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HPV Vaccinations in Lublin Region, Poland

Szczepienia przeciwko HPV w regionie lubelskim

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Summary

Introduction: Secondary prophylaxis of cervical cancer consisting in cytology screening tests, despite its effectiveness, does not achieve the desired results. For several years, primary prophylaxis has been available in the form of protective vaccinations. At present, two vaccine preparations are available on the market, and studies conducted on these preparations confirm their almost 100% effectiveness in the prevention of types of HPV present in the vaccine.

Objective: Analysis of the programmes of protective vaccinations against HPV carried out during the period 2008–2013 in the Lublin Region.

Material/Methods: The material used in the study was data obtained from the relevant organs of the territorial self-government concerning programmes of vaccinations against HPV, demographic data pertaining to girls aged 10–18 living in the Lublin Region, as well as data published by the National Institute of Public Health – National Institute of Hygiene (NIZP–PZH). The method applied in the study was analysis of records.

Results: During the period 2008–2013, in the Lublin Region a total of 5,496 girls were vaccinated within the health programmes. The mean immunization coverage in Lublin is 50%, and in Radzyń Podlaski 59%. The percentage contribution of vaccinations guaranteed free by the local authorities, with relation to the total number of vaccinations performed in the Lublin Region, was from 60 to 77%. The units of territorial self-government allocated the amount of PLN 5,125,359 for the performance of projects associated with execution of free vaccinations.

Discussion: Among the total number of girls vaccinated against HPV, a considerable percentage were those vaccinated within the prophylactic programmes carried out by the units of territorial self-government. The programmes of free protective vaccinations against HPV began in 4 cities in the Lublin Region, and are continued only in two (Lublin and Radzyń Podlaski). Long-term observation of girls subjected to vaccinations from the aspect of maintenance of the immune response after vaccination should become an important element of performance of health programmes concerning vaccinations against HPV.

Conclusions: Among the total number of girls vaccinated against HPV, those vaccinated within prophylactic programmes carried out by territorial self-government units made up a considerable percentage. Programmes of free preventive vaccinations against HPV began in 4 cities in the Lublin Region, but are continued in only 2. Long-term observation of girls subjected to vaccinations from the aspect of duration of maintaining immunity after vaccination should become an important element of the performance of health programmes concerning vaccinations against HPV.

Key words: **Human papillomavirus (HPV) • prophylactics vaccinations • health programmes • Lublin Region**

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Abbreviations: **HPV** – human papillomavirus, **CIN** – cervical intraepithelial neoplasia.

Introduction

Malignant cervical cancer constitutes 4% of all cancer cases in Poland. Since the 1980s, there has been observed a decrease in morbidity by approximately 30% and in mortality by approximately 45%. According to the data of 2010, in Poland, slightly more than 3,000 cases are diagnosed annually, and the number of deaths is approximately 1,700. In Poland, the incidence is 15% higher than the mean incidence in European countries, and mortality is approximately 70% higher than the mean value for the remaining European countries [4]. The factors increasing the risk of contracting the disease include genetic predispositions, early sexual initiation, a large number of sexual partners, poor socio-economic standard, chronic use of hormonal contraception, cigarette smoking, and primarily long-term infection with oncogenic types of the HPV virus [2,13]. To date, approximately 200 types of human papilloma virus have been distinguished, divided into oncogenic high-risk (HPV 16, 18, 45, 33, 31, 35, 39, 51, 52, 56, 58, 59, 68, 73, 82) and low-risk (most important: HPV 6 and 11) [3,26]. Genetic material of HPV virus identified in cancers is most often related to the type HPV 16 (approximately 60% of cases), followed by HPV 18 (18%) [2,15]. More than 50% of sexually active individuals have contact with HPV, and the presence of HPV DNA is detected in 99.7% of materials from 10,000 cervical cancer biopsies as it was concluded on the basis of a meta-analysis from several countries of the world [16]. Secondary prophylaxis consisting in cervical cytology screening, despite its high effectiveness, does not provide the desired results. For example, in recent years in Poland, the reporting rate for cytology screening among women aged 25-59 is as low as 27% [24]. Primary prophylaxis in the form of protective vaccinations has been available for several years. The first vaccine against HPV virus was registered in the Unites States in 2006 by Merck & Co under the name Gardasil. Since November 2006, in Europe, this vaccine has functioned under the trade name Silgard. Since 2007, the vaccine Cervarix, produced by GlaxoSmithKline, also became available. Both preparations are designed for the performance of vaccinations in girls aged over 9, via the intramuscular route, by a 3-dose vaccine schedule (Silgard 0-2-6, Cervarix 0-1-6), or, from 2014, by a 2-dose schedule (0–6), exclusively in girls aged a minimum of 13 years (Silgard) and 14 (Cervarix) [27]. In contrast to the 3-dose schedule, at the moment, the effectiveness of the 2-dose schedule is not known. Gardasil/Silgard is a quadrivalent vaccine directed against oncogenic high-risk types of the HPV virus – 16, 18, and HPV 6 and 11 responsible for the development of benign growths in the genital area (genital warts). In this preparation, the adjuvant system is based on amorphous aluminium hydroxyphosphate sulphate. In turn, Cervarix is a bivalent vaccine indicated for oncogenic high-risk types of HPV 16 and 18 containing the new generation adjuvant system 3-O-desacyl-4′-monophosphoryl lipid A (MPL) which, according to the studies available, induces a stronger immune response than the standard aluminium adjuvant [1,9,29]. Both the safety and effectiveness of vaccines against HPV available on the market are based on many-year studies. The effectiveness of the quadrivalent vaccine (Silgard) was confirmed by randomized studies conducted by the double blind sampling method FUTURE I (in 5,455 women aged 16-23 in 16 countries), and FUTURE II (among 6,087 women aged 15–26 in 13 countries) [6,7]. The results of these studies indicate a 100% decrease in the risk of development of non-cancerous changes in the genital area, and 100% decrease in the occurrence of precancerous changes of the cervix CIN 1–CIN 3, and preinvasive adenocarcinoma of the cervix (AIS) related to infections with HPV 16, 18, 11, 6 in women, who before vaccination had no contact with HPV. In addition, the studies show relatively high cross-protection (38%) in the prevention of precancerous and cancerous changes caused by HPV types other than those contained in the vaccine (31, 33, 35, 39, 45, 51, 52, 56, 58, 59) [1,21]. The first stage of studies of the bivalent vaccine (Cervarix) indicated 100% effectiveness in the prevention of the CIN changes associated with HPV 16 and 18. A more detailed study was conducted within the project PATRICIA, which covered 18,644 young women aged 15-25 in 14 countries. After 3 years of observations, the risk of precancerous changes CIN 2 and CIN 3 decreased by 70% and 87% respectively. Analysis of acquiring cross immunity showed 100% for the 31 and 45 types of the virus, and 62% for HPV 33,

35, 39, 45, 51, 52, 56, 58, 59 [8,19,20]. These results, in the case of both bi- and quadrivalent vaccines, concern girls and young women before sexual initiation. In the case of two vaccine preparations, no significant complications were observed in the form of severe undesirable post-vaccination reactions. Only typical local symptoms occurred: swelling, redness, and pain complaints at the injection site [1,21]. The preliminary results of studies of the effectiveness of application of bivalent vaccine in women older than 25 also seem to be promising. The preliminary results of the study VIVIEN (randomized by the double blind sampling method) among 5,752 women aged 25–45 showed that the effectiveness of the vaccine in the case of persistent infections with HPV 16 and 18 was 81%. A high level of cross immunity (79%) was also found in the case of HPV 31, and 77% with respect to HPV 45 [23]. The new, examined nine-valent anti-HPV vaccine contains types of viruses present in the quadrivalent vaccine as well as 5 additional oncogenic types (31, 33, 45, 52 and 58) [19].

In the past decade many countries included anti-HPV vaccinations in national protective vaccination programmes. However, Poland is one of 8 European Union countries that did not introduce this vaccination to the compulsory programmes. Prophylactic vaccination against HPV is charged extra in basic medical centres; therefore the coverage of Polish teenagers vaccinated against human papilloma virus is between 7.5% and 10% [17,18]. Some territorial self-government units in Poland decided to introduce programmes of prophylactic vaccinations and finance them, but knowledge on their efficiency is not known. Therefore the objective of the study was to analyse the programmes of protective vaccination against HPV virus carried out during the period 2008–2013 in the area of several towns in the Lublin Region by territorial self-government units.

Material and methods

The material analysed in the study was data concerning the performance of protective vaccinations against HPV in the Lublin Region. The source data were obtained from the relevant units at the Lublin Municipal Office (343.5 thousand inhabitants), Zamość Municipal Office (65.2 thousand inhabitants), Świdnik Municipal Office (40.3 thousand inhabitants), and Radzyń Podlaski Municipal Office (16.1 thousand inhabitants). The inhabitants of these 4 cities and towns comprise 22% of all inhabitants of the Lublin Voivodeship (2 096 thousand inhabitants). These were the only 4 cities and towns in the Lublin Region that introduced free vaccination programmes against HPV. In addition, demographic data were used concerning the female population aged 10-18 living in the Lublin Region, and data pertaining to protective vaccinations in Poland published in the form of reports by the National Institute of Public Health – National Institute of Hygiene. The study was conducted by the method of analysis of records, using instruments of descriptive statistics.

Results

Programmes of free protective vaccinations against HPV virus were carried out by the City of Zamość during the period 2010–2011, and the City of Świdnik in 2009 and 2010. Such programmes have continuously functioned in the City of Lublin since 2008, and the City of Radzyń Podlaski from 2009. Both in Lublin and Radzyń Podlaski, the continuation of the programmes is planned in future years. All vaccinations carried out within health programmes by the units of territorial self-governments

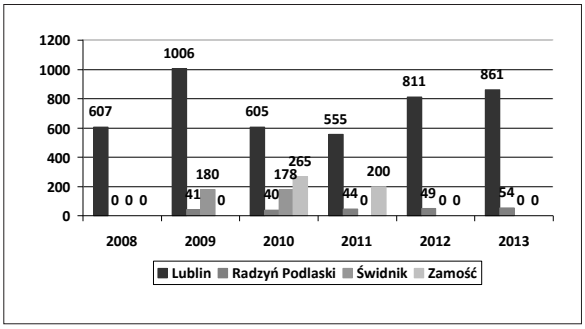


Fig. 1. Number of girls vaccinated against HPV within the prophylactic programmes carried out by the units of territorial self-government in the years 2008–2013 in the Lublin Region

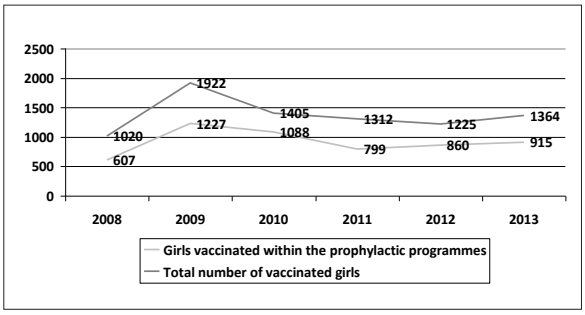


Fig. 2. Number of girls vaccinated against HPV within the prophylactic programmes carried out by the units of territorial self-government among the total number of girls vaccinated against HPV in the years 2008–2013 in the Lublin Region

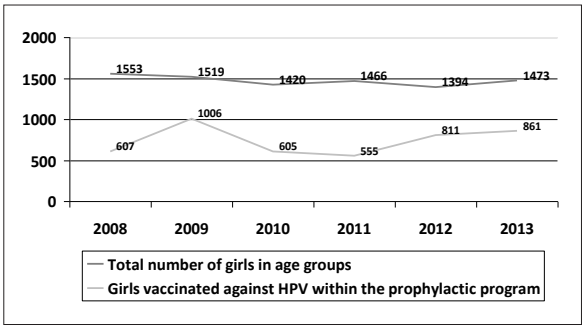


Fig. 3. Number of girls vaccinated against HPV within the prophylactic programme carried out by the self-government of Lublin among total number of girls in the age group for which the vaccination was proposed in the years 2008–2013 in the City of Lublin

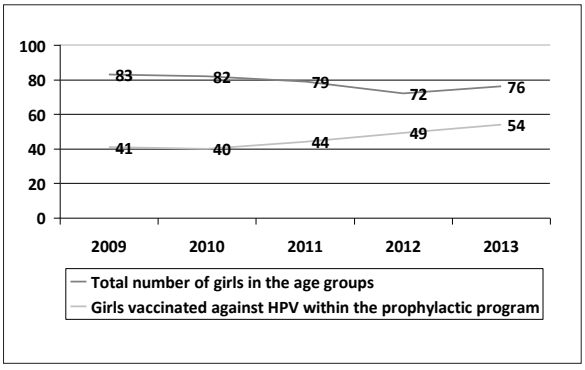
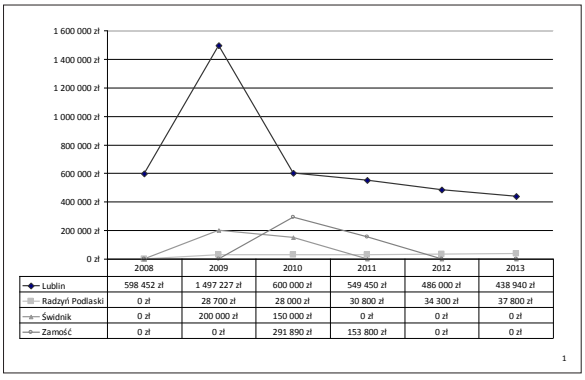


Fig. 4. Number of girls vaccinated against HPV within the prophylactic programme carried out by the self-government of Radzyń Podlaski among the total number of girls in the age group for which the vaccination was proposed in the years 2009–2013 in the City of Radzyń Podlaski



	2008	2009	2010	2011	2012	2013
Lublin	598 452 zł	1 497 227 zł	600 000 zł	549 450 zł	486 000 zł	438 940 zł
Radzyń Podlaski	0 zł	28 700 zł	28 000 zł	30 800 zł	34 300 zł	37 800 zł
Świdnik	0 zł	200 000 zł	150 000 zł	0 zł	0 zł	0 zł
Zamość	0 zł	0 zł	291 890 zł	153 800 zł	0 zł	0 zł

Fig. 5. Amount of money allocated for the performance of projects associated with execution of free vaccinations by the units of territorial self-government in the years 2008–2013 in Lublin Region

were performed in girls; in Lublin, Zamość, and Świdnik 12-year-old girls were vaccinated, while in Radzyń Podlaski 10-year-olds were vaccinated. In each of the above-mentioned cities the service providers engaged in the vaccination programmes against HPV were selected based on competitive offers. The task of service providers participating in the programmes consisted primarily in medical examinations, qualification for vaccinations, their performance, and keeping appropriate records. At the same time, their actions were biased towards education and promotion of health behaviours related to the prophylaxis of cervical cancer. Within the health programmes implemented by territorial self-government units in the Lublin Region from 2008 until 2013, a total number of 5,496 girls were vaccinated against HPV, including 4,445 living in Lublin, 465 in Zamość, 358 in Świdnik, and 228 in Radzyń Podlaski (Fig. 1). The majority of vaccinations against HPV performed during the period 2008–2013 in the Lublin Region were performed within prophylactic programmes. The percentage contribution of vaccinations guaranteed free by self-governments in the above-mentioned cities in relation to the total number of vaccinations performed in the Lublin Region in successive years starting from 2008 is: 60%, 64%, 77%, 61%, 70%, and 67% in 2013 (Fig. 2). In Lublin, the number of girls who used the prophylactic programme, compared to the total number of girls in the age group for which the vaccination was proposed was, successively, starting from 2008, 39%, 66%, 43%, 38%, 58%, and 58% in 2013, which resulted in a mean coverage of approximately 50% in an individual age group (Fig. 3) In Radzyń Podlaski, the vaccination coverage was: 49% in 2008, followed by 49%, 56%, 68%, and 71% in 2013, which is 59% on average (Fig. 4). The number of girls aged 10–18 (all age groups covered by vaccinations during the period 2008–2013) in the Lublin Region is 100,887 (data according to the Statistical Office in Lublin). In this age group, the number of girls who were vaccinated (according to the reports from performance of preventive vaccinations) in the last 6 years is 7,543, which is approximately 7.5%. From the beginning of implementation of prophylactic programmes related to the performance of vaccinations against HPV, the territorial self-government units allocated for this purpose PLN 5,125,359, including in Lublin PLN 4,170,066, Radzyń Podlaski PLN 159,600, Świdnik PLN 350,000, and Zamość PLN 445,690. The last two cities discontinued the performance of the programme after two years (Fig. 5).

Discussion

According to the position of the European Centre for Disease Prevention and Control of 2012, until 2011, vaccinations against HPV were implemented in 19 from among 29 European Union member states. The cost of protective vaccinations is totally covered from the public resources in: Denmark, Germany, Greece, Holland, Ireland, Island, Italy, Latvia, Luxemburg, Malta, Norway, Portugal, Romania, Slovenia, Spain, Sweden, and the United Kingdom. In France, 35% of the costs of vaccines is covered by the patient, whereas in Belgium the amount of co-financing by the patient is 25%. Since 2012, free vaccinations have also been introduced by the Czech Republic, Slovakia, and Hungary. The age of girls subjected to vaccinations varied according to the country; eventually, girls aged 9–18 will be covered by vaccinations. In 10 of the above-mentioned countries (Austria, Belgium, Denmark, France, Holland, Italy, Luxemburg, Portugal, Romania, and the United Kingdom), programmes of catch-up immunization were implemented directed to patients aged 12-40 [5]. According to the data of 2010, in Portugal and the United Kingdom, the percentage of girls fully immunized exceeded 80%, in Italy and Denmark 50–60%, while in France, Luxemburg and Norway it reached maximally 30%. Within the catch-up immunization programmes, vaccinations covered 29–73% of the population of girls and women for whom they were intended [5]. For several years in Poland, vaccinations against human papilloma virus (HPV) have been recommended by the Polish Gynaecological Association [12] and the Polish Society for HPV Prevention [14] as an essential element of cervical cancer prevention. From 2008, this vaccination has been introduced into the Programme of Protective Immuniza-

tion, as recommended, i.e., according to Article 19 of the Act of 5 December 2008 in the matter of prevention and control of infections and infectious diseases in humans, Journal of Laws 2008, No. 234, Clause 1570, although not financed from the State budget [10]. The vaccination was not included in free vaccinations considering the negative recommendation by the Consultation Council of the Agency for Evaluation of Medical Technologies, which in the justification emphasized the lack of reliable data concerning the effect on morbidity and mortality of women due to cervical cancer, and primarily the high cost of implementation of protective immunization, without the possibility to resign from secondary prevention [25]. This situation has not changed until today; in the Programme of Protective Vaccinations for the year 2015, immunization against HPV is still placed in Part 2 – recommended vaccinations [11]. However, the Transparency Council of the Agency for Evaluation of Medical Technologies considered it justifiable to cover the preparation Cervarix (Position No. 169/2013 of 19 August 2013) with 50% reimbursement, and the preparation (Position No. 254/2013 of 9 December 2013) with 30% of the cost paid by the patient. At present, vaccines against HPV are available on the pharmaceutical market only at full price. Some territorial self-government units carry out the programmes of free vaccinations against HPV from their own funds. In a pharmacy, the price of a single vaccine most often remains within the range PLN 400–600 for one dose, which means that the full series of vaccinations costs from PLN 1,200 to PLN 1,800. For comparison, in the case of ordering a greater amount of vaccine for the needs of the prophylactic programme performed in Lublin (the largest number of vaccines purchased), in 2008, the cost of one dose of the vaccine was approximately PLN 329, and in the last year it was approximately PLN 170. According to the reports from the whole country, in the last 5 years (2008–2013) in Poland, a total number of 139,243 girls and women were vaccinated, including 118,787 girls aged 0–19, which constitutes 2% of girls in this age group. According to the all-Polish analysis for the years 2009–2011, within the self-government health programmes, vaccinations against HPV were performed in 3% of girls in the age group 10–17 [22]. The number of girls vaccinated within health programmes in individual regions is not proportional to the total number of girls at that age living in these regions. This probably results from the number of territorial self-government units which carry out such programmes. The largest number of girls were vaccinated within the programmes carried out by the territorial self-government units in the Poznań Region, and the smallest number in the Kielce Region. In the Rzeszów Region, prophylactic programmes related to the performance of vaccinations against HPV financed from public resources were not conducted. The Lublin Region occupies the third position according to the largest number of vaccinations performed from public funds [22]. Considering the low vaccination coverage against human papilloma virus in Poland, especially compared to other countries of the European Union, it is necessary to promote territorial self-government units which carry out programmes of vaccination against HPV. Also, the aspect of unification of the system of purchasing vaccination preparations for all units conducting immunization is also noteworthy, in order to negotiate the most beneficial offer. An increase in awareness among adolescents and their parents concerning cervical cancer prophylaxis, and the contribution of medical staff to this education, should become an important aspect of the performance of preventive vaccinations against HPV.

The obtained results prove that free vaccination programmes introduced in some cities and towns in the Lublin Region had a considerable impact on the vaccination coverage in that area. Although only 7.5% of all girls in the relevant age were vaccinated, the majority of them underwent vaccination in the course of free programmes. This testifies to the fact that such programmes should be continued and developed as they prove advantageous in prophylaxis of HPV infection.

Conclusions

1. Among the total number of girls vaccinated against HPV, a considerable percentage were those vaccinated within prophylactic programmes carried out by territorial self-government units.

2. Programmes of free preventive vaccinations against HPV began in 4 cities in the Lublin Region, but are being continued in only 2 of them (Lublin and Radzyń Podlaski).

3. Long-term observation of girls subjected to vaccinations from the aspect of duration of maintaining immunity after vaccination should become an important element of the performance of health programmes concerning vaccinations against HPV

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