

Barbara Owsianka¹, Maria Gańczak²

EVALUATION OF HUMAN PAPILLOMA VIRUS (HPV) VACCINATION STRATEGIES AND VACCINATION COVERAGE IN ADOLESCENT GIRLS WORLDWIDE

¹Multispecialty Hospital in Zgorzelec

²Department of Public Health, Pomeranian Medical University in Szczecin

ABSTRACT

STUDY OBJECTIVE. An analysis of HPV vaccination strategies and vaccination coverage in adolescent girls worldwide for the last eight years with regard to potential improvement of vaccination coverage rates in Poland.

METHODS. Literature search, covering the period 2006–2014, was performed using Medline. Comparative analysis of HPV vaccination strategies and coverage between Poland and other countries worldwide was conducted.

RESULTS. In the last eight years, a number of countries introduced HPV vaccination for adolescent girls to their national immunization programmes. Vaccination strategies differ, consequently affecting vaccination coverage, ranging from several percent to more than 90%. Usually, there are also disparities at national level. The highest HPV vaccination coverage rates are observed in countries where vaccines are administered in school settings and funded from the national budget. Poland is one of the eight EU countries where HPV vaccination has not been introduced to mandatory immunization programme and where paid vaccination is only provided in primary health care settings. HPV vaccination coverage in adolescent girls is estimated at 7.5-10%.

CONCLUSIONS. Disparities in HPV vaccination coverage rates in adolescent girls worldwide may be due to different strategies of vaccination implementation between countries. Having compared to other countries, the low HPV vaccination coverage in Polish adolescent girls may result from the lack of funding at national level and the fact that vaccines are administered in a primary health care setting. A multidimensional approach, involving the engagement of primary health care and school personnel as well as financial assistance of government at national and local level and the implementation of media campaigns, particularly in regions with high incidence of cervical cancer, could result in an increase of HPV vaccination coverage rates in Poland.

Key words: *human papillomavirus HPV, vaccination against HPV, strategies, vaccination coverage, Poland*

INTRODUCTION

Human papillomavirus (HPV) belongs to *Papilloma-viridae* family. HPV infects the cells of the basal layer of epithelium or mucous membranes of epidermis. Approximately 100 HPV types were identified. Of these, more than 40 may be transmitted via sexual route. HPV types may be classified as oncogenic (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58) and non-oncogenic (1, 2, 3, 4, 6, 7, 10, 11, 40, 42, 43, 44, 54, 61) (1,2).

An estimated 630 million persons are infected with HPV worldwide. Approximately 500 thousands new HPV infections occur every year (2,3). Nearly 80% of cervical cancer cases are reported in developing countries. Epidemiological data vary substantially between geographical regions. A significant population risk is

noted in the countries of Africa, Latin America as well as Asia with the examples being: Thailand, India, Korea, Philippines, Taiwan. Infections with HPV are prevalent in both females and males aged 15-24 years. Up to 50-80% of all sexually active females become infected with HPV at least once in their lifetime (1,2).

Oncogenic potential of HPV. The majority of cervical cancer cases are attributed to high-risk HPV types, especially 16 and 18. They are also associated with serious complications in males, including cancers of penis, anus and genital warts (2,4). For example, since 1970 the prevalence of anal cancer in the Great Britain has increased twofold in females and males (5). These HPV types can also cause malignant oropharyngeal neoplasms and recurrent respiratory papillomatosis (2,6).

It was noted that an association between HPV 16/18 infections and cervical cancer is stronger than that compared to HCV and liver cancer (1). A risk of cancer in daughter of an affected mother is twofold higher compared to the general population (7). Due to population ageing, an increase of HPV infections is expected, especially in developing countries. IARC (International Agency for Research on Cancer) suggests that the number of females who develop and die due to cervical cancer worldwide to 2050 would be threefold higher than in 1990 [1].

Vaccines against HPV. In 2008, Harald zur Hausen was awarded a Nobel Prize for Physiology or Medicine for the discovery of HPV role in causing cervical cancer. His discovery enabled the creation of vaccines against 4 types of HPV (8).

Three HPV vaccines are licensed in Poland, i.e. Silgard (Merck Sharp Dohme: MSD), a quadrivalent vaccine against the following HPV types: 6, 11, 16, 18, Cervarix (GlaxoSmithKline Biologicals), a bivalent vaccine against 16 and 18 types and Gardias (Merck Sharp Dohme) against 6,11,16,18 types (2,9). WHO (World Health Organization), CDC (Centers for Disease Control and Prevention), AAP (American Academy of Pediatrics), ECDC (European Centers for Disease Prevention and Control) as well as a number of other scientific societies recommend HPV vaccination for girls aged 11–12 years and a catch-up vaccination for those at the age of 13–18 as well as persons who are not yet sexually active (10,11). It should be noted that vaccinated persons should also undergo cytology-based screening.

Immunogenicity studies in young females vaccinated with Cervarix demonstrated that HPV16 and

18-specific antibodies are still detectable in 100% of cases up to 8.4 years following vaccination. For females aged 16–26 years vaccinated with Silgard, HPV16-specific antibodies were present in more than 98% of persons tested up to 4 years after vaccination (1). Both vaccines showed 90%–100% effectiveness in the prevention of conditions such as CIN 2/3 and AIS, caused by HPV 16 and 18 in females who were not previously infected with these HPV types (2,8).

MATERIAL AND METHODS

Analysis of data on HPV vaccination strategies in Poland and worldwide was performed, based on literature from 2006 to 2014 accessible in Medline and Science Direct. The following search string was employed: HPV, vaccination, adolescent girls, strategies, costs, funding. Vaccination coverage rates and vaccination financing systems in particular countries were subject to comparative analysis.

RESULTS

Vaccination coverage and HPV vaccination strategies. Since 2006, HPV vaccines (quadrivalent vaccines – Silgard, Gardias and bivalent vaccine – Cervarix) were licensed in more than 100 countries while 6 years later they were introduced to national immunization programmes in at least 40 countries (12). Percentages of vaccinated adolescent girls differ between countries. Fig. 1 presents estimated HPV vaccination coverage in countries worldwide based on literature data.

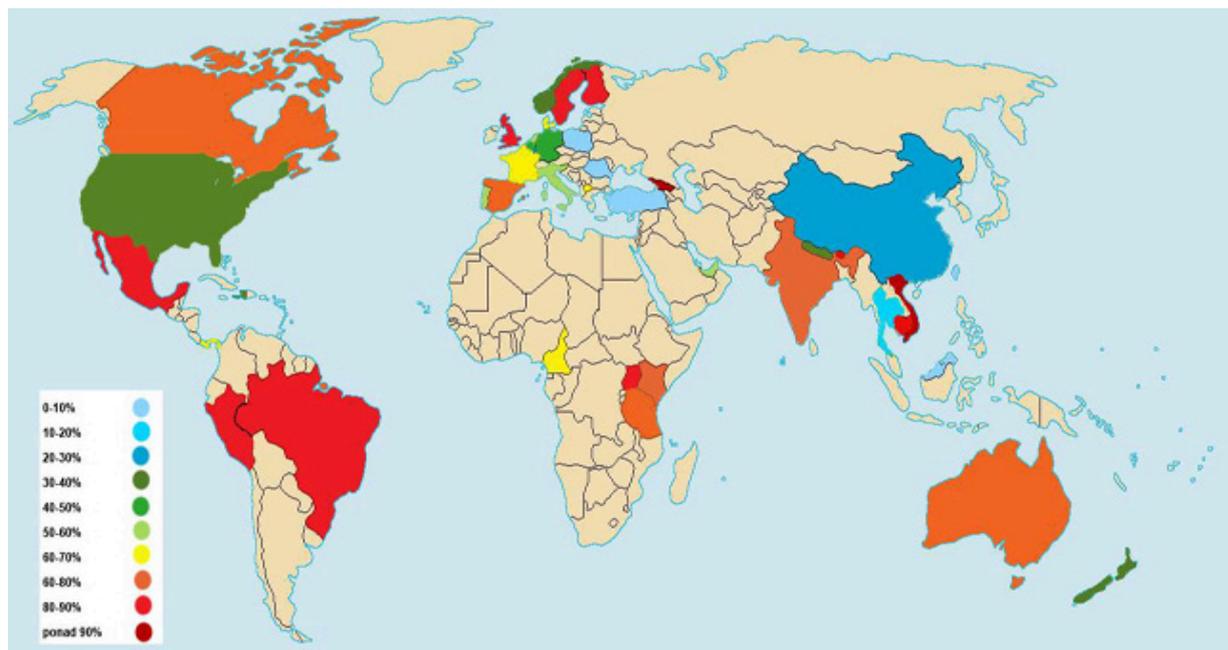


Fig. 1. Estimated HPV vaccination coverage in adolescent girls in selected countries (based on medical literature review).

Australia. Australia was the first country worldwide which in 2007 introduced HPV vaccination free of charge for adolescents aged 12-13 years to the national immunization programme. In 2009, a catch-up programme for young females from 13 to 26 years old was implemented. Vaccination for younger adolescents is offered within school-based immunization programme, thus, vaccination coverage in this group is 75%. The percentage of vaccinated young females aged 18-26 years is lower, amounting to 38% (13).

North America. At the end of 2006, HPV vaccination started to be funded by the government of the United States. There were differences in vaccination implementation with regard to age, gender and place of residence. The highest vaccination coverage (32%) was reported in persons aged 13-17 years and living in north-eastern states. Vaccination outcomes depend substantially on the state's health policy. HPV information is mainly disseminated by media campaigns (14).

Having approved the use of HPV vaccine in 2006 in Canada, it was recommended for girls aged 9-26 years. Since 2010, HPV is also recommended for males at the age of 9-26 years. Irrespective of the similarities regarding vaccination funding between the United States and Canada (public resources), vaccination coverage rates in Canada are higher: 75% and 41% in public schools and catholic schools, respectively. Parents are provided with information on HPV vaccination for children by means of school-based education. Disparities in vaccination coverage rates in adolescent girls results mainly from the fact that girls from less affluent districts cannot attend schools in which vaccination is provided (15).

In Mexico, HPV vaccination was introduced in 2008 to the national public health programme for girls aged 12-16 years. A total of 125 communities of the lowest human development index, classifying as areas of the highest incidence of cervical cancer, were enrolled into the programme. As many as 81% of girls were vaccinated with three doses of HPV vaccine. In 2011, the National Immunization Council has approved the augmentation of the recommendations by HPV vaccination for all 9-year-old girls within a 'school-based vaccination programme' (16).

Central America. In developing countries, HPV infections account for 86% of all sexually transmitted infections (17). Haiti is one of such countries. There, HPV vaccination is funded by the PAHO Revolving Fund (*Pan American Health Organization*). Only 31% of girls aged 9-13 years benefited from such an opportunity. Little interest in vaccination among parents results from the lack of adequate information on HPV infection and its association with cervical cancer that should be provided by medical personnel and schools. In Haiti,

HPV vaccination is provided within the public health care system, even at times of economic crisis (18).

South America. In Peru, 23% of girls aged 15 years are sexually active. It prompted local authorities to bear the costs of HPV vaccination from public resources. The Ministry of Health ensured that 90% of adolescents would be vaccinated against HPV. Cooperation between departments, engaged in health care-related actions, resulted in achieving a high vaccination coverage rate in Peruvian adolescent girls, i.e. 89% (17).

HPV vaccination coverage rates in adolescents in other South America countries are also high with examples being Brazil and Bolivia with 85% and 77% girls aged 10-16 years and 9-13 years, respectively (17). In Brazil, the Ministry of Health approved the introduction of quadrivalent vaccine in 2006, however, due to high costs it is only provided in the private sector. Wide-spread implementation of HPV vaccination is feasible due to the PAHO (17). In Bolivia, vaccination for girls is provided within the NGO's programme free of charge. High vaccination coverage rates may be achieved by providing vaccination in schools which are enrolled into school-based immunization programme as well as gradual vaccinating girls who were not subject to primary vaccination schedule (19).

Africa. In many regions of Africa, cervical cancer is the most prevalent cancer in females (1). Low- and middle-income countries frequently meet serious obstacles in introducing new vaccines to national immunization programmes. Due to PATH (*Programme of Advancement Through Health and Education*), such countries are provided with assistance to launch HPV vaccines free of charge.

Uganda is one of the countries selected to be enrolled into the PATH. High vaccination coverage rate in adolescents (83%) was achieved as vaccines were administered in schools (17). In Tanzania, HPV vaccination was introduced within the project of the National Institute for Medical Research and the London School of Hygiene and Tropical Medicine. A total of 76% of adolescents received three doses of the vaccine (20).

Asia. Asian countries succeeded in achieving high HPV vaccination coverage rates in adolescents. Vietnam is one of such countries where high vaccination coverage rate (96%) was achieved in girls aged 9-14 years due to a pilot immunization programme within PATH (2008-2009) (17). In Thailand, HPV vaccination coverage rate in 12-year-old girls amounted to 60% (21).

Europe. Countries which first introduced HPV vaccination in 2007 were: Belgium, France and Germany. In the successive year, vaccination was introduced to

Greece, Luxembourg, the Netherlands, Italy, Spain and Switzerland. In 2009, HPV vaccination for girls was also introduced in Denmark, Norway, Portugal, San Marino, Macedonia and Great Britain (22).

Different HPV vaccination strategies (cost entirely covered by patients, free of charge or co-financed from public resources) with regard to adolescents and adult females in European countries result in disparities between vaccination coverage rates. The highest vaccination coverage rates are reported in Western Europe and Scandinavia. For example, in Sweden, where a school-based immunization programme was introduced, vaccination coverage rate in girls aged up to 14 years amounts to even 98% (23). In England, where vaccines are funded from public resources, 80% of girls aged 12-13 years were vaccinated while in Scotland – vaccination coverage rate in adolescents was 92% (24). In Belgium, the Netherlands and France, vaccination coverage rates in girls are slightly lower, ranging from 44% to 68%. In Italy, where immunization programmes are planned locally, the vaccination coverage rate in girls aged 12-13 years is 62% (22).

In Central and Eastern Europe, HPV vaccination was introduced to national immunization programme in 2007 in Bulgaria, Bosnia, Czech, Lithuania, Estonia, Slovenia, Hungary, Latvia, Poland and Slovakia while a year later also in Macedonia, Romania and Serbia (12). HPV vaccines are funded from public resources exclusively in Romania. In several countries, vaccines are provided within school-based health protection programmes while in others vaccines are administered in health care units, including fully paid vaccines. Vaccination coverage rates in these countries range from a few to several percent (12).

In Poland, pursuant to the recommendations of the PGS (Polish Gynecological Society) and PS-HPVIP (Polish Society of HPV Infection Prophylaxis), since 2008 HPV vaccination has been recommended in the national immunization programme for girls aged 11-12 years. The Expert Committee, appointed on the initiative of the PPS (Polish Pediatric Society) in 2010, recommends HPV vaccines also for girls aged 13-18 years who have not been vaccinated previously (11). The cost of vaccine is entirely covered by the patient. No national register of HPV vaccinations operates. HPV vaccination in adolescents is provided free of charge exclusively within programmes financed by local authorities (12,25,26). In 2009–2011, only 3% of target population was vaccinated within such programmes. Its cost was estimated at nearly PLN 33 million (25). An estimated 10% of girls aged 11-13 years were vaccinated by means of various strategies at national level (26). Results of our study demonstrate that 7.5% of girls attending the first classes of post-secondary schools were vaccinated against HPV in 2013 in Zgorzelec (27).

DISCUSSION

Having considered the differences between HPV vaccination implementation, determinants of such disparities should be identified. Poland, as well as Cyprus, Estonia, Finland, Hungary, Lithuania, Malta and Slovakia, belongs to EU countries which have not introduced HPV vaccination to mandatory immunization programmes (11). Such a fact should raise concerns, especially while collated with data on cervical cancer incidence. In 2010, it was diagnosed in 3,270 females, of whom 1,745 died (28). Due to the fact that the cost of HPV vaccine is borne by patients, as well as insufficient knowledge on HPV vaccination and HPV-cervical cancer association, the vaccination coverage rate in Polish girls is alarmingly low, i.e. 10-fold lower compared to other EU countries on average (26,11). Lack of knowledge on diseases caused by HPV, as well as a shortage of adequate wide-spread awareness raising programs result in low acceptance of HPV vaccination among parents and their adolescent children. Several parents express concerns that vaccination against sexually transmitted disease would lead to risky sexual behaviour in their children (3).

The aforesaid analysis of data on HPV vaccination implementation and factors influencing high vaccination coverage rates in different regions of the world enables to formulate recommendations which could enhance HPV vaccination coverage rates in Polish adolescents and young females. Analysis of costs suggests that school-based HPV vaccination in adolescent girls is the most cost-effective (11). Experiences of a number of countries demonstrate that such a strategy ensures high vaccination coverage rates as well as completion of full series (15,16,19, 23).

In Poland, mandatory as well as recommended vaccines are provided for children and adolescents in primary health care settings. Having referred to HPV vaccination, it was demonstrated that compared to a school-based programme, such a strategy incurs higher costs (11), i.e. due to difficulties in exacting the completion of full series. To obtain high vaccination coverage rates, it is necessary to initiate multidimensional actions, with engagement of local medical personnel and the government sector as well as with the use of media campaigns. Such campaigns aimed at motivating parents to vaccinate their children against HPV are effectively employed in a number of countries worldwide with an example being the United States (14). On the other hand, Canada turns its attention to education funding for parents (school) with regard to the prevention of HPV infections (15). In Poland, parents could be educated by qualified experts during periodic parent-teacher meetings. Educational programme on cervical cancer and

HPV prevention for secondary school students, which is performed in several provinces in cooperation with i.a.: provincial and district sanitary and epidemiological stations and Education Offices, should be considered as an initiative in the right direction. Within the framework of this programme, teachers are offered training. Due to this programme, an estimated 393 thousand students obtained knowledge on the risks associated with HPV (26).

In studies, where factors influencing the implementation of HPV vaccination were analyzed, special attention was drawn to the physicians' actions aimed at educating persons eager to undergo vaccination (11,28). Medical personnel should be able to inform on the safety of vaccination and present health-related risks for unvaccinated persons (30). It was demonstrated that general practitioners (GPs) play a significant role in actions directed at enhancing HPV vaccination coverage rates (11,29,12). Thus, GPs should be a target group of future interventions. Consequently, they would become an important element of prevention against HPV infection. Not only GPs, but also other medical specialities, including paediatricians, gynaecologists and midwives, should be aware of the importance of recommending vaccination to risk groups.

It is not simply young persons who should be provided with information by medical personnel, but also their parents, especially those who do not have access to other information sources as well as those for whom stress resulting from visiting GP precludes asking questions. Having considered the fact that patients usually trust their GPs, a more optimal mechanism of cooperation between physician and patient should be introduced.

It could be of benefit to introduce a centralized electronic database, including information on administered vaccines. It would facilitate searching for unvaccinated patients. Consequently, such patients could be then contacted to visit vaccination points, also if patient would change his place of residence, e.g. due to commencing education at another school. In order to inform of the need to receive a third dose of vaccine in the case of patients aged 15 years and older, it seems to be important to have updated patient's address, telephone number or e-mail. Consequently, sending an invitation, letter or SMS would substantially enhance the percentage of fully vaccinated persons.

As it was stated earlier, HPV vaccination coverage rates are high in countries, where the cost of vaccination is covered from the national budget. In Poland, the cost of a full series is high (ca PLN 500). Thus, persons with low or middle income could not afford to purchase the vaccine. If vaccination is to be even partially refunded from the budget of the Ministry of Health or local governments or sponsors, it could result in the enhancement

of vaccination coverage rates (22,25). Such actions are especially recommended in areas where there is high cervical cancer incidence (16). It may be presumed that covering the cost of vaccination in case of the groups of the lowest income would lead to an increase in the percentage of vaccinated individuals. The new, investigational 9-valent vaccine against HPV which includes the HPV types in the quadrivalent HPV vaccine and five additional oncogenic types (31, 33, 45, 52, and 58) gives promise to prevent more cervical cancer cases in the future (31).

SUMMARY

1. Disparities in HPV vaccination coverage rates in adolescent girls worldwide result mainly from different strategies of HPV vaccination implementation adopted in particular countries.
2. Compared to other countries, low HPV vaccination coverage rate in adolescent girls in Poland may result from the fact that it is not funded from the national budget and is provided only in primary health care settings.
3. Increase in HPV vaccination coverage rate could be achieved through multidimensional actions with the engagement of primary health care personnel, schools and the financial assistance of governmental sector at national and local level and the use of media campaigns, especially in areas of the highest cervical cancer incidence.

REFERENCES

1. Spaczyński M, Kędzia W, Nowak-Markwitz E. Rak szyjki macicy. Profilaktyka, diagnostyka i leczenie. Ed. 1. Warszawa: Wyd. Lek. PZWL; 2009:5.
2. Couto E, Sæterdal I, Juvet LK, et al. HPV catch-up vaccination of young women: a systematic review and meta-analysis. *BMC Public Health*. 2014;14(1):867.
3. Trojanczyk M. HPV – szczepić czy nie szczepić? *Probl Hig Epidemiol*. 2012;93(3):623-626.
4. Gross G. Genitoanal human papillomavirus infection and associated neoplasias. *Curr Probl Dermatol*. 2014;45:98-122.
5. Howell-Jones R, Soldan K, Wetten S, et al. Declining Genital Warts in Young Women in England Associated With HPV 16/18 Vaccination: An Ecological Study. *J Infect Dis*. 2013; 208(9):1397-403.
6. Omland T, Lie K,A, Akre H. Recurrent Respiratory Papillomatosis: HPV Genotypes and Risk of High-Grade Laryngeal Neoplasia. *PLoS One*. 2014;9(6):e 99114.
7. Hemminiki K, Dong C, Vaittinen P. Familial risk in cervical cancer: is there a hereditary component? *Int J Cancer*. 1999;82(6):775-781.

8. Majewski S, Sikorski M. Szczepienia przeciw HPV jako pierwotna profilaktyka raka szyjki macicy oraz innych zmian wywołanych przez HPV. *Przew Lek.* 2008;1:228-33.
9. Van Kriekinge G, Castellsague X, Cibula D, et al. Estimation of the potential overall impact of human papillomavirus vaccination on cervical cancer cases and deaths. *Vaccine.* 2014;32(6):733-9.
10. Bonanni P, Levi M, Latham NB, et al. An overview on the implementation of HPV vaccination in Europe. *Hum Vaccin.* 2011;7 Suppl:128-35.
11. Wysocki J, Jackowska T, Małecka I, et al. Szczepienia przeciw wirusowi brodawczaka ludzkiego (HPV) u dzieci i młodzieży jako element profilaktyki raka szyjki macicy *Ped Pol.* 2012;87:637-44.
12. Seme K, Maver PJ, Korać T, et al. Current status of human papillomavirus vaccination implementation in Central and Eastern Europe. *Acta Dermatovenerol Alp Panonica Adriat.* 2013; 22(1):21-5.
13. Garland SM, Skinner SR, Brotherton JM. Adolescent and young adult HPV vaccination in Australia: achievements and challenges. *Prev Med.* 2011;53(1):29-35.
14. Markowitz LE, Hariri S, Lin C, et al. Reduction in human papillomavirus (HPV) prevalence among young women following HPV vaccine introduction in the United States, National Health and Nutrition Examination Surveys, 2003-2010. *J Infect Dis.* 2013;1;208(3):385-93.
15. Remes O R. Determinants of non-uptake of the quadrivalent HPV vaccine; The Ontario Grade 8 HPV Vaccine Cohort Study. <http://hdl.handle.net/1974/7801>.
16. Sanchez Anguiano LF, Lechuqa Quinones AM, Milla Villeda RH, Lares Bayona EF. Knowledge and acceptance of vaccine against human papillomavirus among mothers of students from Durango city, Mexico. *Ginecol Obstet Mex.* 2013;81(2):77-85.
17. Penny M, Bartolini R, Mosqueira NR, et al. Strategies to vaccinate against cancer of the cervix: feasibility of a school-based HPV vaccination program in Peru. *Vaccine.* 2011;29(31):5022-30.
18. Kobetz E, Menard J, Hazan G, et al. Perceptions of HPV and cervical cancer among Haitian immigrant women: implications for vaccine acceptability. *Educ Health (Abingdon).* 2011; 24(3): 479.
19. Fregnani JH, Carvalho AL, Eluf-Neto J, et al. School-Based Human Papillomavirus Vaccination Program in Barretos, Brazil: Final Results of a Demonstrative Study. *PLoS One.* 2013; 8(4):e62647.
20. Watson-Jones D, Baisley K, Ponsiano R, et al. Human papillomavirus vaccination in Tanzanian schoolgirls: cluster-randomized trial comparing 2 vaccine-delivery strategies. *J Infect Dis.* 2012;206(5):678-86.
21. Songthap A, Pitisuttithum P, Kaewkungwal J, et al. Knowledge, attitudes, and acceptability of a human papillomavirus vaccine among students, parents and teachers in Thailand. *Southeast Asian J Trop Med Public Health.* 2012;43(2):340-53.
22. Dorleans F, Giambi C, Dematte L, et al. The current state of introduction of human papillomavirus vaccination into national immunisation schedules in Europe: first results of the VENICE2 2010 survey. *Euro Surveill.* 2010;15(47):19730.
23. Leval A, Herweijer E, Ploner A, et al. Quadrivalent human papillomavirus vaccine effectiveness: a Swedish national cohort study. *J Natl Cancer Inst.* 2013;105(7):469-74.
24. Hilton S, Hunt K, Bedford H, Petticrew M. School nurses' experiences of delivering the UK HPV vaccination programme in its first year. *BMC Infect Dis.* 2011;11:226.
25. Saniewska-Kilim A, Kujawa J. Samorządowe programy szczepień przeciwko ludzkiemu wirusowi brodawczaka w Polsce. *Medycyna Praktyczna Szczepienia* 2014/01 <http://www.mp.pl/szczepienia/specjalne/show.html?id=97459>.
26. Fundacja MSD dla Zdrowia Kobiet. Profilaktyka HPV w Polsce. 2010. Wytyczne dla organizacji programów profilaktycznych przez jednostki samorządu terytorialnego <http://koalicjarsm.pl/download.php?rid=3>.
27. Owsianka B, Gańczak M, Dmytrzyk-Daniłó G. Ocena stopnia wyszczepialności przeciw HPV oraz wiedzy młodzieży szkół średnich na temat HPV, w tym szczepień. V Krajowa Konferencja Polskiego Towarzystwa Wakcynologii. 24-26.X.2013.
28. Wojciechowska U, Didkowska J. Zachorowania i zgonu na nowotwory złośliwe w Polsce. Krajowy Rejestr Nowotworów. Warszawa, Centrum Onkologii, Instytut im. M. Skłodowskiej-Curie. <http://onkologia.org.pl/raporty> (cyt. 17.12.2013).
29. Majewski S. Implementacja szczepień przeciwko HPV w praktyce lekarza rodzinnego. *Przew Lek.* 2009;1:231-3.
30. Wysocki J. Rodzice a szczepienia ochronne - wiedza czy intuicja? [in:] *Szczepienia w społeczności lokalnej. II konferencja Polskiego Towarzystwa Wakcynologii, Wrocław, 24-26 IX 2006*;30.
31. Joura EA, Giuliano AR, Iversen OE, et al. A 9-valent HPV vaccine against infection and intraepithelial neoplasia in women. *N Engl J Med.* 2015; 372 (8): 711-23.

Received: 22.09.2014

Accepted for print: 10.12.2014

Address for correspondence:

Barbara Owsianka, MA
Multispecialty Hospital in Zgorzelec
Lubańska 11-12
59-900 Zgorzelec
Tel. +48 75 77 22 900
e-mail: barbara10201@wp.pl