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EXPERIENCE OF IMPLEMENTATION VACCINATION PROGRAMS AGAINST HUMAN PAPILLOMAVIRUS IN THE WORLD, REASONS FOR REJECTION OF THE VACCINE (LITERATURE REVIEW)

Vaccines against human papilloma virus (HPV), a potential instrument for the prevention of cervical cancer and some other cancers. High coverage of the target group in the ongoing program of HPV vaccination is cost-effective and successful event, depending on the knowledge and the trust to the ongoing program.
***Keywords**: human papillomavirus, HPV-associated diseases, HPV vaccine, vaccination programs, recommendations, safety, efficacy.*

Introduction: Human papillomavirus (HPV) is the most common viral infection of the reproductive tract. HPV is sexually transmitted, but penetrative sex is not required for transmission. Skin-to-skin genital contact is a well-recognized mode of transmission. Cervical cancer is by far the most common HPV-related disease. Though data on annogenital cancers other than cancer of the cervix are limited, there is an increasing body of evidence linking HPV with cancers of the anus, vulva, vagina, and penis. In 2005, the World Health Organization (WHO) initiated the establishment of the global HPV Laboratory Network (LabNet) [1]. The first vaccine to prevent cancer cervix and HPV-associated diseases in woman was approved in US on June, 2006 by the U.S. Food and Drug Administration (FDA). Currently, there are three HPV vaccines that are safe and efficacious in preventing HPV infection: bivalent (Cervarix, GlaxoSmithKline), quadrivalent (Gardasil, Merck), and ninevalent (Gardasil, Merck) HPV vaccines which protects against HPV 16 and 18; HPV 6, 11, 16 and 18; and HPV 6, 11, 16, 18, 31, 33, 45, 52 and 58, respectively [2]. HPV16 and 18 are the primary cause of 70% of all cervical cancers worldwide. [3], HPV 6 and 11 are present in over 90% of all anogenital warts [4]. In clinical trials, the HPV vaccine demonstrated more than 90% efficacy against HPV 16 and 18 related with precancerous lesions in women aged 15-26 years. [5]. Vaccines showed a high percentage of efficacy against cervical intraepithelial neoplasia and invasive cancers related to virus types 16,18. In four randomized, double-blind, placebo-controlled researches, where as an endpoint was persistent infection, the effectiveness of HPV vaccine was 100%. [6] The data of another randomized, placebo-controlled, double-blind research conducted at 62 research centers in 16 countries during the period from January 2002 to March 2003 were published in 2007 and presented the 100% effectiveness of HPV vaccine (95% CI, 94% -100 %). [7] The data on the safety and efficacy of vaccines allow many countries to start using the vaccine prevention at the level of public vaccination programs. According to the World Health Organization's monitoring system, HPV vaccine had been introduced in 57 countries by 2013. [8]. Although the age range for comparison varies internationally, there is a vast difference in HPV vaccine uptake across these countries, from very high—86.7 % for 3 doses in adolescent females of the target age in the UK (2013–2014) [9] —to very low—37 % for 3 doses the adolescent age group in the US [13]. Uptake needs to be consistently high for a comprehensive reduction in HPV disease burden to be achieved at a population-level. In particular, vaccination coverage can be increased from 67 to 90 %, models predict that the long-term reduction in incident infection will be increased from 76 to 95 % [10].

Most developing countries, participating in vaccination, primarily propose the introduction of vaccination strategies at schools. This experience today remains the main, close coordination with the education sector is a key element and the overall immunization coverage is high enough. [12]. The spread of correct information about the vaccine is key in ensuring public support. There is little evidence available to guide strategies for school-based vaccination. The systematic review of practices for school-based vaccination implementation conducted by S. Rachel Skinner, Cristyn Davies, Spring Cooper identified only one randomised controlled trial in 14 studies, which evaluated process. [13-14]. We can trace how the introduction of vaccination programs developed by example of some developed countries.

The National Human Papillomavirus (HPV) Vaccination Program in Australia commenced in 2007 for females and in 2013 for males, using the quadrivalent HPV vaccine (HPV 6,11,16,18). Australia is one of the first countries where the program of HPV immunization was launched. Post-vaccination reductions have already been documented in Australia in genital warts high-grade cervical abnormalities, and most recently, HPV prevalence, in young women. There is some evidence that in Australia was the decrease of ervical abnormalities (CAX) (CIN2+ or adenocarcinoma *in situ*) in women younger than 18 years involved in the vaccination programme when comparing the period 2003–2007 (prevaccination) with the period 2007–2009 (postvaccination). Such a decline from an incidence of 0.85% in 2006 to 0.22% in 2009 represents a more than 50% decline in incidence (p = 0.003) [15]. Further Australian data, collected during the first 5 years of their national immunization program, found that the incidence of genital warts decreased more than 50% among females under 30 and more than 70% in heterosexual males of the same age. [16]

Similarly, incidence data from Denmark shows that genital warts have declined an average of 3.1% every year since 2007. Denmark has reached very high vaccination rates (3-dose coverage of over 80%) through administration by general practitioners. [17] The implementation of immunization program in the United States has been very successful, with the provision of 90% coverage [18] However, immunization was not achieved with the same success for adolescents and adults. [19].

In US within 4 years of vaccine introduction, the vaccine-type HPV prevalence decreased among females aged 14–19 years to 50 %. [20]

In Switzerland during four years in a multicenter randomized controlled research the effectiveness of preventive vaccination against HPV (6, 11, 16 and 18) was evaluated relatively to low risk of cervical intraepithelial neoplasia, vulvar, vaginal, and anogenital warts. The efficiency of the vaccine was 100% for I class intraepithelial neoplasia of vulva and vagina (95% CI 74%

to 100%, 64% and 100%, respectively), and 99% for anogenital warts (96% to 100%) and led to a significant reduction of the prevalence of HPV in the follow-up period of 42 months.
France, which offered vaccination on request and reimbursed only a proportion of the costs, achieved only 28.5% coverage with a doses. [21].
In Hong Kong, HPV vaccination does not provide by government program and patients have to pay out of pocket to be immunized in the private sector.
In German, German Standing Vaccination Committee (STIKO) recommends HPV vaccination for Girls aged 12-17, before the first sexual intercourse if possible.
Thus, the effectiveness of the vaccine can be measured only in the long term, when sufficiently numerous cohort of immunized teens reach the age of developing cancer pathology. Nevertheless, despite these limitations, the data accumulated in a number of countries approves the efficiency of HPV vaccination.
Also studying the literature on the subject of vaccination, we note that the relevant issue is the study of factors affecting the coverage of HPV vaccination and parental attitude towards vaccination against HPV. According to the literature, many researches tell us that parent's lack of knowledge about the virus and HPV vaccines to make an informed decision about vaccination.
There are some reviews indicated that recommendation from a doctor is the main driver of vaccination, safety is a key parental concern, HPV vaccine-related knowledge is positively associated with vaccination uptake and) school-based immunization programs increase vaccination coverage. [21, 22]
The data of systematic review based on 23 studies of European countries, conducted by Victoria Fernández de Casadevante et all, showed that vaccination coverage is related to ethnicity of the population, high socioeconomic status, regular participation of mothers in cervical cancer screening programs, as well as obtaining vaccinations by the vaccination schedule since childhood. Also the author noted that few parents have some problems with the HPV vaccination, and that we should find ways to influence these vulnerable groups for the prevention of HPV-associated diseases. [23].
In the literature there is a surprising consistent pattern of general knowledge about vaccination in respect to parental hesitancy: parents who refuse to do vaccination tend to be more educated whereas those who accept vaccination have a lower educational level. One of the theories is that educated parents are much more likely to have access to specific sources of media such as the Internet, where they can receive negative information regarding the HPV vaccine. In addition, highly educated parents feel more confident and able to interpret complex scientific and clinical health information that allows them to ignore the advice of practitioner doctors, if there are contradictions.
With regard to vaccination in general literature review reflects the fact that the parents, who agree to the vaccination for their children, often have limited knowledge of the diseases which may be prevented by vaccine. Also, these solutions of the parents are often based on the provider recommendations and not on knowledge of the specific vaccine or disease that can be prevented. [24-26]. Furthermore, research has shown that parents who do not have their children vaccinated have researched the topic extensively and overall show an interest in health-related issues. [27].
Uncertainty about the level of protection offered by the HPV vaccine was evident among parents, and to a lesser extent among vaccination-aged girls. There was a lack of understanding among parents and girls that cervical screening would be required irrespective of vaccination status; several parents had believed that the vaccine would eliminate the need for cervical screening. [28]. It is important that parents and girls make informed decisions about accepting the HPV vaccine based on accurate understandings of the advantages and disadvantages that vaccination offers, particularly the level of protection it provides against cervical cancer.
Conclusions: As we can see from the literature low level of knowledge and understanding of HPV and HPV vaccines among parents of vaccinated girls occurs everywhere [29]. These studies suggest that girls know little about how the human papillomavirus is transmitted, how to reduce the risk of HPV infection, [30] knowledge and understandings about HPV infection and its link to cervical cancer. In addition, girls are unaware about the level and duration of protection HPV vaccine, [31] and they had a lack of knowledge about the role of passing further screening for cervical cancer. Based on published data, barriers to the introduction of vaccines are multifactorial, but nevertheless, vaccination against HPV - is a cost effective public health strategy, the implementation of which will prevent the financial cost of the state associated with the risk of developing HPV-related diseases in perspective. HPV vaccination program is based on a voluntary agreement, which gives parents the opportunity to avoid vaccination. Well-known fact is that today the level of vaccination coverage, not only against HPV, but immunization by schedule began to decline. The differences between HPV vaccination coverage rates of teenage girls all over the world may be caused by the implementation of different vaccination strategies among countries. A multidimensional approach involving the participation of medical and school staff, financial support of the government at national and local level and the implementation of campaigns in the media, especially in regions with high rates of cervical cancer, may lead to an increase HPV vaccination coverage rate in any country.

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ДҮНИЕ ЖҮЗІНДЕГІ АДАМ ПАПИЛЛОМАСЫ ВИРУСЫНА ҚАРСЫ, ВАКЦИНАЦИЯ ПРОГРАММАСЫН ЕНГІЗУ ТӘЖІРИБЕСІ, ВАКЦИНАДАН БАС ТАРТУ СЕБЕПТЕРІ.
(ӘДЕБИЕТКЕ ШОЛУ)

Түйін: Адам папилломасы вирусы (АПВ) – жатыр мойны рагы мен басқа рак түрлерінен профилактикалық потенциалды инструмент№ Жүргізілген программаларға сенімді қарым-қатынаспен білімге байланысты, экономикалық эффективті және сәтті іс-шаралар, АПВ-ға қарсы вакцинациялық программалар жоғары мақсатты халық тобына жүргізіледі.
Түйінді сөздер: адам папилломасы вирусы, АПВ-ассоциацияланған аурулар, эффективтілік, қауіпсіздік, ұсыныстар, вакцинациялар программалары.

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ОПЫТ ВНЕДРЕНИЯ ПРОГРАММ ВАКЦИНАЦИИ ПРОТИВ ВИРУСА ПАПИЛЛОМЫ ЧЕЛОВЕКА В МИРЕ, ПРИЧИНЫ ОТКАЗОВ ОТ ВАКЦИН
(ЛИТЕРАТУРНЫЙ ОБЗОР)

Резюме: Вакцины против вируса папилломы человека (ВПЧ) потенциальный инструмент для профилактики рака шейки матки и некоторых других видов рака. Высокий охват целевой группы в проводимой программе вакцинации против ВПЧ является экономически эффективным и успешным мероприятием, зависящим от знаний и доверительного отношения к проводимой программе.
Ключевые слова: вирус папилломы человека, ВПЧ-ассоциированные заболевания, вакцинация против ВПЧ, программы вакцинации, рекомендации, безопасность, эффективность