Research articles

THE BURDEN OF GENITAL WARTS IN SLOVENIA: RESULTS FROM A NATIONAL PROBABILITY SAMPLE SURVEY

I Klavs (irena.klavs@ivz-rs.si)¹, M Grgič-Vitek²

1. AIDS, Sexually Transmitted Infections and Healthcare Associated Infections Unit, Communicable Diseases Centre, Institute of Public Health of the Republic of Slovenia, Ljubljana, Slovenia

2. Immunization Programme Unit, Communicable Diseases Centre, Institute of Public Health of the Republic of Slovenia, Ljubljana, Slovenia

The objective of this study was to estimate the lifetime age-specific cumulative incidence of self-reported genital warts diagnosis in Slovenia and to explore the association with demographic characteristics and self-reported sexual behaviour. Data were collected in the period from November 1999 to February 2001 from a national probability sample of the general population aged 18-49 years through a combination of face-to-face interviews at the respondents' homes and anonymous self-completed questionnaires. In total, 849 men and 903 women were interviewed (response: 63.3% men, 70.9% women). Among sexually experienced respondents with available information (752 men and 842 women), previous diagnosis of genital warts was reported by 0.3% of men (95% confidence interval (CI): 0.0%-1.3%) and 0.4% of women (95% CI: 0.1%-1.1%), and in the age group of 40-49 year-olds by 0.5% of men (95% CI: 0.0-3.2) and 0.7% of women (95% CI: 0.2%-2.9%). In comparison to women with fewer than 10 lifetime male partners, those who reported to have had at least 10 male partners were more likely to have a previous diagnosis of genital warts (adjusted odds ratio: 7.2 (95% CI: 1.1%-47.8%). The lifetime cumulative incidence of self-reported genital warts diagnosis among Slovenians was relatively low in comparison to other published estimates from probability sample surveys in the general population in European countries. Our findings will inform the Slovenian vaccination policy against human papillomaviruses (HPV) and contribute to a better understanding of the differences between European countries regarding the burden of genital warts.

Introduction

Anogenital infections with human papillomavirus (HPV) types 6 and 11 are responsible for almost all genital warts, in Slovenia as well as in other countries [1-3]. Prophylactic quadrivalent HPV vaccine has been shown to be highly effective in preventing anogenital disease, including genital warts, associated with HPV types 6, 11, 16, and 18 in young women [4]. Since this vaccine has recently become available, and many Member States of the European Union (EU) consider introducing HPV vaccination into their national immunisation schedules [5], understanding the burden of genital warts in the general population is important in order to make informed vaccination policy decisions. Few studies about the overall and age-specific lifetime cumulative incidence of self-reported genital warts diagnosis have been conducted in probability samples of the general population of European countries [6,7].

Surveillance of sexually transmitted infections in Slovenia, including genital warts, is based on mandatory notification of all diagnosed cases by clinicians. The annual reported incidence of newly diagnosed genital warts in the period from 2001 to 2007 was relatively low. The lowest rate, 3.5 per 100,000 general population, was reported in 2001, and the highest rate in 2002, with 6.7 per 100,000. The incidence in 2007 was 4.7 per 100,000 general population [8]. Although the sensitivity of our surveillance system has not been formally assessed, these reported rates are assumed to underestimate the true incidence [8].

We used data from the Slovenian national Sexual Lifestyles, Attitudes and Health Survey to estimate the overall and age-specific lifetime cumulative incidence of self-reported genital warts diagnosis in Slovenia and to explore the association with selected demographic characteristics and self-reported sexual behaviours.

Methods

Details on the employed methods have been published previously [9]. In brief, data were collected over the period between November 1999 and February 2001 from a national probability sample of the general population aged 18-49 years by a combination of face-to-face interviews conducted at respondents' homes and anonymous self-administered pencil and paper questionnaires. The data collection methods were an adaptation from the British National Survey of Sexual Attitudes and Lifestyles conducted in 1990 and have been thoroughly piloted in Slovenia [10,11]. They were very similar to the methods used in the second British survey conducted in 2000 [6,12]. Ethical approval was obtained from the Medical Ethics Committee of the Republic of Slovenia. Informed consent was obtained from each study participant.

We used stratified two-stage probability sampling. Individuals aged between 18 and 24 years were sampled with twice the probability of older individuals. The sampling frame was designed using the list of enumeration areas provided by the Central Population Registry. Within each of the 12 statistical regions of Slovenia, communities were implicitly stratified according to their type and size as follows: rural communities with less than 2,000 inhabitants, non-rural communities with less than 2,000, communities with 2,000-9,999 inhabitants, those with 10,000-100,000, and two cities with more than 100,000 inhabitants. The entire sampling frame included 9,850 primary sampling units of approximately 120 inhabitants at 18-49 years of age. 270 primary sampling units were sampled

independently from the 12 regions with the probability proportional to the size of the eligible population, which was defined as the sum of the individuals at 25-49 years of age and twice as many individuals at 18-24 years of age. On average, 10 individuals at the age of 18-49 years were randomly selected from each unit.

Questions about demographic characteristics and first heterosexual intercourse were asked in face-to-face interviews. Only those who reported any sexual experience were asked to anonymously complete self-administered questionnaires that included questions on the details of sexual lifestyles, risk behaviours and previous diagnosis of sexually transmitted infections. The question designed to estimate age-specific lifetime cumulative incidence of self-reported genital warts diagnosis was: "Have you ever been told by a doctor that you have genital warts?"

Weights were computed to adjust for over-sampling of the age group of 18-24 year-olds and the differences in survey response between different regions, and different types and sizes of communities. A multidimensional calibration procedure was applied to adjust for any remaining differences between the achieved sample and available Slovenian population estimates according to statistical regions, types of communities, and gender and age groups, based on Central Population Registry data for the year 2000.

Analyses were conducted using STATA version 7.0 statistical methods for complex survey data (svy commands) to account for stratification, clustered sampling, over-sampling of 18-24 year-olds. Response rates were calculated from unweighted data.

Weighted estimates of cumulative proportions of respondents who reported genital warts diagnosis, overall and according to different demographic and sexual behaviour characteristics, were obtained together with 95% confidence intervals (CI). Tests for independence for complex survey data (the Pearson chi-squared statistics corrected for the survey design) were computed. For women only, multivariate analyses of the association between self-reported genital warts diagnosis and marital status as well as having at least 10 heterosexual partners in one's lifetime (two variables associated with self-reported genital warts diagnosis in the univariate analyses, $p < 0.05$) were performed by logistic regression accounting for complex survey design (svylogit command) to obtain pseudo-maximum likelihood estimates of adjusted odds ratio (AOR) together with 95% CI, and adjusted Wald tests of significance.

Results

A total of 849 men (survey response: 63.3% of those selected) and 903 women (survey response: 70.9%) were interviewed. The 807 men and 874 women who reported sexual experience were asked to anonymously complete self-administered questionnaires.

The question for previous diagnosis of genital warts was answered by 752 sexually experienced men and 842 sexually experienced women (item response: 93.2% among men; 96.3% among women). Overall, two men and three women (unweighted counts) reported previous diagnosis of genital warts. Table 1 shows the proportions of those who reported previous diagnosis of genital warts, overall and by selected demographic characteristics and sexual behaviours with the results of univariate analyses of association (p values). Previous diagnosis of genital warts was reported more often by

TABLE 1

Proportion (cumulative incidence) of sexually experienced* men and women aged 18-49 years who reported previous diagnosis of genital warts, Slovenia, 1999-2001

	Men				Women			
	% (95% CI)	Base WT	Base UWT	p value†	% (95% CI)	Base WT	Base UWT	p value†
All	0.3 (0.0 - 1.3)	801	752		0.4 (0.1-1.1)	823	842	
Age				0.58				0.37
18-29 years	0	280	363		0	283	381	
30-39 years	0.5 (0.0 - 3.7)	254	174		0.4 (0.0-2.7)	265	235	
40-49 years	0.5 (0.0 - 3.2)	268	215		0.7 (0.2-2.9)	276	226	
Marital status				0.55				0.04
Married/cohabiting	0.5 (0.1 - 2.1)	497	391		0.3 (0.0 - 1.3)	605	553	
Widowed/separated/divorced	0	17	12		2.9 (0.4 -18.4)	34	27	
Single	0	286	349		0	184	262	
Heterosexual partners in lifetime				0.58				0.04
Less than 10	0.3 (0.0 - 1.8)	547	528		0.3 (0.0 - 1.1)	762	778	
10 or more	0.5 (0.1 - 3.7)	227	203		2.1 (0.3 -13.8)	47	49	
Concurrent heterosexual partners				0.07				0.41
Never	0	454	439		0.3 (0.0 - 1.2)	658	668	
At least once	1.0 (0.2 - 3.7)	271	245		0.8 (0.1 - 5.6)	123	133	

* Sexually experienced respondents are defined as those who reported to have had sexual intercourse (oral, vaginal or anal).

† Pearson's chi-squared statistics corrected for the survey design were computed (univariate analyses of association between self-reported genital warts diagnosis and selected demographic and sexual behaviour characteristics).

CI: confidence interval; WT: weighted count of individuals; UWT: unweighted count of individuals.

Numbers of individuals (bases) vary according to the number of missing values for individual variables.

The data were weighted to be representative of the Slovenian population based on the Central Population Registry data for the year 2000 and analysed using STATA version 7.0 to account for complex survey design (stratification, clustered sampling, over-sampling of 18-24 year-olds).

older than by younger respondents: by 0.5% of the 40-49 year-old men (95% CI: 0.0-3.2) and by 0.7% of the 40-49 year-old women (95% CI: 0.2-2.9).

We found no evidence of association of previous genital warts diagnosis with the level of education, first heterosexual intercourse before the age of 16, having ever paid for sex, or condom use.

In multivariate analysis, women with at least 10 lifetime partners had higher odds of previous genital warts diagnosis (AOR (adjusted for marital status): 7.2 (95% CI: 1.1-47.8)) in comparison to those with fewer than 10. In comparison to married/cohabiting and single women, women who had been married previously were also more likely to have a previous genital warts diagnosis (AOR (adjusted for 10+ lifetime partners): 5.8 (95% CI: 0.9-38.8)); however, the statistical significance was borderline (p=0.07).

Discussion and conclusion

Our findings indicate a relatively low overall and age-specific lifetime cumulative incidence of self-reported genital warts diagnosis in the general population of Slovenia.

The lifetime cumulative incidence of self-reported genital warts seems to vary substantially between European countries. In the general population probability sample of 16-44 year-old British men and women interviewed in 2000, 3.6% (95% CI: 3.1-4.2) of sexually experienced men and 4.1% (95% CI: 3.6-4.7) of sexually experienced women reported ever being diagnosed with genital warts [6]. In the general population probability sample of 18-45 year-old women interviewed in the period 2004-2005 in four Nordic countries, clinically diagnosed genital warts were reported by 10.1% (95% CI: 9.7-10.5) in Denmark, 12.0% (95% CI: 11.5-12.6) in Iceland, 9.5% (95% CI: 9.0-9.9) in Norway, and 11.3% (95% CI: 10.8-11.8) in Sweden [7]. These differences in the estimated lifetime cumulative incidence of self-reported genital warts between the studies in Slovenia, the United Kingdom (UK) and the Nordic countries are consistent with a recent review on the epidemiology of sexually transmitted infections in the European Union which concluded that the prevalence of herpes simplex virus type 2 (HSV-2) in Scandinavia was higher than in other countries [13].

Differences in sexual behaviours may contribute to the differences in the lifetime cumulative incidence of self-reported genital warts

diagnosis between these European countries. The occurrence of genital warts has been linked to higher-risk sexual behaviours, most often with higher numbers of sexual partners [7,14,15]. Both of the above-mentioned European studies conducted in general population probability samples, reported higher mean numbers of lifetime sexual partners than our study (see Table 2).

Our results provide some evidence that Slovenian women with at least 10 lifetime male partners were more likely to have a previous genital warts diagnosis than those with fewer partners. Since the numbers were small and we used logistic regression accounting for the complex survey design (svylogit command) to obtain pseudo-maximum likelihood estimates of adjusted odds ratio (AOR) together with 95% CI and adjusted Wald tests of significance, it is possible that the statistically significant association we calculated may have been an association of only borderline significance. The lack of evidence in our data for an association of previous genital warts diagnosis with the level of education, first heterosexual intercourse before the age of 16, having ever had concurrent heterosexual partnership, having ever paid for sex, and condom use may be due to the relatively low prevalence of self-reported genital warts diagnosis as well as the relatively small sample size.

We may have underestimated the true overall and age-specific lifetime cumulative incidence of genital warts among Slovenian men and women due to the survey limitations that include validity constraints of self-reported information and to possible participation biases inherent to all behavioural surveys. Another possible factor is under-diagnosis caused by people that do not consult a doctor for genital warts or by barriers with respect to referral to sexually transmitted infections (STI) outpatient clinics. The ability to self-diagnose genital warts, a precondition to seeking health care, has been questioned [14]. However, we have no reason to believe that differences of such magnitude exist between general populations of Slovenia, Britain and Nordic countries with regards to the ability to self-diagnose genital warts, health-care seeking behaviour or access to STI outpatient clinics. Nor do we think that the ability to recall a previously diagnosed episode of genital warts or the number of lifetime sexual partners is responsible for the differences between these European studies [6,7,12].

It is noteworthy that our estimates, for both men and women, of the self-reported lifetime cumulative incidence of any STI (rather than of genital warts only), although still lower, were closer to the estimates obtained in the British survey (Slovenian men: 5.5%; Slovenian women: 5.1%; British men: 10.8%; British women: 12.6%) [6,17]. Further, the measured prevalence of sexually transmitted Chlamydia trachomatis infection among sexually experienced Slovenians aged 18-24 years in our survey was substantial, at 4.7% (CI 2.5%-8.5%) in both sexes, while the corresponding estimates for the UK were appreciably lower, with 2.7% (CI 1.2%-5.8%) among men and 3.0% (CI 1.7%-5.0%) among women, although the differences between the two countries were not statistically significant [6,18].

In conclusion, we found a relatively low lifetime cumulative incidence of self-reported genital warts diagnosis among Slovenian men and women in comparison to other published estimates from general population probability sample surveys in European countries. Differences in high-risk sexual behaviours may have contributed to these differences. Our findings will inform the Slovenian HPV vaccination policy as well as broader sexual and reproductive health

TABLE 2
Estimates of mean numbers of lifetime sexual partners from surveys conducted in representative samples of general populations in selected European countries

Country	Mean numbers of lifetime sexual partners		Year of study	Reference
	Men	Women		
United Kingdom	12.7	6.5	2000	[12]
Denmark	n.i.	8.4	2004-2005	[7]
Iceland	n.i.	8.8		
Norway	n.i.	7.4		
Sweden	n.i.	8.6		
Slovenia	8.3	3.2	1999-2001	Unpublished results

n.i.: not included in the study.

policies. Our results also contribute to a better understanding of the differences in the burden of genital warts between European countries and may inform mathematical models aimed at projecting the long-term benefits and costs of vaccination with prophylactic quadrivalent HPV vaccine.

Acknowledgements

We thank the study participants and the interviewers.

Financial support:

In addition to internal funding, the study was supported by numerous small grants from the Slovenian Ministry of Health, Ministry of Science and Technology, City Council of Ljubljana, Health Insurance Institute of Slovenia, Slovenian Research Agency and donations from Merc Sharp and Dohme Idea, Inc., Roche Diagnostics, Krka, and Lek. None of them were involved in the study design, in the collection, analysis, and interpretation of the data, in the writing of the paper or in the decision to submit the paper for publication.

References

- Greer CE, Wheeler CM, Ladner MB, Beutner K, Coyne MY, Liang H, et al. Human papillomavirus (HPV) type distribution and serological response to HPV type 6 virus-like particles in patients with genital warts. *J Clin Microbiol*. 1995;33(8):2058-63.
- Lacey CJ, Lowndes CM, Shah KV. Chapter 4: Burden and Management of non-cancerous HPV-related conditions: HPV-6/11 disease. *Vaccine*. 2006;24 Suppl 3:S3/35-41.
- Potočnik M, Kocjan BJ, Seme K, Poljak M. Distribution of human papillomavirus (HPV) genotypes in genital warts from males in Slovenia. *Acta Dermatovenereol Alp Panonica Adriat*. 2007;16(3):91-6, 98.
- Garland SM, Hernandez-Avila M, Wheeler CM, Perez G, Harper DM, Leodolter S, et al. Quadrivalent vaccine against human papillomavirus to prevent anogenital diseases. *N Engl J Med*. 2007;356(19):1928-43.
- King LA, Lévy-Bruhl D, O'Flanagan D, Bacci S, Lopalco PL, Kudjawi Y, et al. Introduction of human papillomavirus (HPV) vaccination into national immunisation schedules in Europe: Results of the VENICE 2007 survey. *Euro Surveill*. 2008;13(33):pii=18954. Available from: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=18954>
- Fenton KA, Korovessis C, Johnson AM, McCadden A, McManus S, Wellings K, et al. Sexual behaviour in Britain: reported sexually transmitted infections and prevalent genital Chlamydia trachomatis infection. *Lancet*. 2001;358(9296):1851-4.
- Kjaer SK, Tran TN, Sørensen P, Tryggevadottir L, Munk C, Dasbach E, et al. The burden of genital warts: a study of nearly 70,000 women from the general female population in the 4 Nordic countries. *J Infect Dis*. 2007;196(10):1447-54.
- Klavs I, Kustec T, Bergant N, Kastelic Z. Sexually transmitted infections in Slovenia in 2007: annual report. [In Slovene]. Ljubljana: Institute of Public Health of the Republic of Slovenia; 2008.
- Klavs I, Rodrigues LC, Wellings K, Weiss HA, Hayes R. Increased condom use at sexual debut in the general population of Slovenia and association with subsequent condom use. *AIDS*. 2005;19(11):1215-23. 2005 Jul 22;19(11):1215-23
- Johnson AM, Wadsworth J, Wellings K, Field J. *Sexual Attitudes and Lifestyles*. Oxford: Blackwell Scientific Publications; 1994.
- Klavs I, Rodrigues LC, Wellings K, Keše D, Švab I. Feasibility of testing for Chlamydia trachomatis in a general population sexual behaviour survey in Slovenia. *Int J STD AIDS*. 2002;13 Suppl 2:5-8.
- Johnson AM, Mercer CH, Erens B, Copas AJ, McManus S, Wellings K, et al. Sexual behaviour in Britain: partnerships, practices, and HIV risk behaviours. *Lancet*. 2001;358(9296):1835-42.
- Fenton KA, Lowndes CM. Recent trends in the epidemiology of sexually transmitted infections in the European Union. *Sex Transm Infect*. 2004;80(4):255-63.
- Munk C, Svare EI, Poll P, Bock JE, Kjaer SK. History of genital warts in 10,838 women 20 to 29 years of age from the general population. Risk factors associated with Papanicolaou smear history. *Sex Transm Dis*. 1997;24(10):567-72.
- Habel LA, Van Den Eeden SK, Sherman KJ, McKnight B, Stergachis A, Daling JR. Risk factors for incident and recurrent condylomata acuminata among women. A population based study. *Sex Transm Dis*. 1998;25(6):285-92.
- Wiley DJ, Grosser S, Qi K, Wisscher BR, Beutner K, Strathdee SA, et al. Validity of self-reporting of episodes of external genital warts. *Clin Infect Dis*. 2002;35(1):39-45.
- Grgič-Vitek M, Švab I, Klavs I. Prevalence of and risk factors for self-reported sexually transmitted infections in Slovenia in 2000. *Croat Med J*. 2006;47(5):722-9.
- Klavs I, Rodrigues LC, Wellings K, Keše D, Hayes R. Prevalence of genital Chlamydia trachomatis infection in the general population of Slovenia: serious gaps in control. *Sex Transm Infect*. 2004;80(2):121-3.

This article was published on 6 November 2008.

Citation style for this article: Klavs I, Grgič-Vitek M. The burden of genital warts in Slovenia: results from a national probability sample survey. *Euro Surveill*. 2008;13(45):pii=19032. Available online: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19032>