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Human papillomavirus infection in women with and without cervical cancer in Tbilisi, Georgia

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ABSTRACT

Background: No accurate estimates of cervical cancer incidence or mortality currently exist in Georgia. Nor are there any data on the population-based prevalence of high-risk (HR) human papillomavirus (HPV) infection, which, in the absence of good-quality screening, is known to correlate with cervical cancer incidence. *Methods*: We obtained cervical cell specimens from 1309 women aged 18–59 years from the general population of Tbilisi, and also from 91 locally diagnosed invasive cervical cancers (ICC). DNA of 44 HPV types was tested for using a GP5+/6+-based PCR assay. *Results*: In the general population (of whom 2% reported a previous Pap smear) HPV prevalence was 13.5% (95% CI: 11.6–15.9), being highest in women aged 25–34 years (18.7%) and falling to between 8.6% and 9.5% for all age groups above 34 years. HR HPV prevalence was 8.6% overall, being 6.8% and 38.9% among women with normal and abnormal cytology, respectively. HPV45 (1.6%) was the most common type in women with normal cytology, whereas HPV16 predominated among women with cervical abnormalities (including 7 of 10 histologically confirmed cervical intraepithelial neoplasia 2/3) and among ICC (57.6%). The next most common types in ICC in Georgia were HPV45 and 18 (13.2 and 11.0%, respectively). *Conclusions*: We report a relatively high burden of HPV infection in Tbilisi, Georgia. Improving cervical cancer prevention, through screening and/or HPV vaccination, is an important public health issue in Georgia, where 70% of ICC are theoretically preventable by HPV16/18 vaccines.

1. Introduction

Georgia has a population of approximately five million and is situated at the South Eastern limit of Europe, at the juncture with Western Asia. Cervical cancer is reported as the second most commonly diagnosed malignancy among women in the country [1]. However, as is the case for most former Soviet Republics, accurate population-based incidence and mortality data are unavailable. Contrary to elsewhere in Europe, upward trends in cervical cancer incidence and mortality have been reported in some Eastern European countries [2,3] particularly in young women [4]. Furthermore, no data are available on the population prevalence of high-risk (HR) human papillomavirus (HPV) infection in Georgia, which, in the absence of good-quality screening, is known to correlate with cervical cancer incidence [5].

The establishment of the viral aetiology of cervical cancer has raised hopes for primary and secondary prevention through HPV vaccination and HPV DNA test-based screening, respectively. The rationale and planning of such measures greatly benefit from knowledge of overall, age- and type-specific HPV prevalence in women with and without cervical cancer. To this end, the International Agency for Research on Cancer (IARC) has carried out surveys in representative samples of women worldwide [6]. In the present paper, we report on an HPV prevalence survey conducted in a representative sample of the general female population, and in women with invasive cervical cancer (ICC) in Tbilisi, Georgia.

2. Materials and methods

2.1. General female population

Study methods were similar to those used for previous IARC HPV Prevalence Surveys [6]. The study area included a residential district (Isani-Samgori) near the center of Tbilisi, the capital of

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Georgia. The study purpose was to enrol approximately 100 women from the general population in each five-year age group between 15–19 and 54–59 years. All mentally and physically competent women aged 15–59 years were eligible for the study, regardless of marital status. All women were enumerated at their homes by local community workers and invited to a local community clinic between September and December 2007.

Of the 3009 invited women, 1569 (52%) did not accept the invitation, including 197 unmarried and 81 pregnant women. Otherwise, the most common reasons for refusal were "no time" ($N = 603$) and "fear of gynaecological exam" ($N = 127$). Refusal rates were 54%, 49%, 43% and 57% among women aged 15–24, 25–34, 35–44 and 45–59 years, respectively. In addition, among the 1440 women who accepted the invitation to come to the study clinic, 96 refused to undergo a vaginal examination (including 88 unmarried women), and hence did not provide a cervical cell specimen.

An interview was administered by one of two female interviewers. The structured questionnaire included information on socio-demographic characteristics, reproductive and menstrual factors, sexual habits of women and their husbands, and lifetime use of contraceptive methods.

A total of 1344 women underwent a vaginal examination by a midwife or gynaecologist. After the preparation of a conventional Pap smear, a sample of exfoliated cervical cells from the endocervix and ectocervix was collected with a cervexbrush (Rovers Medical Devices B.V., Oss, The Netherlands). After being inserted into the endocervical canal and rotated gently, the brush containing cellular material was placed in a vial containing PreservCyt media (Hologic, Marlborough, MA, USA).

2.2. Cytopathology

Pap smears were first read at the Alexandre Natishvili Institute of Morphology, Tbilisi, Georgia, and reported using the 2001 Bethesda system terminology [7]. A total of three women were diagnosed with high-grade squamous intraepithelial lesions (HSIL), and were immediately referred for colposcopy.

As a quality-control step, when HPV results became available approximately six months later, all Pap smears from women positive for HPV and/or with abnormal cytology ($N = 318$), plus an additional random sample of HPV-negative women with normal cytology ($N = 143$), were blindly reviewed by an expert pathologist (FJvK) at the VU University Medical Center (VUMC), Amsterdam, the Netherlands, where cytological diagnosis was formulated according to the CISOE-A classification [8] and translated into the 2001 Bethesda system terminology [7]. Following the VUMC review, an additional 12 women were diagnosed with HSIL (of which 10 were HPV-positive) and, together with 18 women with HPV-positive low-grade cytological lesions, were also referred for colposcopy. For all reviewed Pap smears, the VUMC diagnosis is henceforward considered as the reference.

2.3. Women with invasive cervical cancer

ICC cases were identified at the National Cancer Center, Tbilisi, Georgia between July 2008 and December 2009. For 102 women diagnosed with ICC, tumour biopsies were immediately frozen in liquid nitrogen and stored at −80 °C before being sent to the VUMC, where they were sectioned for HPV testing using a 'sandwich' approach: inner sections were destined for HPV testing (see below) and outer sections for histological confirmation. After exclusion of biopsies without histological evidence of tumour ($n = 9$) or suspected to be of endometrial origin ($n = 2$), 91 valid ICC cases remained.

2.4. Ethical approval

All participants signed informed consent forms according to the recommendations of the IARC and the Alexandre Natishvili Institute of Morphology ethical review committees, both of which approved the present study.

2.5. HPV detection

HPV DNA testing on exfoliated cervical cells stored in PreservCyt media (Hologic, Marlborough, MA, USA) and frozen ICC biopsies was performed at the Department of Pathology at the VUMC, according to a protocol similar to that used in previous IARC HPV Prevalence Surveys [6]. DNA was extracted from the PreservCyt sample using magnetic beads (Macherey-Nagel, Düren, Germany) on a robotic system (Hamilton Robotics, Martinsried, Germany), according to the manufacturer's instructions. For ICC biopsies, one or more 5 μM sections representing approximately 1 cm^2 of tissue were pre-digested with Proteinase K, after which DNA was extracted using magnetic beads (Macherey-Nagel, Düren, Germany).

Beta-globin PCR analysis was performed firstly on all specimens in order to assess the quality of the DNA to be submitted to HPV PCR. The overall presence of HPV DNA was determined by performing a general primer GP5+/6+-mediated PCR [9]. HPV positivity was assessed by hybridisation of PCR products in an enzyme immunoassay using two HPV oligoprobe cocktails that, together, detect the following 44 HPV types: HPV6, 11, 16, 18, 26, 30–35, 39, 40, 42–45, 51–59, 61, 64, 66–70,71 (equivalent to CP8061), 72, 73, 81 (equivalent to CP8304), 82 (IS39 and MM4 subtypes), 83 (equivalent to MM7), 84 (equivalent to MM8), cand85, 86, cand89 (equivalent to CP6108) and JC9710. Subsequent HPV typing was performed by reverse-line blot hybridisation of PCR products, as described previously [10]. HPV types considered high-risk for this analysis included HPV16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73 and 82 [11]. All other HPV types were considered low-risk.

2.6. Statistical analysis

HPV prevalence was standardised by age using the world standard population [12] as a reference population. Odds ratios (ORs) for HPV positivity and corresponding 95% confidence intervals (CIs) were calculated by means of unconditional logistic regression equations, adjusted for age (<25, 25–34, 35–44, ≥ 45 years) and lifetime number of sexual partners (1, ≥ 2), where appropriate. The statistical significance of trends for ORs was assessed by considering the categorical variables as a continuous variable in the logistic model.

Prevalence ratios and corresponding 95% CIs were used to compare the relative frequency of HPV types in HPV-positive women with ICC and HPV-positive women with normal cytology from the general female population.

The fraction of ICC potentially preventable by HPV vaccines that target HPV16/18 or other types was defined as the fraction of ICC in which the DNA of the corresponding types could be demonstrated [13].

3. Results

3.1. General female population

Of 1344 women who provided cervical cell samples, 34 women with inadequate HPV DNA (including 1 HSIL) and/or inadequate cytology results, and one prevalent ICC case already under treatment, were excluded, leaving 1309 women in the following analyses. Among them, 62 (4.7%) had an abnormal cytological diagnosis, including 34 (2.6%) atypical squamous cells of undeter-

Table 1
Prevalence of HPV types overall and by cytological findings among 1309 women. Tbilisi, Georgia, 2007.

HPV type	Normal cytology ($N=1247$)		Abnormal cytology ($N=62$)[a]		All ($N=1309$)	
	Single	Total (%)	Single	Total (%)	Single	Total (%)
Any	109	143 (11.5)	26	33 (53.2)	135	176 (13.5)
Any low-risk	58	88 (7.1)	6	8 (12.9)	64	96 (7.3)
Any high-risk	54	85 (6.8)	21	28 (45.2)	75	113 (8.6)
High-risk						
16	5	6 (0.5)	7	10 (16.1)	12	16 (1.2)
18	4	8 (0.6)	1	1 (1.6)	5	9 (0.7)
31	12	15 (1.2)	2	3 (4.8)	14	18 (1.4)
33	2	6 (0.5)	1	1 (1.6)	3	7 (0.5)
35	1	3 (0.2)	1	3 (4.8)	2	6 (0.5)
39	2	3 (0.2)	0	1 (1.6)	2	4 (0.3)
45	8	20 (1.6)	2	5 (8.1)	10	25 (1.9)
51	5	9 (0.7)	1	1 (1.6)	6	10 (0.8)
52	0	4 (0.3)	0	0 (0.0)	0	4 (0.3)
56	3	8 (0.6)	3	4 (6.5)	6	12 (0.9)
58	6	8 (0.6)	3	4 (6.5)	9	12 (0.9)
59	1	3 (0.2)	0	0 (0.0)	1	3 (0.2)
68	1	2 (0.2)	0	0 (0.0)	1	2 (0.2)
73	3	4 (0.3)	0	0 (0.0)	3	4 (0.3)
82	1	3 (0.2)	0	0 (0.0)	1	3 (0.2)
Uncharacterised	2	2 (0.2)	0	0 (0.0)	2	2 (0.2)

HPV, human papillomavirus.
[a] Including 10 CIN2/3, positive for types: 16 only (four women), 16+35, 16+45, 16+56, 31, 56 and 58.

mined significance, atypical squamous cells cannot exclude high-grade lesion or atypical glandular cells of undetermined significance (ASCUS/ASC-H/AGUS), 14 (1.1%) low-grade squamous intraepithelial lesions (LSIL), and 14 (1.1%) HSIL. Final histological confirmation could be obtained for 17 women (including 11 HSIL), of whom 10 were diagnosed with cervical intraepithelial neoplasia (CIN)2/3, 6 with CIN1 and one with no CIN.

Overall HPV prevalence was 13.5% (95% CI: 11.6–15.4), and 11.5% (95% CI: 9.8–13.4) among women with normal cytology (Table 1). Corresponding overall prevalence age-standardised to the world population was 13.8%. In total, 135 (10.3%) women had single-type and 41 (3.1%) had multiple-type infections. Prevalence of HR types was 8.6%, compared to 7.3% for low-risk types. Age-standardised prevalence of HR HPV was 8.9%. The most common types among women with normal cytology were HPV45 (1.6%), HPV31 (1.2%), and HPV66 (1.1%). HPV prevalence among women with abnormal cytological diagnosis was 53.2%. HPV16 was detected in 0.5% (95% CI: 0.2–1.0) of women with normal cytology, but predominated among women with cervical abnormalities (16.1%), including seven out of 14 women with HSIL and seven out of 10 women with histologically confirmed CIN2/3.

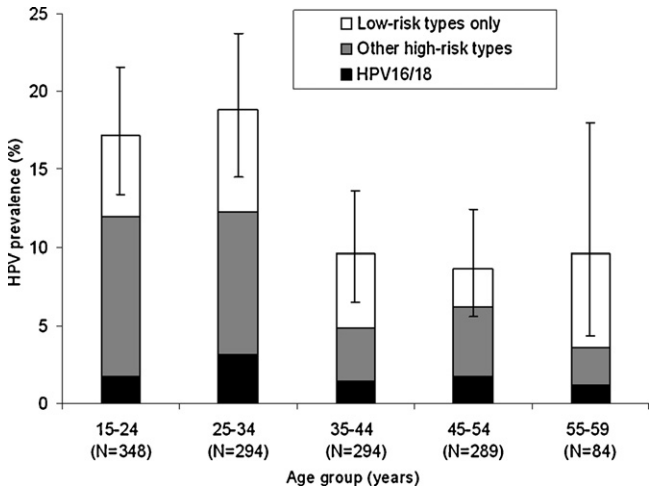

Fig. 1. Age-specific prevalence of human papillomavirus (HPV) DNA by HPV type among 1309 women. Tbilisi, Georgia, 2007. Vertical bar represents 95% confidence interval of overall HPV prevalence.

Fig. 1 shows the age-specific prevalence of HPV, classified hierarchically into (1) HPV16 or 18, (2) other HR types and (3) low-risk types only. Overall HPV prevalence was 17.2% among women younger than 25 years, and remained similar (18.7%) in the 25–34-year age group. Thereafter, it decreased, being between 8.7% and 9.5% for all age groups above 34 years. Age-specific patterns were not significantly different for the prevalence of HPV16 and/or 18, or for other HR types (Fig. 1). When women below the age of 25 years were further subdivided into two age groups, overall HPV prevalence was similar in 182 women aged 18–22 (18.1%) and 166 women aged 23–24 years (16.3%).

Table 2 shows the relationship between overall HPV positivity and various characteristics of study participants after adjustment for age. Significant differences in HPV positivity were observed by lifetime number of sexual partners (OR for ≥2 versus 1 partner = 3.8; 95% CI: 2.1–6.8), marital status (OR for unmarried versus married women = 2.1; 95% CI: 1.3–3.3), number of full-term pregnancies (OR for parous versus nulliparous = 0.5; 95% CI: 0.3–0.7), history of intrauterine device use (OR for ever-user versus never-user = 0.5; 95% CI: 0.3–0.8) and smoking status (OR for current versus never = 2.0; 95% CI: 1.3–2.9), particularly among heavy smokers (OR for ≥15 cigarettes/day versus never = 3.3; 95% CI: 1.7–6.4). The reporting of husband's extramarital sexual relationships was also associated with higher HPV prevalence, albeit with only borderline statistical significance (OR = 2.1, 95% CI: 1.0–4.8). Age at first sexual intercourse was not significantly related to HPV positivity in either adjustment model (Table 2). Additional adjustment of the model for lifetime number of sexual partners did not materially effect these associations (data not shown).

Education level (college or higher education reported by 66.4% of women), hormonal contraceptive use (12.5%), condom use (23.3%), history of spontaneous (23.9%) or induced abortion (68.2%), and history of Pap smear (2.2%) were not associated with HPV positivity (data not shown).

3.2. Women with invasive cervical cancer

Type-specific HPV prevalence is reported in Table 3 for 91 ICC cases, including 87 squamous cell carcinomas and four adeno-

Table 2
ORs for HPV positivity and corresponding 95% CIs according to selected characteristics among 1309 women. Tbilisi, Georgia, 2007.

Characteristics	Number of women[a]	HPV DNA positive		OR (95% CI)[b]
		N	%	
Age (years)				
<25	348	60	17.2	1
25–34	294	55	18.7	1.1 (0.7–1.7)
35–44	294	28	9.5	0.5 (0.3–0.8)
45–54	289	25	8.7	0.5 (0.3–0.7)
≥55	84	8	9.5	0.5 (0.2–1.1)
χ^2_1 for trend				$p=0.002$
Marital status				
Married	1162	147	12.7	1
Unmarried[c]	147	29	19.7	2.1 (1.3–3.3)
Number of full-term pregnancies				
Nulliparous	149	36	24.2	1
Parous	1160	140	12.1	0.5 (0.3–0.7)
1	378	60	15.9	0.6 (0.4–0.9)
2	576	63	10.9	0.4 (0.3–0.7)
≥3	206	17	8.3	0.4 (0.2–0.7)
χ^2_1 for trend among parous				$p=0.14$
Age at first sexual intercourse				
≥22	419	54	12.9	1
19–21	462	54	11.7	0.7 (0.5–1.1)
<19	428	68	15.9	1.0 (0.6–1.4)
χ^2_1 for trend				$p=0.94$
History of intrauterine device use				
Never	1060	158	14.9	1
Ever	249	18	7.2	0.5 (0.3–0.8)
Lifetime number of sexual partners				
1	1247	156	12.5	1
≥2	60	20	33.3	3.8 (2.1–6.8)
Husband's extramarital sexual relationships				
No	99	9	9.1	1
Yes, only before marriage	510	68	13.3	1.5 (0.7–3.1)
Yes, during marriage	221	30	13.6	2.1 (1.0–4.8)
Uncertain	479	69	14.4	1.9 (0.9–4.0)
Smoking status				
Never	1024	121	11.8	1
Former	63	9	14.3	1.2 (0.6–2.5)
Current	222	46	20.7	2.0 (1.3–2.9)
<15 cigarettes/day	173	32	18.5	1.7 (1.1–2.6)
≥15 cigarettes/day	48	14	29.2	3.3 (1.7–6.4)

CI, confidence interval; HPV, human papillomavirus; OR, odds ratio.
[a] Some figures do not add up to the total because of a few missing values.
[b] Adjusted for age.
[c] Including seven single, 61 separated/divorced and 79 widowed women.

Table 3
Prevalence of selected human papillomavirus (HPV) types in 91 HPV-positive ICC cases and 143 HPV-positive women with normal cytology. Tbilisi, Georgia, 2007.

HPV type	ICC (*N*=91)	Normal cytology (*N*=143)	ICC:normal cytology
	Total (%)	Total (%)	Prevalence ratio (95% CI)
16	53 (58.2)	6 (4.2)	13.9 (6.0–39.5)
45	12 (13.2)	20 (14.0)	0.9 (0.4–2.0)
18	10 (11.0)	8 (5.6)	2.0 (0.7–5.7)
33	4 (4.4)	6 (4.2)	1.0 (0.2–4.4)
58	3 (3.3)	8 (5.6)	0.6 (0.1–2.5)
31	2 (2.2)	15 (10.5)	0.2 (0.0–0.9)
35	2 (2.2)	3 (2.1)	1.0 (0.1–9.1)
39	2 (2.2)	3 (2.1)	1.0 (0.1–9.1)
82	2 (2.2)	3 (2.1)	1.0 (0.1–9.1)
Other high-risk types	4[a] (4.4)	27 (18.9)	0.2 (0.1–0.6)
Any low-risk type	2[b] (2.2)	88 (61.5)	0.0 (0.0–0.1)
X	0 (0.0)	2 (1.4)	0.0 (0.0–8.4)
Multiple infections	5[c] (5.4)	34 (23.8)	0.2 (0.1–0.6)
16 and/or 18	62 (68.1)	14 (9.8)	7.0 (3.9–13.5)
16 and/or 18 and/or 45	74 (81.3)	76 (53.2)	1.5 (1.1–2.1)

CI, confidence interval, ICC: invasive cervical cancer; X, uncharacterised HPV type.
[a] One each of HPV51, 56, 68 and 73.
[b] One each of HPV30 and 42.
[c] HPV16/18, 16/33, 31/45, 51/56, and 58/39.

carcinomas. Average age of cases was 45 years (range: 21–64) and the majority were tumour stage I ($n = 62$). All cases were HPV-positive and all but two (97.8%) were HR HPV-positive. HPV16 was found in 53 (58.2%) cases, with the next most common types being HPV45 (13.2%), HPV18 (11.0%) and HPV33 (4.4%). The four adenocarcinoma cases were positive for HPV18 (2 women), 16 and 45. Upon comparison with HPV-positive women with normal cytology, prevalence ratios for women with ICC were 13.9 (95% CI: 6.0–39.5) for HPV16, 2.0 (95% CI: 0.7–5.7) for HPV18, and 0.9 (95% CI: 0.4–2.0) for HPV45. Several HR HPV types including HPV31 were under-represented in HPV-positive ICC compared to normal cytology (Table 3). Low-risk types and multiple-type infections were also much less common in ICC than in HPV-positive women with normal cytology (Table 3).

4. Discussion

The major finding of the present study, the first carried out in Georgia, was the disclosure of a relatively important burden of HPV infection, particularly in women below the age of 35 years, in the general female population of Tbilisi. The age-standardised prevalence of HR HPV types in Tbilisi (8.9%) was slightly lower than that found in the IARC survey in Poland (12.1%) using the same HPV testing protocol, but was higher than in the IARC study carried out in Italy (4.6%). It was similar to that found in areas of South America [6] which are known to have high cervical cancer incidence [14]. In addition, the prevalence of HR HPV types in Georgia can be compared with GP5+/6+-based findings for primary cervical cancer screening in other European studies not carried out by IARC (5.6%, 7.1%, 11.2% and 15.7% in the Netherlands, Sweden, South Wales and Scotland, respectively) [15]. The prevalence of high-grade cervical abnormalities in Tbilisi (1.1%) was also similar to that found in Western Europe [15]. However, in contrast to these countries that have organised cervical screening programmes in place, only 2.2% of women in Tbilisi reported a previous Pap smear.

HPV prevalence in Georgia did not decrease between women aged 18–24 and 25–34 years, but fell significantly thereafter. This slow decline of the HPV peak in young women is similar to that reported in Poland [16] and Italy [17], but differs somewhat from findings in other high-resource countries in Europe [18,19], Asia [18] and the USA [20] where a decrease in HPV positivity is already clear after age 25 years. A relatively later age at sexual debut (mean: 20.8 years in Georgia and 19.6 years in Poland) may explain the persistence of relatively high HPV prevalence in women aged 25–34 years in Eastern European countries like Georgia and Poland.

Lifetime number of sexual partners was an important determinant of HPV positivity in Tbilisi [21]. Nevertheless, the mean number of women's lifetime sexual partners (1.1) was relatively low compared to similar surveys in other areas of the world (range: 1.1–2.7) [16,21]. Husband's extramarital sexual relationships were also associated with HPV prevalence, albeit weakly.

Unmarried and nulliparous women had a significantly higher risk of being HPV-positive, even after adjustment for age and lifetime number of sexual partners, in agreement with a pooled analysis of previous IARC HPV Prevalence Surveys [22]. Among parous women, however, the linear trend by number of full-term pregnancies was not significant, and nulliparous women tended to be both younger (mean age = 28.5 and 36.8 years, respectively) and more sexually active ($\geq$2 partners = 8.7% and 4.1%, respectively) than parous women, so that nulliparity has to be interpreted, as a marker of sexual behaviour.

The use of an intrauterine device was also inversely associated with HPV prevalence, but with no evidence of a relationship with sexual behaviour or parity. No consistent association with intrauterine device use was detected in previous IARC HPV Prevalence Surveys (data not shown). Oral contraceptive and condom use were unrelated to HPV prevalence, as previously reported [22].

Current smoking was associated with higher HPV positivity even after adjustment for sexual behaviour, particularly among heavy smokers. This is consistent with a previous pooled analysis [23] and might be explained by an adverse effect of smoking on the clearance of HPV infection [24]. However, current smokers were considerably more sexually active than non-smokers ($\geq$2 partners = 16.3% and 1.8%, respectively), making residual confounding by sexual behaviour difficult to completely rule out.

With respect to the relative importance of different HPV types, the most frequently detected HR type in the general female population of Tbilisi was HPV45, which is in slightly contrast to similar studies where HPV16 tended to predominate [6]. The relative importance of HPV16, however, was much higher in cervical lesions (including 50% of HSIL) and ICC (57.6%), consistent with a worldwide meta-analysis [25]. HPV45 remained the second most common HPV type in ICC (13.2%) but was not more frequent in ICC in comparison to HPV-positive women with normal cytology.

Strengths of the study include a relatively large sample size, especially among young women, and the use of a standardised and well-validated HPV test allowing comparisons with similar studies around the world [6]. The principal limitation was the substantial number of women who refused to participate. However, as HPV infection is asymptomatic and was not associated with socio-economic class in the present, nor in many previous studies [26], it is unlikely that HPV positivity and lack of participation were strongly correlated. Another caveat is that very few unmarried women ended up providing a cervical cell specimen. Thus, although invitation was not restricted to married women as in some previous HPV prevalence surveys carried out by the IARC, our present study should be considered almost entirely one of ever-married women.

Lastly, we initially relied on locally read Pap smears for the immediate clinical management of study women. However, a blind cytology review revealed that a majority of HSIL had been locally diagnosed as cytologically normal, including six who were later histologically confirmed as having HR HPV-positive CIN2/3. Furthermore, there was considerable local over-diagnosis of ASCUS/AGUS/LSIL, of whom $>$80% proved to be cytologically normal upon blind review. These findings highlight, once again, inherent problems in achieving a high standard of cytological screening in settings where large quality-assured cervical cancer screening programmes are not in place [27].

In conclusion, the prevalence of HPV infection in the general female population would suggest that Georgia is a country of intermediate cervical cancer risk on a global scale, and of relatively high risk compared to other European countries [15]. Improving cervical cancer prevention, through screening and/or HPV vaccination, is thus an important public health issue and calls for new effective interventions in Georgia. The quality of cytology would need to be greatly improved. Alternatively, new much-needed screening programmes should start using HPV testing, as supported by recent encouraging data [28–30]. In such a scenario, about 5% of Georgian women aged 35 or older would test positive for an HR HPV cocktail test and require diagnostic follow-up. With respect to vaccination, the fraction of ICC potentially preventable in Georgia by an HPV16/18 vaccine (68%), is compatible with worldwide estimates [25] but could be even greater if cross-protection against HPV45 would be confirmed [31,32].

Conflict of interest

None to declare.

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