HR-HPV at the age group 30–39 (17.2%), and then rapidly declined in other age groups with a slight increase in the age group 60+ (7.4%). This finding could be explained by the selection bias. Other studies of European and Northern American populations demonstrate similar findings—HR-HPV prevalence rates are high below the age of 25–35 years, then tend to decline, and are lower in women over the age of 45 years. The second HR-HPV peak is also observed in the age group 60+. No such age-specific curves are observed in other populations like Asia and Nigeria, where HR-HPV prevalence is high across all age groups.[17,19,25–27] The exciting phenomenon described in many studies is the second HR-HPV peak in the patient group 60+. There are several hypotheses explaining it, like the reactivation of latent HR-HPV infection due to impaired immune system response, or the second theory is changes in sexual behavior in women and their partners (less condom use because there is no risk of unwanted pregnancy).[15,19,25–29]

The present study found a relationship between HR-HPV prevalence and several behavioral and socioeconomic risk factors. Similar correlations are described in the literature as well. In the general population group, any HR-HPV prevalence was related to such risk factors as single/divorced/widowed marital status (vs. married/cohabiting), a higher number of lifetime sex partners for women with six or more and 3–5 partners, respectively, vs. 1–2 partners. There is robust data showing that any HR-HPV positivity relates to sexual behavior like age <15 years at sexual debut, a higher number of sexual partners, and also patients' relationship status and higher number of sexual partners during the past 12 months because it is well-known that HPV is the most common sexually transmitted infection worldwide.[19,26,30]

In our study's colposcopy population, there was an association of any HR-HPV prevalence with Latvian ethnicity (vs. other) and current smoking status (vs. never). There are very well-known data about the harmful effects of tobacco smoking and HR-HPV infection persistence and the development of cervical precancerous lesions and cancer. This phenomenon is explained by the inhibition of the immune system by smoking and the cancerogenic effect on HPV-infected cells, where HPV oncoproteins block apoptosis and cell cycle arrest.[31] It is thought that the association between Latvian ethnicity and HR-HPV can be explained by some residual confounding factors and, possibly, by age. Although the independent variables were not adjusted by age in the colposcopy group (for which age did not show a statistically significant association with HR-HPV in the univariate analysis), there is a tendency for women aged 25–29 years to have a higher prevalence of HR-HPV. It was observed that the Latvian women in the colposcopy group tend to be younger—the proportion of women of the mentioned age in the Latvian group is 26.4%, and in the non-Latvian group, it is 16.4%.

This study was the first one on HR-HPV prevalence conducted in Latvia; no prevalence data are available to our knowledge. HPV self-sampling is not used in the organized screening program in our country, and that was the first time it was a tool of study in Latvia.

There are some limitations to our research. First, HPV prevalence was analyzed in self-taken samples. Still, there are sufficient data from other studies that self-sampling is comparable to vaginal samples collected by clinicians and is considered a gold standard.[32] The second limitation is the patient behavioral questionnaire with self-reporting. The main disadvantage of self-reporting is underreporting important information and risk factors; this issue has already been addressed in other medical studies, but it is one of the most convenient ways to collect patient behavioral data.[33] Another limitation that our study faced might be the sample size. Although our sample was not developed randomly, we can speculate that the sample size provides adequate statistical power to draw conclusions about HR-HPV prevalence and to extrapolate them to the target populations. The extrapolation is also supported by the fact that the general population sample was derived from 10 GP practices from all 5 regions of Latvia (2 per region). A nonrandom selection of GPs may lead to bias as well; we tried to minimize it by selecting two GPs from all five Latvian regions to catch the probable heterogeneity of the situation across the country. In comparison, the colposcopy population was derived from the leading state colposcopy center in Latvia (which provides the service to about half of the women in Latvia with abnormal CC screening results).

CC screening programs face many limitations, problems, and barriers worldwide. The screening program based on cervical cytology has limitations in sensitivity and is expensive to maintain.[34,35] Another problem is stagnation because there is a population of females that cannot be reached. According to the data provided, as many as one in four women do not participate in the screening program.[10–13,16,27,29,34–36] So, it is essential to consider personalized screening approaches. One of the main cornerstones of personalized screening is HPV-based screening with genotyping of HR-HPV because, as previously mentioned, the positive predictive value of CC progression may change certain patient triage and referral intervals and combined with individual behavioral risk factors create an individualized approach for a better fight against CC. Currently, there are efforts to de-intensify screening for some patient groups and to define high-risk HPV profiles that will progress to HSIL and/or CC.[21,34,35,37] This study helped to assess HR-HPV prevalence in Latvia. Based on this study, primary and secondary prevention should be targeted and specified. The study will provide a good background for developing and implementing a personalized CC screening program in Latvia, like intensifying risk groups based on smoking, marital status, and number of sexual partners, and also working on increasing health literacy activities.

Conclusions

We documented a comparable HR-HPV infection burden in Latvia to European data. Any HR-HPV positivity was significantly associated with sexual and other health behaviors. The prevalence of multiple HR-HPV infection was relatively low in the Latvian population.

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Conflict of interest: None declared.

Data availability

The data that support the findings of this study are not openly available due to reasons of sensitivity and are available from the

corresponding author upon reasonable request. Data are located in controlled access data storage at Riga Stradins University.

Key points

- Latvia has a high incidence of cervical cancer compared with the average incidence in the European Union.
- There is no data available on HR-HPV prevalence in Latvia.
- The study showed comparable to European data on HR-HPV infection burden in Latvia.

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