

EXPERIENCE OF THE NATIONAL VACCINATION PROGRAM IMPLEMENTATION AGAINST HUMAN PAPILLOMA VIRUS IN THE REPUBLIC OF UZBEKISTAN

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Таянч сўзлар: эмлаш, бачадон бўйни саратони, бирламчи профилактика, инсон папиллома вируси.

Ключевые слова: вакцинация, рак шейки матки, первичная профилактика, вирус папилломы человека.

Introduction. Cervical cancer is one of the most serious threats to women's health. This is the fourth most common cancer in women around the world. According to the forecasts of international experts (taking into account population growth and an increase of life span expectancy), the increase in the incidence and prevalence of cervical cancer will have made up 40% in developing countries and in economically developed countries - 11% by 2020. In the case of non-conducting timely measures for the prevention and treatment of cervical cancer, malignant neoplasms of the cervix will affect up to 1 million women annually after 2050 in the world. **Aim of the study** is primary prevention of cervical cancer by introducing vaccination to 9 years old girls of the Republic of Uzbekistan. **Material and methods.** The Gardasil MK vaccine was imported to the Republic of Uzbekistan in 2019. From October 21 to November 30, 2019, the first dose was vaccinated to 9 years old girls in the republic; the introduction of the 2nd dose is planned in 6 months. **Results and discussion.** Vaccination rates significantly increased after the measures taken on November 30: in the city of Tashkent - 97%, in the Tashkent region - 90.8%, in Bukhara - 90.2%. Refusers made up 66.9% of unvaccinated girls. Temporary left who also did not receive vaccination made up 360 (4%). 1935 girls were not vaccinated by other reasons and they made up 21.4% of the total unvaccinated population. **Conclusion.** As a result of joint efforts by the Government of the Republic of Uzbekistan, the Ministry of Health with the support of international organizations from WHO and UNICEF, the first dose of the tetravalent HPV vaccine - Gardasil MK- was successfully administered to 9 years old girls all over the country. According to the data of Health Ministry of the Republic of Uzbekistan no adverse reactions were observed in 292,867 girls after vaccination.

ЎЗБЕКИСТОН РЕСПУБЛИКАСИДА ОДАМ ПАПИЛЛОМА ВИРУСИГА ҚАРШИ ЭМЛАШ МИЛЛИЙ ДАСТУРИ ТАЖРИБАСИ

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Кириш. Бачадон бўйни саратони аёллар саломатлиги учун энг жиддий таҳдидлардан биридир. Бу дунё бўйлаб аёлларда тўртинчи энг кенг тарқалган саратон ҳисобланади. Ҳалқаро экспертларнинг 2020-йилги прогнозларига кўра (аҳоли сонининг ўсиши ва умр кўриш давомийлигининг ошиши ҳисобга олинган ҳолда) ривожланаётган мамлакатларда бачадон бўйни саратони билан касалланиш ва тарқалишининг ўсиши 40 фоизни, иқтисодий ривожланган мамлакатларда эса 11 фоизни ташкил қилади. Бачадон бўйни саратонининг олдини олиш ва даволаш бўйича ўз вақтида чоралар кўрилмаса, бачадон бўйни саратони 2050 йилдан кейин дунё бўйлаб ҳар йили 1 миллион аёлда касаллик келтириб чиқаради. **Тадқиқот мақсади.** Ўзбекистон Республикасининг 9 ёшли қизларини эмлаш орқали бачадон бўйни саратонининг бирламчи профилактикаси ҳисобланади. **Материаллар ва усуллар.** Гардасил МК ваксинаси Ўзбекистон Республикасига 2019-йилда олиб келинган. 2019-йилнинг 21-октябрдан 30-ноябрга қадар Республикада 9 ёшли қизларга биринчи доза эмланди; 2-доза 6 ой ичида режалаштирилган. **Натижалар ва муҳокама.** 30 ноябрь куни амалга оширилган чора-тадбирлардан сўнг эмлаш кўрсаткичлари сезиларли даражада ошди: Тошкент шаҳрида – 97%, Тошкент вилоятида – 90,8%, Бухорода – 90,2%. Эмлашдан бош тортганлар эмланмаган қизларнинг 66,9%ни ташкил қилади. Вақтинчалик ташлаб кетилганлар, шунингдек, эмланмаганлар 360 (4%) ни ташкил қилади. 1935 нафар қиз бошқа сабабларга кўра эмланмаган ва умумий эмланмаган аҳолининг 21,4%ни ташкил қилади. **Хулоса.** Ўзбекистон Республикаси Ҳукумати, Соғлиқни сақлаш вазирлиги, ЖССТ ва ЮНИСЕФ ҳалқаро ташкилотлари кўмагида биргаликдаги саъй-ҳаракатлари натижасида ИПВ га қарши тўрт валентли вакцина – Гардасил МКнинг биринчи дозаси мамлакат бўйлаб 9 ёшли қизларда муваффақиятли эмланди. Ўзбекистон Республикаси Соғлиқни Сақлаш вазирлиги маълумотларига кўра, 292 867 нафар қиз болада эмлашдан сўнг нолғўя реакциялар кузатилмаган.

ОПЫТ РЕАЛИЗАЦИИ НАЦИОНАЛЬНОЙ ПРОГРАММЫ ВАКЦИНАЦИИ ПРОТИВ ВИРУСА ПАПИЛЛОМЫ ЧЕЛОВЕКА В РЕСПУБЛИКЕ УЗБЕКИСТАН

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Введение. Рак шейки матки представляет одну из серьезнейших угроз здоровью женщин. Это четвертый по распространенности вид рака у женщин всего мира. Согласно оценкам ВОЗ, в мире в 2019 году было зарегистрировано около 600 000 вновь выявленных случаев и более 300 000 случаев смерти от рака шейки матки (руководство ВОЗ). По прогнозам международных экспертов (с учетом роста населения и увеличения ожидаемой продолжительности жизни), к 2020 году в развивающихся странах рост заболеваемости и распространенности РШМ составит 40%, а в экономически развитых странах – 11%. В случае не проведения своевременных мероприятий по профилактике и лечению РШМ, после 2050 года ежегодно в мире злокачественными новообразованиями шейки матки будут заболеть до 1 млн. женщин. **Цель исследования** - Первичная профилактика рака шейки матки, путем внедрения вакцинации 9 летним девочкам Республики Узбекистан. **Материал и методы.** Вакцина Гардасил МК была ввезена в Республику Узбекистан в 2019 году. С 21 октября по 30 ноября 2019 года в Республике проведена вакцинация 1 дозы 9-летним девочкам; введение 2-й дозы запланировано через 6 месяцев. **Результаты и обсуждение.** После проведенных мероприятий 30 ноября показатели вакцинации заметно увеличились: в городе Ташкенте - 97%, в Ташкентской области - 90,8%, в Бухаре - 90,2%. Отказавшиеся от вакцинации составили 66,9% непривитых девушек. Временно выбывшим, которым также не произведена вакцинация составили 360 (4%). По другим разным причинам не вакцинированы 1935 девочек, что составило 21,4% из числа всего невакцинированного контингента. **Заключение.** В результате совместных усилий со стороны Правительства Республики Узбекистан, Министерства здравоохранения при поддержке международных организаций ВОЗ и ЮНИСЕФ успешно осуществлено введение первой дозы четырехвалентной вакцины против ВПЧ - Гардасил МК- была 9 летним девочкам по всей Республике. По данным Минздрава Республики Узбекистан, после вакцинации у 292 867 девочек никаких побочных реакций не наблюдалось.

Introduction. Cervical cancer is one of the most serious threats to women's health. This is the fourth most common cancer in women around the world. According to WHO data, around 600,000 newly diagnosed cases and more than 300,000 death cases from cervical cancer in the world were recorded in 2019 (WHO guidelines). According to the forecasts of international experts (taking into account population growth and an increase of life span expectancy), the increase in the incidence and prevalence of cervical cancer will have made up 40% in developing countries and in economically developed countries - 11% by 2020. In the case of non-conducting timely measures for the prevention and treatment of cervical cancer, malignant neoplasms of the cervix will affect up to 1 million women annually after 2050 in the world [1,5,8].

Indicators of morbidity and mortality from cervical cancer are also unpromising in the Republic of Uzbekistan. The frequency of cervical cancer advanced forms (stage III-IV) remains high, making up 45.3%. 5-year survival at stage III is 30-35%, at stage IV - only 5-7%. In 2018, the number of initially diagnosed cases of cervical cancer was 1,600 cases, and more than 800 patients died from this disease. Below are the intensive indicators of the morbidity rate per 100 thousand population in Uzbekistan.

Recent epidemiological studies have shown that cervical cancer is caused by oncogenic types of human papillomavirus (HPV). Two oncogenic types of HPV that most often cause cervical cancer are types 16 and 18. They together cause approximately 70% of cervical cancer cases in all countries of the world, in other cases the etiological role of the cervical cancer development belongs to other serotypes of viruses [7]. HPV 16 in 41-54% of cases causes the cervical cancer development [10]. Cervical cancer does not occur in the absence of the virus. The development of the disease is slow, so it is detected after decades [9]. In 2008 the Nobel Committee awarded a prize in physiology and medicine for the discovery of viruses that annually take millions of human lives. Half of the prize was awarded to Harald zur Hausen "for the discovery of human papillomaviruses that cause cervical cancer", the other half – to Francoise Barre-Sinoussi and Luc Montagnier "for the discovery of the human immunodeficiency virus" [4]. Currently, two vaccines are approved for the prevention of oncogenic types of HPV infection in most countries. Vaccines contain virus-like particles - the papilloma virus (PV), similar in shape with the human papilloma virus. As far as vaccines consisting of PV do not contain the virus, they cannot cause infection. Vac-

cines stimulate the production of antibodies to PV, which, due to their similarity with HPV, will prevent the infection caused by HPV in contact with it in the future [2,3]. Vaccines are highly safe and can be prescribed along with other vaccines that do not contain live pathogens [6].

There are proven and effective strategies for cervical cancer at all stages of the continuum of medical care in world practice. The first step in this strategy is vaccination against human papillomavirus (HPV) which in 95-98% of cases is the cause of cervical cancer. The WHO Director-General has called for action to eliminate cervical cancer in May, 2018. Partners and countries should work over an increase of access to three main measures for cervical cancer prevention - HPV vaccination, screening and treatment of precancerous conditions and increase of their coverage rates. Uzbekistan is one of six pilot countries in the framework of the United Nations Joint Global Program for the Prevention and Control of Cervical Cancer. The goal of this program is to join the efforts of all seven participating UN organizations to work with the government and other partners in order to promote the development and implementation of a sustainable, comprehensive and high-quality national cervical cancer program that provides women with equal access to services and information. The joint program aims to eliminate cervical cancer at a global level. A national action plan for 2020-2025 was developed for accelerating the implementation of this program and ensure its effectiveness in the country.

Aim of the study is primary prevention of cervical cancer by introducing vaccination to 9 years old girls of the Republic of Uzbekistan.

Material and methods. In 2015, by the Order of the Government of the Republic of Uzbekistan, with the support of GAVI, WHO, UNICEF and the Ministry of Health, the national vaccination schedule included the HPV vaccination for girls aged 9–13 years produced by MerckSharp & Dohme (sometimes called MSD or Merck, USA), which received a license for use in 2006. This vaccine is tetravalent and protects against 4 types of HPV– 6,11,16,18. The Gardasil MK vaccine was imported to the Republic of Uzbekistan in 2019. From October 21 to November 30, 2019, the first dose was vaccinated to 9 years old girls in the republic; the introduction of the 2nd dose is planned in 6 months. A total number of 9 years old girls in the republic is 292617 (100%). Results and discussion

The vaccination process was carried out from October 21 to November 30, 2019. Preparation for vaccination was started in March 2019 by the Ministry of Health with the assistance of international organizations WHO, UNICEF, leaders of the working group (obstetrician-gynecologists, epidemiologists, general practitioners, oncologists). Preparatory activities included the following: creating videos, information brochures, flyers, manuals for doctors, parents and carers in Russian and Uzbek; organization of conferences and seminars with the participation of European experts in the field of vaccination; performances in the media and in social networks. Also, by the UNICEF initiative, a video was created in Uzbek and Russian about cervical cancer, with the participation of leading oncologists of the republic. The video began to be shown a week before vaccination began on several TV channels, in public transport (metro, buses) for a month. Vaccination was carried out in family polyclinics and medical centers of secondary schools, in the presence of the parents of the vaccinated girls, a general practitioner and an epidemiologist. The vaccination was performed by a specially trained, licensed vaccine nurse.

Vaccination coverage by regions (absolute number /%): Autonomous Republic of Karakalpakstan - 15616 (93.4%); Kharezm region - 16507 (99%); Ferghana region - 30829 (95.4%); Tashkent region - 20582 (90.2%); Syrdarya region - 6499 (92.4%); Surkhandarya region - 23501 (97.6%); Samarkand region - 35065 (98.1%); Namangan region - 22332 (95.8%); Navoi region - 7629 (92.4%); Kashkadarya region - 28235 (96%); Jizzakh region - 12345 (98%); Bukhara region - 14175 (90.8%); Andijan region - 26549 (96.2%) and Tashkent city - 19772 (97%) (Tab.1). The analysis of the table showed that the largest number of 9 years old girls in the Samarkand region was 35748, the smallest one was in the Syrdarya (7008), and vaccination coverage in these regions was 98.1% and 95%, respectively. The highest vaccination coverage was observed in the Kharezm region - 99%, the smaller - 93.9% in the Tashkent region and the Autonomous Republic of Kara-

Table 1.

Vaccination coverage in Uzbekistan

Administrative territories	Contingent to be vaccinated n=292617	Vaccinated n=283574	%
Tashkent city	20775	20367	98.0
Andijan region	27359	26782	97.9
Bukhara region	15619	15288	97.8
Djizzak region	12592	12350	98.1
Kashkadarya region	29401	28235	96.0
Navoi region	8253	8024	97.2
Namangan region	23305	22332	95.8
Samarkand region	35748	35069	98.1
Surkhandarya region	24075	23599	98.0
Syrdarya region	7008	6660	95.0
Tashkent region	22815	21423	93.9
Fergana region	32329	31281	96.8
Kharezmi region	16669	16507	99.0
Republic of Karakalpakstan	16761	15657	93.4
Total			96.9

karakalpakstan. Despite the fact that the Autonomous Republic of Karakalpakstan and the Kharezmi region are geographically distant, vaccination activity was quite high, as the specialists involved in vaccination were trained and certified by the Ministry of Health and WHO experts.

When studying the dynamics of vaccination coverage, the smallest number of vaccinated girls was observed in the capital of the Uzbekistan, the city of Tashkent, where coverage was 28%, in Bukhara and Tashkent regions coverage was lower than in other regions - 71.9% and 74.5%, respectively. The main reason for this situation in the capital was the spread by social networks unreasonable audio and video messages about the side effects of HPV vaccination which lead to infertility, allergic reactions, up to the death, that this event is aimed at the destruction or genocide of the nation and etc. a week before the vaccination began. In connection with the above situation, working groups consisting of epidemiologists, gynecologists, oncologists were created, who, according to the approved schedule, visited all schools in Tashkent, gave lectures, made presentations refuting false Internet messages. The Ministry of Health of the Republic of Uzbekistan, UNICEF and WHO actively participated in the coordination of the working groups.

When analyzing the dynamics of the vaccination process, there was a tendency to an increase in the number of vaccinated girls (Fig. 1).

Vaccination rates significantly increased after the measures taken on November 30: in the city of Tashkent - 97%, in the Tashkent region - 90.8%, in Bukhara - 90.2%. It should be noted that adverse reactions were not observed after vaccination. Despite the carried out organizational, sanitary and educational measures, 9043 (3.1%) girls were not vaccinated for several reasons. The main reason was the refusal of parents to vaccinate, despite repeated explanatory discussions about the need for vaccination. The refusal was reasoned by the disagreement of father, grandmother, grandfather and other relatives, religious affiliation, etc. The largest number of refusing was observed in Kashkadarya region - 1166, in Tashkent region - 1114 and the Republic of Karakalpakstan - 914. In the Namangan region 868 girls also refused vaccination. Refusers made up 66.9% of unvaccinated girls. The next reason was medical challenge for one reason or another; the total number of medical challenges in the republic was 702 (7.7%): girls with acute inflammatory and respiratory diseases, exacerbation of chronic diseases, the presence of an allergic reaction at the time of vaccination, etc. However, after the condition improves, the girls will be vaccinated (Fig. 2).

Temporary left who also did not receive vaccination made up 360 (4%). 1935 girls were not vaccinated by other reasons and they made up 21.4% of the total unvaccinated population.

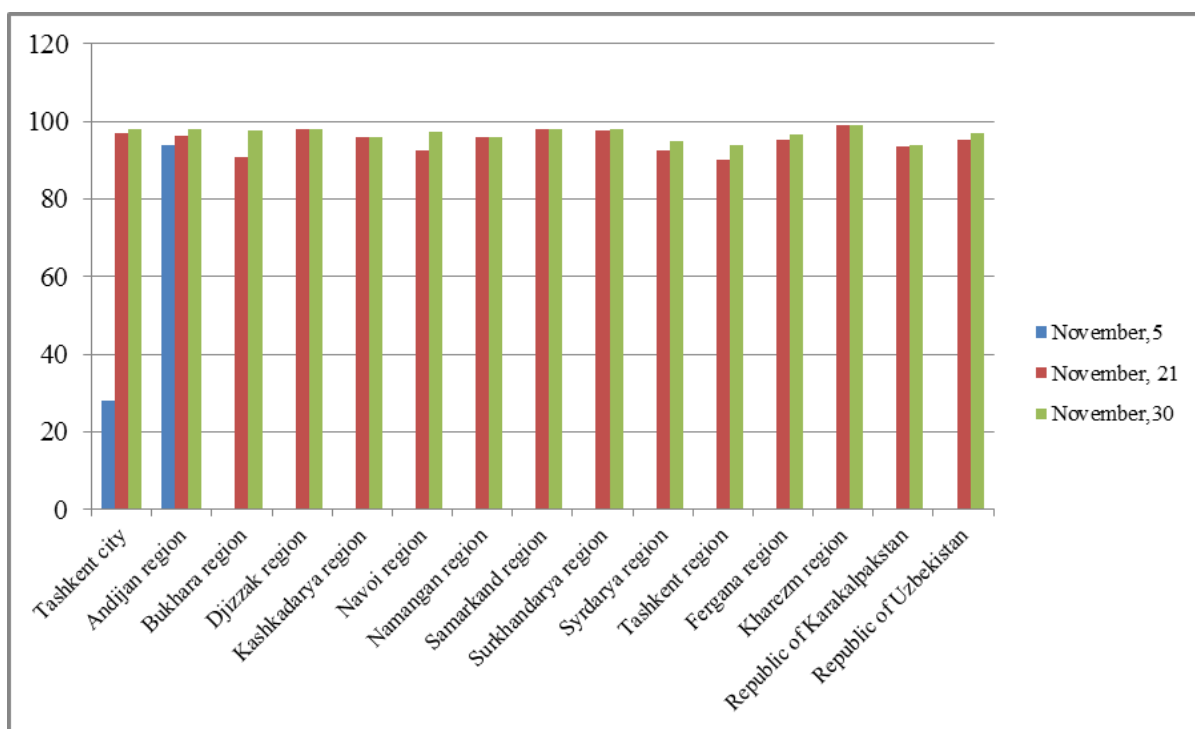


Fig. 1. The dynamics of the vaccination process in Uzbekistan.

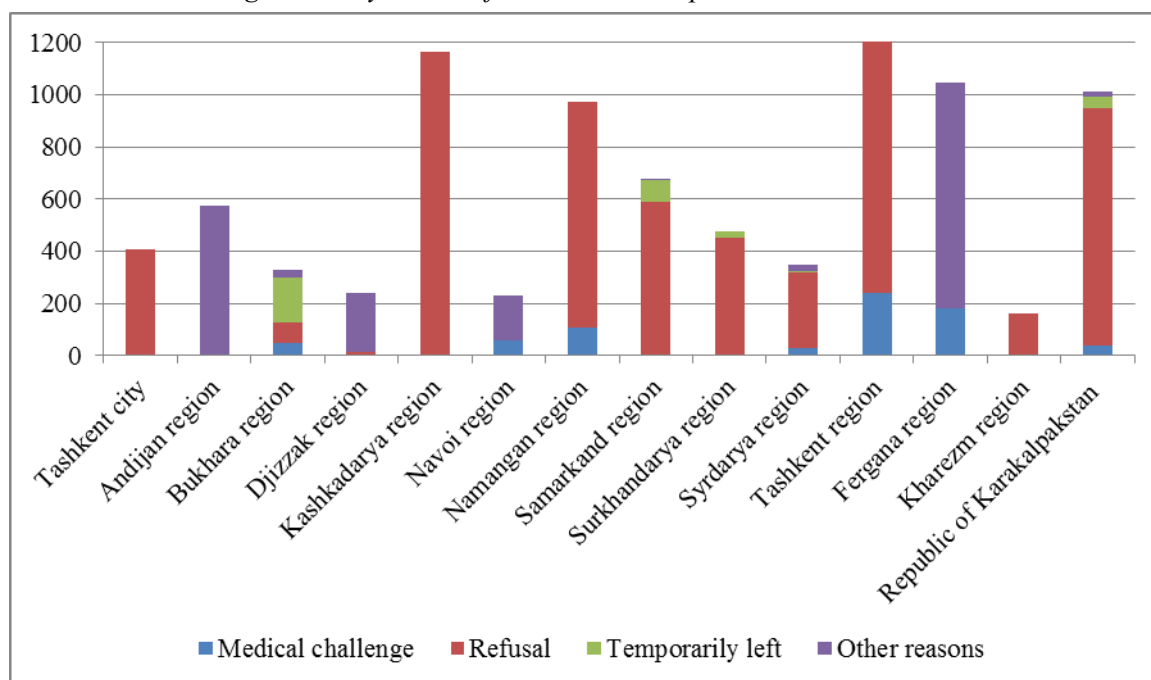


Fig. 3. The reasons of non-vaccination.

Conclusion. Our experience with HPV vaccination has shown that more attention should be paid to educational work (social videos, audio messages, meetings in the media, in magazines, newspapers, etc.), on TV and in social networks a few months earlier than planned vaccination, organize lectures, presentations in schools, polyclinics 2-3 months before the planned vaccination, with the mandatory participation of leading experts in the field of epidemiology, virology, gynecology and oncology. Also, a comprehensive action plan should be drawn up before, during and after vaccination with the involvement of experts from international organizations with sufficient experience in conducting such large-scale events.

As a result of joint efforts by the Government of the Republic of Uzbekistan, the Ministry of Health with the support of international organizations from WHO and UNICEF, the first dose of the tetravalent HPV vaccine - Gardasil MK- was successfully administered to 9 years old girls all

over the country. According to the data of Health Ministry of the Republic of Uzbekistan no adverse reactions were observed in 292,867 girls after vaccination.

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