

GENERAL AWARENESS OF THE HUMAN PAPILLOMAVIRUS (HPV)
INFECTIONS, IMPLICATIONS OF HEALTH EDUCATION
IN CERVICAL CANCER PREVENTION
AND THE PREVALENCE OF HPV:
POPULATION-BASED EPIDEMIOLOGICAL STUDIES

ERIKA MAREK, MSc

PhD thesis



University of Pécs

Medical School

Supervisors:

Péter Gőcze, MD, PhD, D.Sc, UP-MS, Department of Obstetrics and Gynaecology

István Kiss, MD, PhD, UP-MS, Department of Public Health Medicine

Programme leaders:

István Szabó, MD, PhD, D.Sc, UP-MS, Department of Obstetrics and Gynaecology

István Ember, MD, PhD, D.Sc, UP-MS, Department of Public Health Medicine

Head of the Doctoral School:

Sámuel Komoly, MD, PhD, D.Sc, Clinical Medical Sciences Doctoral School, D94

Pécs, 2013

INTRODUCTION

Epidemiology of the human papillomavirus (HPV) infection and cervical cancer

The human papillomavirus (HPV) infection is one of the most prevalent sexually transmitted disease (STD) [1]. The prevalence of genital HPV infection in young women has been estimated to range between 20% and 46% in various countries, but some studies suggest the potential lifetime risk of infection to be around 60% or greater [1,2]. The estimated prevalence of HPV infection in the Hungarian female population is approximately 17.6%, with the highest rates occur in sexually active women among 17-22-year-olds [3,4].

More than 100 different HPV types have been identified about one-third of which infect the genitals [5,6]. Genital HPV types have been classified into two main groups reflecting their oncogenic risk to induce invasive cancer. Since human papillomavirus DNA can be detected from more than 95% of all cervical tumors, epidemiological studies established causal association between persistent infection with certain high-risk (HR) types of HPV and the development of cervical cancer [1,2,7]. Recent studies indicated evidence for the likely role of oncogenic HPV types in the development of 88-94% of anal cancers, 64-91% of vaginal cancers and 25-36% of the oropharyngeal cancers [6,8,9]. Cancer of the cervix uteri is the second most common gynaecological cancer among women [10]. Hungary with approximately 1100 new cases diagnosed and 500 deaths every year takes the fourth place regarding the incidence, and the sixth regarding the mortality of cervical cancer among the member countries of the European Union [11].

HPV infection is a necessary cause of cervical cancer, but it is not a sufficient cause. Promiscuous sexual behaviour (e.g. large number of sexual partners) has been clearly established as a predominant risk factor for acquiring genital HPV infection [1,12,13]. The role of the 'male factor': the male partners' lifetime sex partners should not be neglected as risk [13]. Men having regular intercourse with female sex workers (who can be regarded as reservoirs of HR-HPV) may be considered as vectors carrying the virus to their wives, thus place them at increased risk of developing cervical cancer [12,13].

Primary and secondary prevention of the HPV infections and cervical cancer

Cervical cancer screening with PAP smears complemented with colposcopy is highly effective in reducing incidence and mortality of invasive cervical cancer. In Hungary it is recommended to take part in cytological screening at least every three years after starting sexual activity or between the ages 25-65 years. As no exact data are available, it can only be estimated that in Hungary 36-45% of the female population aged 18 years and above present for regular gynaecological screening (3-year coverage). The estimated one-year coverage of participation is lower, approximately 24.3% [14].

The recognition of the strong causal association between HPV infection and cervical cancer has led two drug companies to develop prototypes of prophylactic vaccines (Merck/Silgard

a quadrivalent and GSK/Cervarix a bivalent vaccine). In order to maximise the effectiveness, the most recent recommendations include the administration of the HPV vaccine to adolescents and young adult females (aged 9-26) preferably before they become sexually active [15]. The vaccines have been available in Hungary since December, 2006. Unlike in several European countries, in Hungary the cost of the HPV vaccine is not even partially subsidised by the National Health Insurance Fund (OEP). On the other hand, vaccinating adolescent girls have been in part or totally subsidised by an increasing number of local governments.

The role of health education in cervical cancer prevention

Since 2010 school-based immunisation programs (i.e. informing the students and their parents about HPV vaccination and directing them to their pediatrician or gynaecologist entitled to administer the vaccine) have been initiated in Hungary. Still, the estimated proportion of the female population vaccinated is nearly 10% in the 12-26 year-old age cohort. This may suggest, that in Hungary the introduction of the HPV vaccination was not accompanied by informing adolescents. This might also contribute to adolescents' knowledge gaps, while parental knowledge remained also low [16]. It is important to note that in Hungary, there is no specific education focusing on the prevention of cervical cancer or STDs incorporated into high school curriculum. These issues are generally discussed in relation to the reproductive system: one or two lessons at primary school (for students aged 13-14) and the same number at high school (for students aged 16-17). Sex education and STD prevention education may vary between schools and usually depend on the preferences of the biology teacher and commitment of the school nurses.

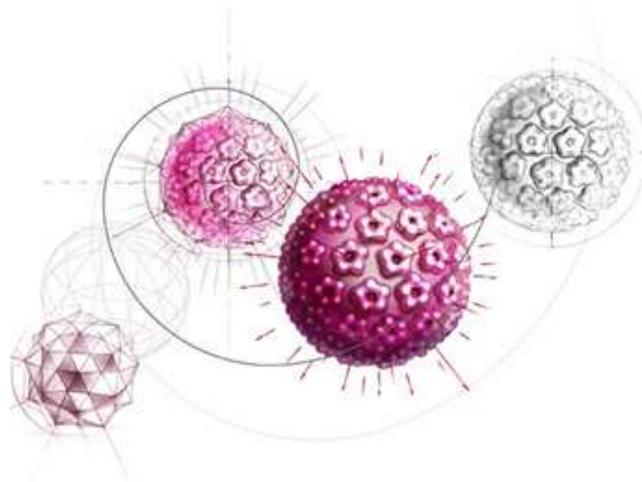
As in Hungary gynaecological screening is mainly opportunistic and the HPV vaccination is optional, it is very important that the general population be educated about the opportunities of cervical cancer prevention, so that informed decision regarding screening and vaccination could be made. The acceptance of HPV vaccination may increase when individuals are properly informed about the risks and benefits of the vaccine [17]. Having a low level of knowledge was reported to be a considerable barrier to the acceptance of the vaccine [18,19]. It has been suggested that interventions targeting at creating understanding of the risks associated with an HPV infection may have positive impact on HPV vaccine acceptability [17-19]. On the other hand, the target population itself has also expressed a sound need for receiving further information on sexual health issues, including HPV vaccination [20]. Furthermore, lack of knowledge about HPV prevalence and its transmission may have direct implication for adolescents' future health practices including sexual behaviour, condom use and participation in cervical screening [16]. Still, the contribution of health education (an integral part of primary prevention) for preventing cervical cancer is often despised and ignored [21].

AIMS

1. **As the first stage of the research, through a nationwide questionnaire survey in a representative sample of the Hungarian population (both males and females):**
 - 1.1. to explore awareness of HPV infection and cervical cancer and to assess beliefs and attitudes towards HPV vaccination 3 years following the introduction of the vaccine in Hungary
 - 1.2. to determine factors affecting the uptake of HPV vaccinations and to identify the main obstacles of the primary and secondary prevention of cervical cancer in Hungary

2. **Based on the results of the first stage, we designed and conducted a brief, HPV-focused educational intervention with the following aims:**
 - 2.1. to evaluate changes in adolescents' awareness, health beliefs, attitudes of cervical cancer prevention as well as to detect improvement in their sexual behaviour due to the intervention
 - 2.2. to assess the present deficiencies and future tasks of health education and health promotion concerning cervical cancer prevention

3. **In the third study we investigated the prevalence of HPV in a highly vulnerable population of female sex workers (FSWs) aiming:**
 - 3.1. to determine the HPV prevalence and type distribution of this high risk population at cervical, anal and oropharyngeal sites in comparison with those of the general female population
 - 3.2. to assess association between HPV prevalence at different locations and sexual behaviour, condom usage



STUDY POPULATION AND METHODS

1. Population-based nationwide survey on knowledge and attitudes

Study population, inclusion criteria

A nationwide questionnaire survey was conducted regarding HPV infections and vaccination in 16 Hungarian cities and towns, covering each of the 7 administrative regions of Hungary between January and May, 2009

Our survey had four main target populations:

1. middle adolescents, represented by students of primary school (age range 12-14 years, 596 persons, 23.3%),
2. late adolescents: students attending secondary school (age range 15-19 years, 1173 persons, 45.9%),
3. young adults represented by college students (appr. 19-30 years of age, 298 persons, 11.7%) and
4. parents of adolescent children to represent the middle-aged generation (487 persons, 19.1%).

The types of schools and classes at schools were represented equally. Neither of the selected schools were involved in the HPV vaccination promoting campaign prior to the survey. The number of participants enrolled in the study was 2554, with a response rate higher than 90%. More than half of the participants were females (1535 persons) and 1019 (40%) were males. The vast majority of respondents (2293 persons) came from urban areas while 10% were from rural settlements (261 persons). Responses from 11 participants who did not indicate their sex or age were excluded from the analysis.

The questionnaire survey

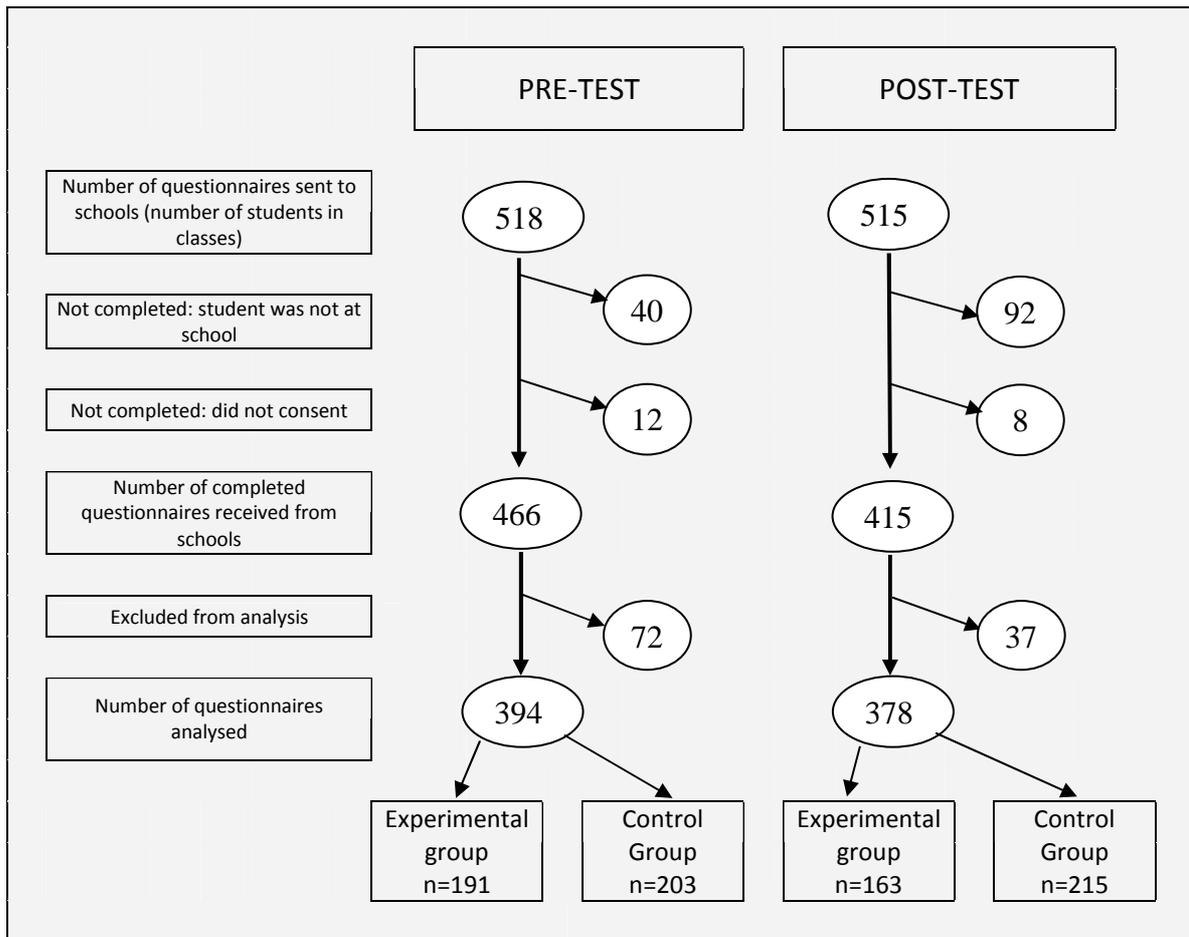
The survey instruments was a self-administered anonymous questionnaire with 31 (34 for adults) items. The questions inquired about basic demographics (age, gender and location), HPV knowledge, cervical cancer knowledge, other STDs, routes of transmission, prevention of STDs and preferred information sources, attitudes and beliefs concerning screening and vaccinating in general, and HPV vaccination in particular. Data regarding participants' exposure to health informants were also obtained.

2. Efficacy assessment of an HPV-focused educational intervention

Study population, the questionnaire survey

Adolescents of public secondary schools were involved in the educational intervention study conducted between September, 2010 and February, 2011 in Baranya County, Southern Hungary. The two vocational schools invited were matched by their profile, benchmark and age-composition. One school was selected to act as 'the experimental-group', in which the education was undertaken, the other school was named as 'the control-group' in which we conducted only two questionnaire surveys with no any intervention between the two occasions (Table 1.).

Table 1 Enrollment of the study population by the intervention study



The survey instrument was a self-administered anonymous questionnaire with 47 items. The items inquired about certain demographics, HPV and cervical cancer knowledge, beliefs and attitudes towards screening and vaccination. Several questions focused on finding out about the participants' past and current sexual behaviour.

The process of the educational intervention

The education was performed during the students' regular classes in October, 2010. The size of the audience per class ranged between 25 and 33. The total number of students educated was 191. The educational program consisted of a 45-min long lesson, including a didactic slide-show presentation covering information about viral life-cycle and the HPV, the female reproductive system focusing on the cervix, the procedure of gynaecological screening, risk factors of cervical cancer and methods of prevention. Cytobrush and Cusco-speculum were demonstrated. The interactive presentation was followed by a short (5-10 min) question and answer session and finally, the students were provided with hand-outs containing key-messages. Three months following the intervention each group was re-evaluated with the same questionnaire.

3. Methods of HPV screening of female sex workers (FSWs)

Enrollment of study population

The study was conducted between April, 2009 and May, 2011 including 34 sex workers (mean age: 28.38, SD:8.14) and a control group of 52 females of the general population matched for age with the FSWs (mean age: 27.65, SD:7.56) in Pecs, Hungary. Sex workers who came for routine STD screening to the local venereologist (obliged by law in every three months) were enrolled into the study. Control females were recruited during their regular visit to their gynaecologist.

Investigating sexual behaviour by questionnaire survey

Self-administered anonymous questionnaires with 27 items were completed by each participants. The items inquired about some demographics, HPV and cervical cancer knowledge, perception of STD prevention and HPV vaccination. Several questions focused on finding out about the participants' sexual behaviour, condom usage.

Collecting clinical specimens from cervical, oropharyngeal and anal sites

Material for HPV analysis was collected by rotating one cervical swab over the entire cervical surface and in the cervical os. Anal specimens were collected by inserting another swab about 1 cm into the rectum, gently rotated and withdrawn. Oropharyngeal sample was obtained by scraping a third swab around the posterior oropharyngeal mucosal membrane. After swabbing, the swab applicator was cut off, and each swabs were placed into a sample transport vial (provided by GenoID). Vials were stored at -20°C until testing.

HPV DNA testing

HPV DNA detection was performed using Full Spectrum HPV PCR amplification and detection, as described earlier [22]. The high-risk HPV positive samples were genotyped with types-specific probes using the same technology.

4. Statistical analysis

Statistical Package for the Social Sciences (SPSS) for Windows Release 6.1.4 Standard Version was used for data analysis. Basic descriptive statistics and frequency calculations were performed on all variables. Bivariate relationship between nominal variables were assessed using Pearson's χ^2 test and Fischer's Exact tests were employed when sample sizes were small (more than 20% of the contingency table cells have expected cell frequencies less than 5). The level of statistical significance was set at 0.05 throughout the whole study. Rank-correlation was used to analyse the relationship between the number of sources and participants' answers.

SUMMARY OF THE THESIS, PRACTICAL APPLICATIONS

1. General awareness of HPV infection and cervical cancer and attitudes towards HPV vaccination: obstacles of prevention

As a first part of our research we conducted a nationwide questionnaire survey that offers a first insight into awareness of the general Hungarian population (both males and females in four age-groups) concerning HPV infection and its consequences as well as into their attitudes towards the prevention of cervical cancer by screening and HPV vaccination 3 years following the introduction of the HPV vaccine in Hungary.

- Three main obstacles to the wide implementation of HPV vaccination program were identified:
 1. Lack of adequate knowledge about HPV infection and vaccination
 - a majority of the target population was unaware of the HPV infection (65%) and the HPV vaccination was even lesser-known (30%);
 - great confusion was detected in the consideration of HPV as an STD, the potential routes of transmission and the role of condoms in prevention;
 - recent extensive school-based AIDS/HIV educational campaigns has overshadowed the education of other STDs, including HPV infection.
 2. Intense distrust in proven scientific facts as well as towards the domestic health care system
 - a considerable proportion (20-25%) of study population did not believe that cervical cancer is caused by HPV and that cervical cancer may be prevented by vaccination. 15% even did not believe in the effectiveness of vaccinations at all;
 - more than half of the Hungarian adults did not trust in domestic health care (55%) as well as in the preparedness of the Hungarian doctors (45%).
 3. Financial concerns of the high cost of the vaccine
 - a vast majority of female respondents (76%) expressed desire towards being vaccinated in case it was free (91% of adolescents), but willingness decreased by half if there is a need to pay for the vaccination;
 - the price of the vaccine was considerably underestimated by study population;
 - 90% of participants found the price of the vaccine disproportionately high correlated to average domestic earnings;
 - 80% of adults were unable to afford this price (appr. 90.000 HUF).
- Sociodemographic determinants of the awareness and acceptability of the vaccine were also explored as well as the exposure to health information:
 - we confirmed that older age, female gender and greater exposure to health informants correlates with better knowledge on STDs including HPV;
 - we correlated the greater exposure to health informants also with more positive attitudes and beliefs towards preventive measures.

- The main anticipated sources of information about STDs were identified (considering the differing expectations of males and females as well as the different age-groups) hoping our results may be useful in designing future educational interventions.

In conclusion, the HPV vaccination has been introduced more than 3 years ago, but the extensive implementation of the vaccinating program has several obstacles to face. Our findings indicate that information on HPV from the media campaign related to the introduction of the vaccination may not have reached sufficiently nor the target adolescents neither the decision-maker adult population. It is encouraging, that despite the difficulties identified (incomplete knowledge, distrust and financial concerns) the study population demonstrated generally positive attitudes towards HPV vaccination and also expressed desire to learn more about STDs, including HPV and its association with cervical cancer. Therefore, in addition to comprehensive financial support of the HPV vaccine, well-designed, HPV-focused educational interventions would be necessary for the efficacious prevention of HPV-related conditions. The increasing knowledge enhances the acceptance of vaccination and it may also improve the awareness about the risks associated with HPV infections. Thus, responsible sexual behaviour may reduce the high incidence and mortality of cervical cancer in Hungary in the future.

2. Effects of an HPV-focused educational intervention on adolescents' knowledge, beliefs, attitudes and sexual behaviour

The alarming morbidity and mortality data of a largely preventable disease, as well as the thought-provoking results of the first stage of the present dissertation (demonstrating considerable gaps in Hungarian adolescents' knowledge) led us to the recognition of the urgent need for well-designed, HPV-focused educational interventions.

The second phase of the dissertation was meant to design, conduct and evaluate the impact of a school-based educational intervention on cervical cancer prevention. At this phase of the research we investigated into **changes** in adolescents' knowledge, beliefs and attitudes towards the prevention of HPV infection and cervical cancer and also explored the effects of the program on adolescents' sexual behaviour following an intermediate, 3-months follow-up period. Results were compared with similar control group of students from another vocational school matched by profile, benchmark and age-composition.

- Considerably increased baseline perception of HPV infection and HPV vaccination was observed in comparison with results of the first phase of the research (nationwide survey, 2009). This improvement may be attributed to some newly developed media-campaign initiatives.

- Sharp rise in adolescents' awareness and also enhanced beliefs towards health care issues (such as screening and vaccination) were demonstrated due to our educational intervention that were sustainable after 3 months:
 - awareness of the absence of symptoms of early cervical cancer has increased significantly only in the group educated (28%→48%, $p<0.05$);
 - similarly, significantly strengthened beliefs were detected in experimental group regarding the question: '*Could HPV cause cervical cancer?*' (65%→81%, $p<0.05$), while no change was observed in the control group.

- These findings indicate that such initiatives may be appropriate in increasing awareness and enhancing beliefs, while we also detected only little impact on attitudes towards prevention. We may confirm that to change attitudes is a complex task which is hard to influence.

- We identified the most common reasons that may prevent girls from attending gynaecological screening:
 - half of girls would visit the gynaecologist in case they experienced trouble, another 50% of girls thought this visit extremely intimate. Fear of pain was indicated as a relevant concern for a quarter of female students.

- No clear changes in sexual behaviour were detected due to the program, however, as a limitation it was noted that both the questionnaire and the intervention was designed focusing specifically on cervical cancer prevention. On the other hand, students' responses provided us a valuable, updated insight into adolescents' current sexual practices, a delicate area of research that still requires further exploration.

- We demonstrated that the general Hungarian adolescent population practises extremely risky sexual behaviour, which is acknowledged as the most significant risk factor for developing cervical cancer:
 - one-third of sexually active adolescents (34%) reported to have initiated sexual contact at the age of 13-14 years and two-third to have had already two or more sexual partners;
 - a considerable part (41%) had already participated in 'one-night relationships';
 - nearly half of them (44%) have already had an intercourse without any protection.

In conclusion, in addition to providing adolescents with clear information about the implications of HPV infection and addressing their fears of screening and vaccination, as they may also be barriers to prevention, health education should also focus on improving safe sex behaviour by promoting the use of condoms and reducing the number of sexual partners.

Further studies with a longer duration and with multiple follow-up points are also needed to investigate the long-term outcomes of various educational interventions in order to highlight their value and effectiveness and also to use their findings for the development of future educational programs. Comprehensive and sustainable HPV and cervical cancer education should be incorporated into health education at schools from the early teen-ages in order to achieve the desired impact, which is to limit the spread of HPV, thus decreasing the risk for cervical cancer.

3. Assessment of HPV prevalence in female sex workers in relation to their sexual behaviour: promiscuity and condom usage

In the third part of our research we investigated into the prevalence of HPV infection in cervical, oropharyngeal and anal samples of a high-risk population for STDs: the sex workers in the Southern Hungarian region. We assessed the association between their sexual behaviour, condom usage and their overall, high-risk (HR) and multiply HPV prevalence and compared those with results of the general female population. Perception of and attitudes towards the prevention of HPV and other STDs were also investigated.

- A significantly higher HPV prevalence, particularly the HR- and multiply HPV prevalence of the cervix and the anal samples of FSWs was demonstrated in comparison with those of the general female population:
 - HPV DNA was detected in at least one location in 82.4% of the FSWs and in 46.2% of control females ($p < 0.05$);
 - as for the cervical swabs:
 - overall HPV: 65% vs. 35% ($p < 0.05$)
 - HR-HPV: 44% vs. 21% ($p < 0.05$)
 - as for the anal swabs:
 - overall HPV: 50% vs. 15% ($p < 0.05$)
 - HR-HPV: 29% vs. 4% ($p < 0.05$)
- Our results confirm studies reporting association between highly promiscuous sexual behaviour and increased risk of acquiring HPV infection.
- Our findings may support the role of promiscuity in the increased prevalence of oropharyngeal HPV infection as well, and confirms that the use of condom may not protect from HPV infection:
 - a great majority of control females practises oral sex without condoms (71%) and only one in ten (11%) was detected positive for HPV DNA, while a majority of FSWs applies condom always (55%) or generally (33%) during oral sex, still, a quarter of them was HPV-infected at oropharyngeal sites (24%).

As a consequence, due to their higher promiscuity, FSWs are at a greater risk for acquiring oropharyngeal HPV-infection and thereby developing oropharyngeal cancer than females of the general population.

- Investigation of HPV prevalence of the anal samples in relation to condom usage during anal sex may reaffirm that there is no relationship between anal sex practices and the HPV infection of the anal mucosa:
 - a significantly higher HPV prevalence was detected from the anal samples of both FSWs and controls who are not practising anal sex than from those who does (59% and 75% vs. 41% and 25%, respectively);
 - furthermore, HPV was detected more frequently from the samples of those participants who had reported consistent condom usage during anal sex (78%).
- We detected a significantly higher proportion of FSWs's reported history of genital warts (71% vs, 27%, $p < 0.05$) and also more considerable history of other STDs.
- Perception of HPV infection and HPV vaccination was significantly lower among FSWs compared to females of the general population ($p < 0.05$). Sex workers showed positive attitudes towards HPV vaccination, the main concern arised was the price of the vaccine.

In conclusion, the findings of this preliminary investigation, which is the first of its kind in Hungary demonstrate a significantly higher HPV prevalence of FSWs at three different sites in comparison with similar control group. These highly infected sex workers are sources of HPV infection for the general population since their male clients, as vectors may infect their wives, thus, FSWs should be considered as priority group for HPV and cervical cancer preventing programmes. Strengthened STD services are proposed supplemented with regular cervical screening, treatment counseling, supply of condoms and education about the risks and consequences of an HPV infection as well as about the methods of prevention. Designing and implementing effective interventions aiming at sexual risk reduction for this high risk population would be of crucial importance from public health aspects.

REFERENCES

- [1] Koutsky L. Epidemiology of genital human papillomavirus infection. *Am J Med* 1997;**102**:3–8.
- [2] Ho GY, Bierman R, Beardsley L, Chang CJ, Burk RD. Natural history of cervicovaginal papillomavirus infection in young women. *N Engl J Med* 1998;**338**:423–8.
- [3] Deák J, Cseh I, Szöllősi J, Pulay T, Kornya L, Bak M, et al. Human papillomavírus-fertőzés kimutatás nukleinsav hibridizációs módszerrel (multicentrikus tanulmány). [Detection of human papillomavirus infection by the nucleic acid hybridization method (a multicenter study)]. *Orv Hetil* 1999;**140(3)**:115–20. [Article in Hungarian]
- [4] Kornya L, Cseh I, Deak J, Bak M, Fulop V. The diagnostics and prevalence of genital human papillomavirus (HPV) infection in Hungary. *Eur J Obstet Gynecol Reprod Biol* 2002;**100(2)**:231–6.
- [5] de Villiers EM, Fauquet C, Broker TR, Bernard, HU, zur Hausen, H. Classification of papillomaviruses. *Virology* 2004;**324**:17–27.
- [6] Munoz N, Castellsague X, de González AB, Gissmann L. Chapter 1: HPV in the etiology of human cancer. *Vaccine* 2006;**24(S3)**:1–10.
- [7] zur Hausen H. Viruses in human cancer. *Science* 1991;**254**:1167–73.
- [8] Clark MA, Hartley A, Geh JI. Cancer of the anal canal. *The Lancet Oncology* 2004;**5**:149–57.
- [10] Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. *CA Cancer J Clin* 2005;**55**:74–108.
- [9] Gillison ML, Lowy DR. A causal role for human papillomavirus in head and neck cancer. *The Lancet* 2004;**363(9420)**:1488–9.
- [11] WHO/ICO Information Centre on HPV and Cervical Cancer (HPV Information Centre). Human Papillomavirus and Related Cancers in Hungary. Summary Report 2010. Available at: www.who.int/hpvcentre [Accessed 23 May, 2012].
- [12] Bosch FX, Muñoz N, de Sanjosé S, Guerrerro E, Ghaffari AM, Kaldor J, et al. Importance of human papillomavirus endemicity in the incidence of cervical cancer: an extension of the hypothesis on sexual behavior. *Cancer Epidemiol Biomarkers Prev* 1994;**3(5)**:375–9.
- [13] Burk RD, Ho GY, Beardsley L, Lempa M, Peters M, Bierman R. Sexual Behavior and Partner Characteristics Are the Predominant Risk Factors for Genital Human Papillomavirus Infection in Young Women *J Inf Dis* 1996;**174(4)**:679–89.
- [14] Boncz I, Sebestyén A, Dobrossy L, Kovacs A, Budai A, Székely T. A méhnyakszűrés részvételi mutatói Magyarországon. (The coverage of cervical screening in Hungary.) *Orv Hetil* 2007;**148(46)**:2177–82 [Article in Hungarian]
- [15] Editorial: Who should be vaccinated against human papillomavirus? *The Lancet Infectious Diseases* 2006;**6(1)**:1.
- [16] Robbins SCC, Bernard D, McCaffery K, Brotherton J, Garland S, Skinner SR. 'Is cancer contagious?': Australian adolescent girls and their parents: Making the most of limited information about HPV and HPV vaccination. *Vaccine* 2010;**28**:3398–408.

- [17] Davis K, Dickman ED, Ferris D, Dias JK. Human papillomavirus vaccine acceptability among parents of 10- to 15-year-old adolescents. *J Low Genit Tract Dis* 2004;**8**(3):188–94.
- [18] Pelucci C, Esposito S, Galeone C, Semino M, Sabatini C, Piccioli I, et al. Knowledge of human papillomavirus infection and its prevention among adolescents and parents in the greater Milan area, Northern Italy. *BMC Public Health* 2010;**10**:378–89.
- [19] Woodhall SC, Lehtinen M, Verho T, Huhtala H, Hokkanen M, Kosunen E. Anticipated Acceptance of HPV Vaccination at the Baseline of Implementation: A Survey of Parental and Adolescent Knowledge and Attitudes in Finland. *J Adol Health* 2007;**40**(5):466–9.
- [20] Marek E, Dergez T, Rebek-Nagy G, Kricskovics A, Kovacs K, Bozsa S, et al. Adolescents' awareness of HPV infections and attitudes towards HPV vaccination 3 years following the introduction of the HPV vaccine in Hungary. *Vaccine* 2011;**29**:8591–8.
- [21] Shepherd J, Weston R, Peersman G, Napuli IZ. Interventions for encouraging sexual lifestyles and behaviours intended to prevent cervical cancer (Cochrane Review). *Cochrane Database Syst Rev*. 2000;**(2)**:CD001035.
- [22] Jeney C, Takács T, Sebe A, Schaff Z. Detection and typing of 46 genital human papillomaviruses by the L1F/L1R primer system based multiplex PCR and hybridization. *J Virol Methods* 2007;**140**(1-2):32–42.

ACKNOWLEDGEMENT

Hereby, I would like to express my thanks and gratitude...

- ...to my supervisors, Prof. Dr. Péter Gőcze and Prof. Dr. István Kiss for their thought-provoking ideas and professional advice during my PhD studies;
- ...to my doctoral programme leaders, Prof. Dr. István Szabó and Prof. Dr. István Ember for the opportunity to work and improve myself in their Departments;
- ...to Dr. Gábor Rébék-Nagy for his kind help in the English proofreading of my papers;
- ...to Timi for the statistics;
- ...to Nóra and Anti for their support and friendship;
- ... and especially to my husband and my sweet twinnies for their patience and love.

PUBLICATIONS IN THE TOPIC OF THE THESIS

1. **Marek E.**, Dergez T., Rebek-Nagy G., Kricskovics A., Kovacs K., Bozsa S., Kiss I., Ember I., Gocze P. Adolescents' awareness of HPV infections and attitudes towards HPV vaccination 3 years following the introduction of the HPV vaccine in Hungary.
Vaccine 2011;**29(47)**:8591-8. IF: 3.766
2. **Marek E.**, Dergez T., Kricskovics A., Kovacs K., Rebek-Nagy G., Gocze K, Kiss I., Ember I., Gocze P. Difficulties in the prevention of cervical cancer: adults' attitudes towards HPV vaccination 3 years after introducing the vaccine in Hungary.
Vaccine 2011;**29(32)**:5122-9 IF: 3.766
3. **Marek E.**, Dergez T., Bozsa Sz., Gocze K., Rebek-Nagy G., Kricskovics A., Kiss I., Ember I., Gocze P. Incomplete knowledge – unclarified roles in sex education: results of a national survey about human papillomavirus infections.
Eur J Cancer Care 2011;**20(6)**:759-68. IF: 1.171
4. **Marek E.**, Gőcze P., Bózsza Sz., Molnár G., Stefanovits Á., Gőcze K.: A HPV fertőzéssel és méhnyakrákkal kapcsolatos ismeretek pécsi iskolások és szülők körében.
Magyar Epidemiológia 2010;**7(1)**:35-42. IF: ---
5. **Marek E.**, Dergez T., Rebek-Nagy G., Szilard I., Kiss I., Ember I., Gocze P., D'Cruz G. Effect of an educational intervention on Hungarian adolescents' awareness, beliefs and attitudes on the prevention of cervical cancer
Vaccine 2012;**30(48)**:6824-32 IF: 3.766
6. **Marek E.**, Dergez T., Szilárd I., Kiss I., Gőcze P. Méhnyakrák-prevenció az iskolában: egy rövid oktatási program hatékonysága a serdülőkorúak ismereteire, attitűdjeire és szexuális magatartására.
Egészségfejlesztés (under publication) IF: ---

Cummulative IF: 12.469

Independent citations: 10

Oral presentations

1. **E. Marek**, P. Gőcze, Sz. Bózsza, G. Molnár, Á. Stefanovits, M. Benczik, R. Koiss, K. Gőcze: Survey of knowledge about the HPV infection and cervical cancer among students and parents in Hungary. Bridges in Life Sciences US –CEE Regional Networking Meeting IV, 4, April, 2009, Debrecen, Hungary
2. **E. Marek**, Sz. Bózsza, G. Molnár, Á. Stefanovits, K. Gőcze, M. Benczik, P. Gőcze. Knowledge about HPV infection and attitudes toward HPV vaccination in Hungary. Symposium for Graduate Students in Biology, 12-13, Nov, 2009, Pécs, Hungary

3. **E. Marek**, A. Cseh, K. Gőcze, M. Benczik, D. Várszegi, P. Gőcze, Sz. Bózsa. Prostitutes' cervical, pharyngeal and anal HPV status and attitudes toward HPV vaccination. Symposium for Graduate Students in Biology, 12-13, Nov, 2009, Pécs, Hungary
4. Bózsa Sz., Cseh A., Gőcze K., Gőcze P., Benczik M., Bódis J., **Marek E.** Cervicalis, pharyngealis és analis HPV status felmérése a prostituáltak STD szűrése során. Fiatal Nőorvosok V. Kongresszusa, Balatonfüred, 2009. nov. 12-14.
5. Bózsa Sz., **Marek E.**, Cseh A., Gőcze K., Várszegi D., Benczik M., Gőcze P.: Humán Papillomavírus fertőzés gyakorisága a prostituáltak cervicalis, pharyngealis és analis mintáiban a Dél-Dunántúlon. A MNT XXIX. Nagygyűlése, Debrecen, 2010. május 20-22.
6. Cseh A., Bózsa Sz., Benczik M., Várszegi D., Gőcze K., Gőcze P., **Marek E.** Dél-dunántúli prostituáltak HPV statusa és HPV oltás iránti affinitása. Magyar Szexuális Medicina Társaság I. Tudományos ülése – Továbbképző Tanfolyam, Budapest, 2010. május 13-15.
7. **Marek E.**, Gőcze P., Molnár G., Stefanovits Á., Benczik M., Koiss R., Gőcze K, Bózsa Sz.: HPV-fertőzésekkel kapcsolatos ismeretek felmérése különböző hazai populációkban. MSZMT I. Tudományos ülése -Továbbképző Tanfolyam, Budapest, 2010. május 13-15.
8. **Marek E.**, Cseh A., Gőcze K., Várszegi D., Benczik M., Gőcze P., Bózsa Sz.: Female Sex Workers' HPV status and affinity toward HPV vaccination in Southern Hungary. 3rd Conference of Migrant and Ethnic Minority Health in Europe, 27-29, May, 2010, Pécs, Hungary
9. **E. Marek**, T. Dergez, K. Gőcze, A. Kricskovics, Sz. Bózsa, K. Kovács, I. Kiss, I. Ember, P. Gőcze: Difficulties in the primary prevention of cervical carcinoma in Hungary. International Conference of Preventive Medicine and Public Health, 19-20, Nov, 2010, Pécs, Hungary
10. **E Marek**, T Dergez, G Rebek-Nagy, I Szilard, Z Katz, I Kiss I Ember, P Gocze: Evaluation of the impact of a brief, HPV-focused educational intervention on Hungarian adolescents' knowledge, beliefs, attitudes and sexual behaviour. 5th European Public Health Conference, 8–10, Nov, 2012, Portomaso, St. Julian's, Malta
Abstract: *Eur J Public Health* 2012;**22(Suppl 2):67** IF:2.728

Poster presentations

1. **Marek E.**, Gőcze P., Bózsa Sz., Molnár G, Stefanovits Á., Gőcze K.: Ismeretek a Human Papilloma Vírus (HPV) fertőzések következményeiről és a megelőzés lehetőségeiről általános-, középiskolás, egyetemista és szülői populációkban Pécsen. A Magyar Család- és Nővédelmi Tudományos Társaság XXXIII. Kongresszusa, Gyula, 2008. november 13-15.
Best poster of the Congress, 1st prize
2. **E. Marek**, P. Gőcze, Sz. Bózsa, G. Molnár, Á. Stefanovits, R. Koiss, M. Benczik, K. Gőcze. Survey of knowledge about HPV infection in Hungary. 25th International Papillomavirus Conference, May, 8-14, 2009, Malmö, Sweden

3. **Marek E.**, Bózsa Sz., Cseh A., Benczik M., Várszegi D., Gőcze K., Gőcze P. Prostitúáltak cervicalis, pharyngealis és analis HPV statusának elemzése. Magyar STD Társaság XIV. Nagygyűlése – 3. Venerológiai Továbbképző Tanfolyam. Budapest, 2009. nov. 26-28.
4. **Marek E.**, Gőcze P., Bózsa Sz., Molnár G., Stefanovits Á., Benczik M., Koiss R., Gőcze K. Hazai felmérés a HPV-fertőzésekkel kapcsolatos ismeretekről. Magyar STD Társaság XIV. Nagygyűlése – 3. Venerológiai Továbbképző Tanfolyam. Budapest, 2009. nov. 26-28.
5. **Marek E.**, Gőcze K., Cseh A., Bózsa Sz., Várszegi D., Benczik M., Gőcze P. Evaluation of cervical, pharyngeal and anal HPV status of prostitutes. EUROGIN 2010 Conference, CERVICAL CANCER PREVENTION: 20 YEARS OF PROGRESS AND A PATH TO THE FUTURE, 17-20, February, 2010, Monte-Carlo, Monaco
6. **Marek E.**, Cseh A., Gőcze K., Várszegi D., Benczik M., Gőcze P., Bózsa Sz. Evaluation of cervical, pharyngeal and anal HPV status of Female Sex-Workers in Hungary. RECOOP HST Bridges in Life Sciences Annual Scientific Meeting V. 9-11, April, 2010, Lviv, Ukraine
Abstract: *Biopolymers and cell* 2010;26.(N2suppl):102.
7. **Marek E.**, Bózsa Sz., Molnár G., Stefanovits Á., Benczik M., Koiss R., Gőcze K., Gőcze P. Ismeretek a Human Papillomavírus fertőzésről Magyarországon. MAGYAR NŐORVOS TÁRSASÁG XXIX. NAGYGYŰLÉSE, Debrecen, 2010. május 20-22.
8. **Marek E.**, Bózsa Sz., Molnár G., Stefanovits Á., Benczik M., Koiss R., Gőcze K., Gőcze P.: A HPV fertőzések és a méhnyakrák megelőzésével kapcsolatos ismeretek Magyarországon 3 évvel a védőoltás bevezetését követően. MNT Dél- nyugat Dunántúli Szekciójának XII. Kongresszusa, Siófok, 2010. szeptember 10-11.
9. **E. Marek**, T. Dergez, K. Gőcze, Sz. Bózsa, K. Kovacs, P. Gőcze. Nationwide survey of adolescents' attitudes towards HPV vaccination in Hungary. 4th Vaccine and ISV Annual Global Congress, 3-5, October, 2010, Vienna, Austria
10. **Marek E.**, Bózsa Sz., Cseh A., Gőcze K., Benczik M., Várszegi D., Gőcze P.: Csökkenti-e az óvszerhasználat a HPV fertőzés gyakoriságát? MCSNTT XXXIV. Kongresszusa, Pécs, 2010. november 19-20. **Best poster of the Congress, 1st prize**
11. **Marek E.**, Cseh A., Bózsa Sz., Gőcze K., Benczik M., Várszegi D., Gőcze P.: Does condom usage decrease the prevalence of HPV infections? International Conference of Preventive Medicine and Public Health, 19-20, Nov, 2010, Pécs, Hungary
12. **Marek E.**, Bózsa Sz., Cseh A., Stefanovits Á., Gőcze K., Benczik M., Világi Sz. Panka T., Várszegi D., Gőcze P. Promiszkuitás és óvszerhasználat hatása a HPV-fertőzés gyakoriságára. Magyar Nőorvos Társaság Cervixpatológiai Szekció XIX. Tudományos Ülése, Hajdúszoboszló, 2011. március 25-26.
13. **E. Marek**, T. Dergez, A. Kricskovics, G. Rebek-Nagy, Sz. Bózsa, K. Kovacs, K. Gőcze, I. Kiss, P. Gőcze. Major obstacles in the prevention of cervical cancer in Hungary. The 27th International Papillomavirus Conference 17-22, September, 2011, Berlin, Germany