Rates and predictors of genital warts burden in the Czech population

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SUMMARY

Objective: To describe the burden and the predictors of genital warts (GWs) in Czech men and women.
Methods: A population-based cross-sectional study was conducted of 32 974 randomly selected health clinic attendees from all 14 regions of the Czech Republic. Information on GWs and lifestyle behaviour was collected using a questionnaire.
Results: Results revealed a 5.8% prevalence rate of self-reported GWs in the Czech population aged 16–55 years. There was an increase in the incidence of GWs in the years 2010–2013 when compared to lifetime incidence rates, from 205.4 (95% confidence interval (CI) 191.0–219.7) to 441.8 (95% CI 393.1–490.6) per 100 000 person-years. No significant differences were observed between genders. The strongest risk factors found for GWs were an infected sexual partner (adjusted odds ratio (OR) 114.3, 95% CI 78.9–165.4) and a high number of lifetime sexual partners (adjusted OR 3.36, 95% CI 2.72–4.17 for >14 partners vs. one partner). A novel finding was that 22.7% (95% CI 20.9–24.6%) of participants claimed that the pathology had disappeared spontaneously without medical assistance.
Conclusions: The results provide baseline information for the development and monitoring of prevention strategies against GWs in the Czech Republic.

1. Introduction

Genital human papillomavirus (HPV) causes broad morbidity among men and women, ranging from cancer to genital warts (GWs). Although the latter disease is not life-threatening, the lesions can cause not only clinical symptoms, such as burning, itching, bleeding, and pain, but also psychosocial stress, embarrassment, and anxiety.[1,2] Two HPV types (HPV6 and 11) cause up to 90% of all GWs cases.[3]

Links between GWs and various health-related behaviours and lifestyle factors have been suggested by other investigators, and there is now widespread concern regarding the growing problem of GWs.[4–6] Despite the existence of several works on the prevalence and incidence of GWs, only a few have provided data on the general population.[5,7,8] As such, new knowledge on the overall rates and dynamic acquisition of GWs in the general population is crucial in order to develop national strategies to control and prevent HPV infection. This has become even more relevant since a prophylactic quadrivalent vaccine (4HPV) against HPV6, 11, 16, and 18 has become available.[9] The same prevention

of GWs is expected from new 9-valent HPV vaccine, which includes the HPV types in the 4HPV vaccine and five additional oncogenic types (31, 33, 45, 52, and 58).[10] Of note, the absence of a response against antigens HPV6 and 11 indicated that the bivalent vaccine (2HPV) against HPV16 and 18 could never fully control GWs. For this reason, routine HPV vaccination in the United Kingdom was switched from the bivalent to the quadrivalent vaccine.

The objective of this study was to describe the prevalence and incidence rates of GWs in the Czech Republic using a questionnaire survey that captures a larger cross-section of the general population than clinic-based data. The study also sought to identify and evaluate predictors for the pathology.

2. Materials and methods

2.1. Study population

A cross-sectional survey on GWs was conducted in all 14 regions of the Czech Republic. Volunteers were recruited randomly from people attending outpatient health clinics and were offered a paper-based self-administered questionnaire. To guarantee confidentiality, participants were asked to seal the completed questionnaire in an envelope supplied for this purpose. Physicians or parents could complete the survey for children or adolescents

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younger than 18 years of age. The goal was to include at least 1500 participants from each region.

Between January 2013 and March 2014, valid data were collected from 32 974 attendees at 268 outpatient clinics who agreed to engage in the survey. Paediatricians (n = 166), gynaecologists (n = 57), and other specialists including dermatologists and allergists (n = 45) were involved, as well as immunization and transfusion centres. The percentage of subjects in each region ranged from 5% to 11%. The study was approved by the Executive Committee of Preventive Medicine at Charles University in Prague.

2.2. Data collection

The questionnaire enquired on several lifestyle factors, including residence (rural or urban), education, smoking (age when first started smoking and number of cigarettes per day), number of lifetime sexual partners, and HPV immunization status (also type of commercial HPV vaccine received, year of last dose, and if they had received all three doses), as well as date of birth and gender.

Information on GWs was obtained with the question, "Have you ever had genital warts?" Study participants were also asked for the year of their first outbreak of GWs and of recurrent episodes if any occurred, the treatments received, and the GWs status of their sexual partner. The questionnaire also contained six illustrative pictures representing three different types of GWs for men and women, from which the respondents had to choose the one most similar to theirs.

2.3. Statistical analysis

The overall and age-specific lifetime prevalence of self-reported GWs was estimated with a 95% confidence interval (CI). Associations between the various lifestyle factors and GWs were examined using univariate and multiple logistic regression, from which odds ratios (ORs) and the corresponding 95% CIs were estimated. The multivariate analysis of the effects of different lifestyle factors on GWs prevalence was initially performed separately for the two genders, but data were later pooled as no statistically significant differences were found between the two gender groups.

Incidence rates were calculated as the number of GWs claims divided by the total person-years at risk (reported per 100 000 person-years). Person-time started to accumulate at birth and ended at the date of the first GWs episode, or, if none had occurred, at the survey date.

Analyses were performed using StatsDirect Statistical Software, version 3.0.117 (StatsDirect Ltd, UK).

3. Results

Study participants had a mean age of 35.8 years (95% CI 35.7–35.9 years), with only 1.0% (95% CI 0.9–1.1%) aged 15 years or younger and less than 6% older than 56 years of age (up to 80 years of age). Most of the participants were in the age group 16–55 years, i.e. 93.1% (95% CI 92.9–93.4%). Subjects were studied in 5-year age groups. The study population consisted predominantly of women (81.4%, 95% CI 81.0–81.8%).

Current smoking was 25.2% (95% CI 24.7–25.6%) and was more frequent in men than in women (age adjusted OR 1.4, 95% CI 1.3–1.5). More than 90% of adults aged 23 years or older had a minimum basic level of schooling of 13 years (high school). The median lifetime number of sexual partners was three for both genders, with a mean of 11.1 (95% CI 6.0–16.2) for men and 4.3 (95% CI 4.2–4.3) for women. While the majority of the study population lived in urban areas (77.7%; 95% CI 77.2–78.2%), there

was no difference in age distribution between urban and rural residents (age adjusted OR 1.0, 95% CI 0.97–1.03).

Interestingly, despite the low HPV vaccination rate in the study population (7.2%, 95% CI 6.9–7.5%), 29.4% (95% CI 28.1–30.7%) of girls and young women aged 11–25 years had been immunized. Although the HPV vaccination rate of men was submarginal, i.e. 0.8% (95% CI 0.6–1.1%), no man reported the acquisition of GWs after immunization.

Overall, 1968 participants (6.0%, 95% CI 5.7–6.2%) reported one or more episodes of GWs. The lifetime prevalence of self-reported GWs was independent of gender, with rates of 5.7% (95% CI 5.2–6.3%) for men and 6.0% (95% CI 5.7–6.3%) for women. The prevalence rate was not different between men and women with regard to their age, number of sexual partners or sexual partner having ever had GWs, area of residence, or smoking habit (Table 1).

Of the participants with clinically diagnosed GWs, 76.2% (74.3–78.1%) reported having required treatment with topical cytotoxic agents and/or ablative techniques, while 22.7% (95% CI 20.9–24.6%) claimed that the pathology disappeared without medical assistance.

The prevalence of self-reported GWs increased with age, peaking at 7.6% (95% CI 6.9–8.4%) in the age group 26–30 years, after which it declined to 4.9% (95% CI 4.0–6.0%) in the oldest age group. The sex-, age- and region-standardized GWs prevalence rate reached 5.8% (95% CI 5.4–6.2%) in the Czech population aged 16–55 years.

The lifetime incidence rate of GWs per 100 000 persons-years was 165.7 (95% CI 158.4–173.1) for the study participants and 141.6 (95% CI 158.4–173.1) for the Czech population. This rate increased to 291.6 (95% CI 278.7–305.1) in the study and 205.4 (95% CI 191.0–219.7) in the Czech population when only individuals aged 16–55 years were considered. A slightly lower incidence was found in men than in women, but this was not statistically significant, i.e. OR 1.11 (95% CI 0.99–1.26) for study participants and 1.12 (95% CI 0.97–1.28) for the Czech population.

The sex- and age-standardized incidence rate between the years 2010 and 2013 was 441.8 (95% CI 393.1–490.6) per 100 000 persons-years at risk, revealing an increasing tendency for GWs infection among the population aged 16–55 years during this period when compared with lifetime rates. This observation was further supported by the increase, in 2013, of first GWs infections: up to 0.83% (95% CI 0.67–1.03%) among subjects aged 16–35 years and 0.58% (95% CI 0.47–0.70%) among those between 16 and 55 years of age.

Figure 1 shows the lifetime incidence rate of self-reported GWs by gender and age. The highest incidence in attendees with a history of GWs was found in the age group 21–25 years (459.2, 95% CI 424.9–495.6 per 100 000 person-years). No significant differences were observed between men and women, except in two age groups: the group of subjects between 16 and 20 years of age in which more women than men reported a first episode of GWs, and the group aged 31–35 years in which the exact opposite occurred.

Risk factors were estimated for both genders independently because no significant differences in GWs prevalence were observed between men and women.

A sexual partner with GWs was identified as the strongest risk factor for the acquisition of infection (Table 2). The percentage of subjects reporting GWs in both members of the couple was 87.6% (83.2–91.3%), and the mutually adjusted OR, independent of gender, achieved 114.3 (95% CI 78.9–165.4) when compared to participants whose sexual partners had never had the infection.

The second most important predictor of GWs was the lifetime number of sexual partners; the risk of infection was found to increase with the number of partners. The highest GWs prevalence (13.2%, 95% CI 11.5–15.1%) was among subjects who had had more

Table 1
Prevalence rates of self-reported genital warts in men and women, related to predictors

Category, parameter	Men		Women		OR[a]
	No.	% with GWs	No.	% with GWs	
GW status of sexual partner					
Negative	6089	5.0 (4.5–5.6)	26 610	5.3 (5.1–5.6)	0.95 (0.83–1.07)
Positive	48	93.8 (82.8–98.7)	227	86.3 (81.2–90.5)	2.47 (0.82–7.39)
Age, years					
≤15	64	3.1 (0.4–10.8)	255	1.2 (0.2–3.4)	0.96 (0.85–1.08)
16–20	463	2.6 (1.3–4.5)	1794	5.1 (4.1–6.2)	
21–25	529	6.8 (4.8–9.3)	2647	7.5 (6.5–8.6)	
26–30	807	7.1 (5.4–9.1)	3781	7.7 (6.9–8.6)	
31–35	1105	5.9 (4.6–7.4)	5672	6.1 (5.5–6.7)	
36–40	1228	5.9 (4.7–7.4)	5549	5.6 (5.0–6.2)	
41–45	799	6.4 (4.8–8.3)	3009	5.7 (4.9–6.6)	
46–50	465	4.1 (2.5–6.3)	1634	5.8 (4.7–7.1)	
51–55	271	5.9 (3.4–9.4)	961	3.6 (2.5–5.0)	
≥56	406	4.9 (3.0–7.5)	1535	5.0 (3.9–6.2)	
Lifetime No. of sexual partners					
0	139	1.4 (0.2–5.1)	411	1.7 (0.7–3.5)	0.84 (0.24–2.90)
1	1402	3.1 (2.2–4.1)	6429	3.5 (3.1–4.0)	0.87 (0.63–1.21)
2–4	1097	5.4 (4.1–6.9)	7143	5.1 (4.6–5.7)	1.05 (0.79–1.39)
5–9	901	7.8 (6.1–9.7)	4572	7.6 (6.8–8.4)	1.02 (0.78–1.33)
10–14	458	7.0 (4.8–9.7)	1429	9.4 (8.0–11.1)	0.76 (0.51–1.13)
≥15	548	10.6 (8.1–13.5)	834	15.0 (12.6–17.6)	0.69 (0.48–1.01)
Smoking, cigarettes-day					
Never or 1	4335	5.1 (4.5–5.8)	20 558	5.4 (5.1–5.8)	0.96 (0.83–1.11)
2–10	890	6.7 (5.2–8.6)	4255	7.4 (6.6–8.2)	0.92 (0.69–1.22)
>10	726	7.2 (5.4–9.3)	1203	10.4 (8.7–12.3)	0.69 (0.47–1.02)
Residence					
Rural	956	5.3 (4.0–7.0)	4917	4.9 (4.3–5.5)	1.14 (0.83–1.55)
Urban	3701	5.6 (4.9–6.4)	16 722	6.0 (5.7–6.4)	0.93 (0.80–1.09)
HPV immunization					
No	6091	5.8 (5.2–6.4)	24 711	6.3 (6.0–6.6)	0.92 (0.82–1.04)
2HPV	9	0.0 (0.0–33.6)	816	6.7 (5.1–8.7)	NA
4HPV	19	0.0 (0.0–17.7)	1113	0.6 (0.3–1.3)	NA

OR, odds ratio; GWs, genital warts; HPV, human papillomavirus; NA, not applicable.
[a] Age-adjusted OR between men and women.

than 14 sexual partners – adjusted OR 3.36 (95% CI 2.72–4.17) compared to those with just one sex partner.

Other risk factors were being in the age group 21–30 years, smoking more than 10 cigarettes a day, and living in an urban area. Data also appeared to indicate a link between lifestyle and health-related behaviour and lifetime number of sexual partners. In fact, the percentage of heavy smokers with five or more lifetime sexual partners (40.6%, 95% CI 38.4–42.9%) was 1.7 times that of the non-smokers with the same number of partners (24.2%, 95% CI 23.6–24.7). The OR between them was 2.14 (95% CI 1.95–2.36). Reports of at least five lifetime sexual partners were also more frequent among participants from urban areas (28.2%, 95% CI 28.2–29.4%) than those from rural locations (21.7%, 95% CI 20.6–22.8%), i.e. OR 1.5 (95% CI 1.4–1.6).

Immunization with the 4HPV vaccine, on the other hand, substantially decreased the prevalence of GWs, especially among young women. The percentage of 4HPV-immunized women who went on to develop GWs was reduced by 91.2% (95% CI 81.8–96.7%) and 91.8% (95% CI 83.0–96.9%) when compared to the unvaccinated and 2HPV-vaccinated, respectively. Thus, only immunization with 4HPV can be considered a protective factor against the acquisition of GWs.

Although only 0.6% (95% CI 0.5–0.7%) of all individuals reported recurrent disease, the percentage in the affected group increased to 9.5% (95% CI 8.2–10.9). In fact, it was also found that the risk of recurrence was higher than that of a first infection (age-adjusted OR 1.60, 95% CI 1.37–1.88), and it was not influenced by gender (age-adjusted OR 0.99, 95% CI 0.66–1.46).
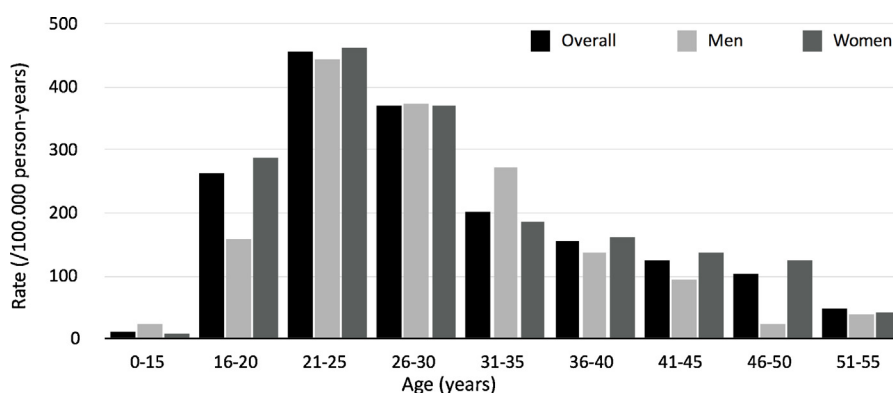

Figure 1. Lifetime incidence rate of self-reported genital warts by gender and age.

Table 2
Predictors associated with self-reported genital warts

Category, parameter	No.	% with GWs	OR[a]	OR[b]
GW status of sexual partner				
Negative	32 699	5.3 (5.0–5.5)	1.0	1.0
Positive	275	87.6 (83.2–91.3)	127.58 (88.3–184.2)	114.25 (78.9–165.4)
Age, years				
≤15	319	1.6 (0.5–3.6)	0.33 (0.13–0.82)	0.55 (0.22–1.38)
16–20	2257	4.6 (3.7–5.5)	1.0	1.0
21–25	3176	7.4 (6.5–8.4)	1.67 (1.32–2.12)	1.33 (1.03–1.72)
26–30	4588	7.6 (6.9–8.4)	1.72 (1.37–2.16)	1.29 (1.01–1.65)
31–35	6777	6.0 (5.5–6.6)	1.34 (1.08–1.68)	0.99 (0.78–1.26)
36–40	6777	5.7 (5.1–6.2)	1.26 (1.01–1.57)	0.97 (0.76–1.23)
41–45	3808	5.8 (5.1–6.6)	1.29 (1.02–1.65)	0.98 (0.75–1.26)
46–50	2099	5.4 (4.5–6.5)	1.20 (0.91–1.58)	0.98 (0.73–1.31)
51–55	1232	4.1 (3.1–5.4)	0.90 (0.64–1.27)	0.72 (0.50–1.03)
≥56	1941	4.9 (4.0–6.0)	1.09 (0.82–1.45)	0.98 (0.73–1.33)
Lifetime No. of sexual partners				
0	550	1.6 (0.8–3.1)	0.61 (0.30–1.26)	0.64 (0.32–1.28)
1	7831	3.5 (3.1–3.9)	1.0	1.0
2–4	8240	5.1 (4.7–5.6)	1.50 (1.28–1.75)	1.37 (1.17–1.62)
5–9	5473	7.6 (6.9–8.3)	2.24 (1.91–2.63)	2.04 (1.73–2.41)
10–14	1887	8.9 (7.6–10.2)	2.41 (2.13–3.20)	2.34 (1.89–2.89)
≥15	1382	13.2 (11.5–15.1)	4.13 (3.39–5.05)	3.36 (2.72–4.17)
Smoking, cigarettes-day				
Never or 1	24 893	5.4 (5.1–5.7)	1.0	1.0
2–10	5145	7.3 (6.6–8.0)	1.35 (1.19–1.52)	1.14 (1.00–1.29)
>10	1929	9.2 (7.9–10.6)	1.74 (1.48–2.05)	1.33 (1.11–1.59)
Residence				
Rural	5874	5.0 (4.4–5.6)	1.0	1.0
Urban	20 425	6.0 (5.6–6.3)	1.22 (1.07–1.39)	1.19 (1.03–1.36)
HPV immunization				
No	30 802	6.2 (5.9–6.5)	1.0	1.0
2HPV	825	6.7 (5.1–8.6)	1.01 (0.76–1.35)	1.17 (0.86–1.58)
4HPV	1132	0.6 (0.2–1.3)	0.10 (0.05–0.20)	0.09 (0.04–0.20)

GWs, genital warts; OR, odds ratio; HPV, human papillomavirus. Note: Missing values were excluded from the analysis.
[a] Adjusted for age.
[b] All factors mutually adjusted.

4. Discussion

This is the first representative study of GWs in the general population of the Czech Republic. Overall, 6.1% of sexually active persons aged 16 to 55 years reported GWs.

Other studies involving self-report have found the lifetime prevalence of GWs to range from 4.0% or 4.4% in Australian men or women aged 16–59 years,[11] to 5.6% in US nationals aged 18–59 years.[12] Slightly higher prevalences were found among Danish women and men aged 18–45 years (10.6% and 7.9%),[13,14] as well as among women of the same age in Iceland (12.0%), Norway (9.5%), and Sweden (11.3%). The estimates in the present study of 5.8% for GWs prevalence in Czech men and 6.1% for Czech women are close to the midpoint of previously published values.

In the present study, the GWs incidence rate of 0.83% in those aged 16–35 years who experienced a first GWs episode in the year 2013, was similar to that documented in 2010 for Czech women.[15] These numbers are slightly higher than the annual incidence rates per 100 000 sexually active persons reported in the United Kingdom,[16] France,[17] Spain,[18] and Germany,[19] but still lower than the percentages of newly acquired GWs per year reported in women in the Nordic countries, i.e. 1.3% in Denmark, 1.9% in Iceland, 1.1% in Norway, and 1.0% in Sweden.[14]

In agreement with the results of others studies,[12,20] the peak occurrence of GWs in men seen in the present study occurred slightly later in life than that in women. As found in a study from the USA, no statistically significant differences in GWs prevalence or incidence rates were identified between adult men and women.[21] However, the results of other surveys have already suggested higher incidence rates in men than women,[18,20] as well as the opposite.[12,19]

Besides methodological differences in study design, differences in the epidemiology of GWs between countries can be explained by geographical and cultural variations in sexual behaviour. In addition, epidemiological knowledge across the world has shown an increasing trend in the occurrence of GWs in the last 30–40 years;[14,20,22] this could also have contributed to the different rates estimated in distinct years over the last 15 years.

Sexual behaviour was found to be the strongest risk predictor for GWs burden in both men and women. This is the first study to estimate the risk of acquiring GWs when having an infected sexual partner. The probability of contracting GWs in these circumstances was found to be almost 17 times higher than with a non-infected partner. In fact, there was an 87.6% chance of becoming infected as well, independent of gender.

An increased risk was also observed in men or women who reported having had at least two to four lifetime sexual partners in comparison to those who reported having had one or no sexual partner. Consistent with other studies, the risk of GWs was found to increase with an increasing number of sexual partners.[12–14] Individuals with a prior history of GWs were identified as being 1.8 times more susceptible to a new infection than those with no previous episodes.

It was also discovered that the frequency of GWs correlated with health-related behaviours (heavy smoking) and demographic variables (urban residence). Although both predictors appeared to be risk factors for the acquisition of GWs, heavy smokers and those living in urban areas also reported five or more lifetime sexual partners more frequently than other participants. Therefore it is uncertain whether smoking and residence are confounding or risk factors for GWs. This could also explain why the association between smoking and GWs incidence has been inconsistent across

studies, with some reporting a positive correlation between smoking and the GWs burden,[13,14,23,24] while others have found no such correlation.[25,26]

To our knowledge, this is the first published survey to include immunization with the quadrivalent HPV vaccine as a protective predictor. It is clear that this vaccine contributes to a substantial reduction in GWs burden;[27–29] at least 90% of individuals were protected against the disease after vaccination in comparison to those not vaccinated or immunized with the bivalent HPV vaccine.

A potential limitation of this survey was the lack of a system to routinely register sexually transmitted infections, like that existing in the United Kingdom,[30] in order to confirm the self-reported sexual behaviour. Despite a high participation rate, the possibility of bias pertaining to non-attendance or interview bias cannot be excluded. Another limitation was the absence of information on other health-related or demographic variables as reported in other studies, such as marriage status, other sexually transmitted infections, pregnancy history, contraceptive use, alcohol consumption, contact with a prostitute, etc.

Nevertheless, this epidemiological survey still has much relevance. First, it is the largest study so far to assess the occurrence of GWs in Czech men and women. Second, it is a nationwide investigation with randomized data from the general population in all 14 regions of the Czech Republic. Third, HPV immunization has only recently been established as a predictor of the disease and had not been studied. Fourth, the survey, in contrast to most studies, was not limited to individuals with clinically diagnosed GWs; this enabled attendees to self-diagnose using the pictures included in the questionnaire.

Interestingly, while treatment was refused by only 10% of those infected in the USA and 7.4% in Australia,[4,31] in the present study almost 23% of attendees did not require treatment for GWs, most likely because they were not aware of the infection.

In conclusion, this study showed the overall prevalence of GWs in the Czech population aged 16–55 years to be 5.8%; however, incidence rates are rising fast, as demonstrated by the growing number of cases per year, increasing from an average of 205.4 lifetime cases to 441.8 cases per 100 000 person-years between 2010 and 2013. As such, vaccination against HPV types 6 and 11 together with types 16 and 18, or eventually with additional types 31, 33, 45, 52, and 58 (and not just HPV16 and 18) must become more widely adopted, because this is the only highly effective instrument against what is an increasingly problematic situation. Because GWs are not restricted to women, the absence of routine immunization for boys and the routine immunization of 13-year-old Czech girls with any type of HPV vaccine will no longer be sufficiently effective to control this disease.

Acknowledgement

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