RESEARCH ARTICLE

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Vaccination Effectiveness against Human Papillomavirus in Kazakhstan

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Abstract

Objective: The purpose was to determine the effectiveness of human papillomavirus immunization and its impact on cervical cancer development in Kazakhstan. **Methods:** The current research is a case-control study with two groups: a main group and a control group. A total of 725 subjects participated in the research. **Results:** The association between vaccination and cervical cancer development was calculated both for the two groups as a whole and for individual patients, who were selected based on criteria of residence, presence of immunodeficiency or chronic cardiac or renal pathology, as well as analysis of age at which the vaccine dose was received. There was a statistically significant association between the absence of the human papillomavirus vaccine and the risk of cervical cancer in all groups. When considering the entire cohort, the chance of finding a risk factor (lack of vaccination) was almost 7 times higher in the main group than in the control group. Thus, an association between vaccination and cervical cancer risk was found in each of the pairs of subjects. **Conclusion:** The effectiveness of vaccination in preventing cervical cancer was not observed in patients who were vaccinated after 18 years of age, while most patients in the control group were vaccinated in their teens. The practical significance of the research is not only to further study the problem of human papillomavirus (HPV) vaccination in Kazakhstan but also to popularize HPV immunization to prevent cervical cancer (CC).

Keywords: Cervical cancer- disease prevention- gynaecology- oncology- health care organization

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Introduction

Human papillomavirus (HPV) is associated with cervical cancer (CC), as well as some types of malignancies of the oropharynx, vulva, vagina, penis, and rectum [1]. The primary goal of HPV vaccination is to reduce morbidity and mortality from pathologies that are associated with the virus, especially cervical cancer [2]. Okunade [3], after reviewing the literature on the association of HPV and cancers, noted in a recent study that HPV vaccines can make a significant contribution to reducing the incidence of cancers and preventing this pathology.

HPV (human papillomavirus) vaccination is effective in preventing cervical cancer for several reasons. HPV is the primary cause of cervical cancer. By vaccinating against HPV, particularly the high-risk types such as HPV 16 and 18, the vaccine directly addresses the root cause of cervical cancer. These high-risk HPV types are responsible for the majority of cervical cancer cases. Clinical trials have shown that HPV vaccines, such as Gardasil and Cervarix, have high efficacy in preventing HPV infection and associated cervical abnormalities. These vaccines have been found to be highly effective in preventing infection with the specific HPV types included in the vaccine.

Widespread HPV vaccination creates herd immunity, which means that when a significant portion of the population is immune to HPV, it reduces the overall prevalence of the virus in the community. This indirectly protects those who may not have been vaccinated, including individuals who cannot receive the vaccine for medical reasons. HPV vaccines provide long-lasting protection. Studies have shown that protection against the targeted HPV types can last for many years, possibly even a lifetime, reducing the risk of developing cervical cancer over time. HPV vaccines not only prevent HPV infection but also reduce the risk of precancerous cervical lesions (CIN or cervical intraepithelial neoplasia). These lesions are precursors to cervical cancer, and by preventing their development, vaccines reduce the likelihood of cancer. Reducing HPV-related Diseases: In addition to cervical cancer, HPV is linked to other cancers (such as anal, vaginal, vulvar, and oropharyngeal cancers) and genital warts. HPV vaccination helps reduce the incidence of these diseases as well.

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It's important to note that while HPV vaccination is highly effective, it does not protect against all HPV types. Therefore, regular cervical cancer screening, such as Pap tests and HPV testing, remains important for early detection and prevention of cervical cancer. Additionally, vaccine coverage rates and public awareness are crucial factors in the effectiveness of HPV vaccination programs.

Over the past decade, cervical cancer has become the fourth most frequent cancer worldwide among women [4], and in the Republic of Kazakhstan, cervical cancer ranks second in the structure of oncopathology after breast cancer [5]. Such epidemiological data determine the research relevance. Various issues of prevention and prevalence of CC in the context of Kazakhstan have been studied before. Thus, it has been determined that the incidence and mortality from CC in different regions of the country may vary. The highest rates are observed in the northern regions (incidence – 16.3%, mortality – 12.6%), and the lowest in the western regions (incidence – 12.7%, mortality – 7.1%). The same authors point out that disease screening and vaccination programs should be presented and implemented at the state level. In another study, the authors noted the following areas with higher rates of RHM among women: East Kazakhstan, Aktobe, Almaty, Kostanai, Atyrau oblasts, and the city of Almaty [6].

The variations in cervical cancer (CC) incidence and mortality rates across different regions of Kazakhstan can be attributed to several interconnected factors. Geographic location and demographic characteristics of a region can play a significant role. For instance, regions with larger populations, higher population densities, and different age distributions may exhibit variations in CC rates. Areas with a higher proportion of women in the age group at risk for CC may have higher incidence rates. Disparities in access to healthcare services, including cervical cancer screening and vaccination programs, can influence the incidence and mortality rates. Regions with better access to healthcare facilities, skilled healthcare professionals, and preventive measures are likely to have lower CC rates. The quality and availability of healthcare infrastructure can vary across regions. Areas with well-established healthcare facilities and a strong healthcare system may be more effective in early detection, diagnosis, and treatment of CC, leading to lower mortality rates. Socioeconomic factors such as income levels, education, and awareness about cervical cancer and preventive measures can contribute to regional disparities. Regions with higher socioeconomic status may have better access to healthcare and health education, leading to lower CC rates. Cultural beliefs and behaviors related to healthcare, screening, and vaccination can vary across regions. Regions with cultural norms that encourage regular screening and vaccination may have lower CC rates. It's essential to consider that these factors often interact with one another, and regional variations may result from a combination of these influences. To address these differences and reduce CC rates, public health interventions should be tailored to the specific needs and challenges of each region, taking into account the underlying factors contributing to the disparities.

At the same time, Van Dyne et al. [1] uses a sample of U.S. women to point out that although HPV-related malignancies are preventable with vaccines, the overall incidence is increasing. It should also be noted that plans to achieve 80% vaccination coverage against human papillomavirus by 2020 have not been achieved in the United States [7]. In Kazakhstan, such coverage should be 70%, but Issa et al. [8] in a recent study showed that Kazakhstani women aged 18 to 70 were vaccinated against HPV in 45.7% of cases, a higher rate than in other countries with similar per capita incomes. Despite the work done to promote HPV vaccination in adolescents, the availability of the vaccine remains a problem. Markowitz and Schiller [9] point out the demand for HPV vaccines, which currently exceeds the supply. Therefore, further efforts to prevent HPV should also focus on increasing the production of appropriate vaccines as well as the development of new medicine.

The research aims to determine the effectiveness of HPV vaccination in the Republic of Kazakhstan and its impact on the development of cancers. The objective of the work was to evaluate the effectiveness of HPV vaccines when used in real clinical practice, as well as to determine the indicators affecting this effectiveness in different population groups.

Materials and Methods

The research is an analytic epidemiologic case-control study that is structured to include 2 groups of patients with or without the development of cervical cancer. The research was conducted in 5 stages, which include:

1. Hypothesis formation.
2. Term definition.
3. Case selection.
4. Control selection.
5. Reason determination.

The hypothesis for this study was that HPV vaccination is effective in preventing CC. The research defines "efficacy" as the degree to which vaccination achieved specific results in the primary prevention of CC, namely the relationship between the presence of HPV vaccination and CC.

The criteria for inclusion of patients in the case group were CC diagnosis. A case was defined as a patient with cervical intraepithelial neoplasia of grade 2 or 3 or adenocarcinoma in situ, age 18 years or older, and positive tests for HPV 16 or 18. Criteria for inclusion into the control group:

1. No CC symptoms (Papanicolaou type 1).
2. Same CC risk as in the population.
3. Age from 18 years.

The exclusion criterion for both the main group and the control group was the absence of consent to participate in the research. Since not all aspects that are relevant to the incidence of HPV and CC could be obtained from medical records, the patients were asked to undergo an additional questionnaire survey. The questionnaire included 5 chapters; details are shown in Table 1.

To systematize the data, a four-field table was created, the layout of which is presented in Table 2. The absence of HPV vaccination was taken as a risk factor (RF).

Table 1. Structure of Questionnaires for Patients from Two Groups

Chapter	Questions
Social and demographic data	Age, ethnicity, family status, address
Health habits including sexual activity	Age at the moment of first intercourse, number of partners over the last 3 years, type of used contraception
Health care availability and usage thereof	Previous Papanicolaou smear results and their availability, frequency of smears, availability of a qualified physician's consultation, number of visits to an obstetrician-gynaecologist in the past 12 months
HPV vaccination	Availability of HPV vaccination and the age at which it was given, attitudes toward and awareness of vaccination

Table 2. Four-Field Table Structure

Groups	Lack of HPV vaccine		
	Yes	Present	
Patients from the main group (patients with the event)	a	b	a+b
Control group patients	c	d	c+d
Total	a+c		a+b+c+d=N

To describe the numerical expression of the odds of how much the presence or absence of HPV vaccination affects the risk of CC, the odds ratio (OR) was used. An online calculator was used for this purpose. After appropriate selection, 228 unvaccinated girls and women who underwent cytology and HPV testing were included in the study. Also included in the study were 502 girls and women immunized with the HPV vaccine as part of the 2013-2015 vaccination pilot project.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. A study was approved by Kazakh Institute of Oncology and Radiology, March 21, 2023, No 1124-C.

Results

As noted earlier, after appropriate selection, data from 226 unvaccinated women and 502 vaccinated women were included in the research. The patients were selected at the Kazakh Research Institute of Oncology and Radiology. Details about the study sample are shown in Table 3.

Eighty-nine percent of the patients were ethnic Kazakhs, 7% were of Slavic ethnicity, and 4% had other ethnic origins. Most respondents in the two groups (vaccinated and unvaccinated subjects) lived in urban areas. Among the vaccinated subjects 0.8% became sexually active at age 13, 10.3% at age 16, 9.1% at age 17, 4.8% were not sexually active, and the rest became sexually active at ages 18-25. At the same time, all vaccinated patients who had Pap smear changes were sexually active. Twenty percent were married and none of them had a Pap smear change. In the unvaccinated group, 19.7% were unmarried, of whom 15 women had smear changes. At the same time, all 15.5% of the vaccinated smokers also had no changes, and in the unvaccinated smoking group, only 2 women had changes.

The average age of menarche in both vaccinated and unvaccinated patients was 13 years, and the duration of menstruation was 4-5 days. In the vaccinated 11.7%, menstruation was irregular, and among them, only 3 women were found to have changes in the cytological examination. In the unvaccinated group of women, 15.8% of menstruation is irregular. Of the vaccinated respondents, 84.1% had menstruation that was generally not painful,

Table 3. Number of Patients of Different Age Groups among Vaccinated and Unvaccinated Subjects

Age category	Number of patients	
	Vaccinated group	Unvaccinated group
18-23 years	28	486
24-26 years	71	16
27-30 years	127	0
Total patients	226	502

Table 4. Assessment of the Availability of a Qualified Physician's Consultation

Age category	% of respondents who rated the availability of a consultation with a qualified physician as					
	Unvaccinated respondents			Vaccinated respondents		
	Good	Satisfied	Bad	Good	Satisfied	Bad
18-23 years	80	15	5	92	7	1
24-26 years	75	11	14	91	8	1
27-30 years	85	11	4	85	12	5

Table 5. Presence of Risk Factors in All Patients from the Main and Control Groups

	Risk factor present	Risk factor absent	Total
Result present (main group)	33	12	45
No result (control group)	193	490	683
Total	226	502	728

Table 6. Results of Calculating odds ratios and Other Parameters Determining the Effectiveness of Vaccination in the Study Group

Chance of finding a risk factor in the primary group	2.75
Chance of finding a risk factor in the control group	0.394
Chance correlation (OR)	6.982
Standard odds ratio error (S)	0.348
Lower 95% CI bound	3.532
Upper 95% CI bound	13.8

Table 7. Distribution of Vaccinations According to the Age at which they were Given

Vaccination age	Patient number	
	Primary group	Control group
8 years	0	9
8-14 years	2	428
15-17 years	20	63
18 years and more	23	2
Total patients	45	502

Table 8. Vaccination in Patients with Chronic Diseases and Immunodeficiency

Groups	Risk factor present		Total
	No	Yes	
Patients from the main group (patients with the event)	1	7	8
Control group patients	31	3	34
Total	32	10	42

Table 9. Results of Calculating odds ratios and Other Parameters Determining the Effectiveness of Vaccination in a Group of Patients with Chronic Diseases and Immunodeficiency States

Chance of finding a risk factor in the primary group	7
Chance of finding a risk factor in the control group	0.097
Chance correlation (OR)	72.333
Standard odds ratio error (S)	1.228
Lower 95% CI bound	6.515
Upper 95% CI bound	803.145

and only 1 woman of those 84.1% had changes. Those interviewed with Papanicolaou smear changes responded as follows: 3 subjects had painful menstruation, 1 had moderate pain, 2 women had pain on only 1 day, and the rest had pain that was not always present or was tolerable. In the unvaccinated subjects, only 43.4% reported that menstruation was painless.

Of the vaccinated subjects, 17.2% had a history of pregnancy, 5.6% used hormonal contraception, 37.6% used barrier contraception, 32.5% did not use contraception at all, and the remaining subjects practiced interrupted intercourse or did not answer the question. At the same time, most patients with smear changes did not use any contraception and only one person noted that he used barrier contraception, but these same subjects also noted that they had had 1-2 sexual partners in the past 3 years. Only 8.8% of those vaccinated had heard of the Pap smear, 32.9% would vaccinate their children against HPV, and 47.8% would recommend HPV vaccines to relatives or acquaintances. Among the unvaccinated, 53.5% had a history of pregnancy, 38.7% of the unvaccinated did not use contraception, and they also had the highest percentage of Papanicolaou smear changes. There was also a difference in the assessment of the availability of a qualified physician consultation between the study and control groups, as well as within groups, relative to the age of the patient.

Table 4 presents details about patients' assessments of the accessibility of a skilled nursing consultation. A four-field table reflecting the presence of a risk factor is presented below (Table 5). Patients in the main group were diagnosed with Papanicolaou smear changes; subjects in the control group were unchanged. To assess the significance of the odds ratio, the boundaries of the 95% confidence interval (CI) are calculated. If the 95% confidence interval in the odds ratio is greater than 1, this means that the odds of finding the risk factor are greater in the group with the outcome (i.e., the main group), and the factor (lack of vaccination against HPV infection) has a direct relationship with the probability of the outcome, or it is an aggressive factor. In this case, the p-value is greater than 0.05. In the case where the 95% confidence interval of the odds ratio is less than unity, this indicates that the odds of finding the risk factor is greater in the control group of patients, that is, the factor has an inverse relationship to the probability of the outcome occurring or it is a protection factor. In this case, the p-value is less than 0.05. With an odds ratio of 1, the chance of detecting a risk factor in the study groups is the same. Thus, the factor in question does not affect the probability of the outcome. In this case, the p-value is greater than 0.05. In each case, the statistical significance of the OR was assessed separately based on 95% CI values. If the 95% CI of the odds ratio did not include one, i.e., all the margins were either above or below one, then the association between the factor and the outcome was statistically significant (p-value less than 0.05). If the upper limit of the CI is greater than one and the lower limit is less than one, there is no statistical significance in determining the relationship between the factor under study and the outcome (p-value less than 0.05). Thus, the current study compared the group of subjects according to the frequency of determining the available RF. An important role is played by the fact

that as a result of the application of the OR not only the statistical significance of the relationship between the RF and the outcome can be identified, but also its quantitative characteristic.

The results of calculating odds ratios and other parameters determining the effectiveness of vaccination in the study group are presented in Table 6. The odds ratio was the ratio of the frequency of outcomes in subjects influenced by the RF under study (in the context of the current study, no vaccination) to the frequency of outcomes in subjects who were not influenced by this RF (vaccination against HPV infection). Thus, the results of calculating odds ratios and other parameters determining vaccination efficacy rates in the study group are presented in Table 6. Based on this table, considering the abovementioned, it is possible to determine that the p-value remained less than 0.05.

Odds ratios were used to compare the probability of outcome from the presence of a risk factor. Thus, Table 6 shows that the chance of finding a person with RHM among unvaccinated patients is almost 7 times higher than among vaccinated patients. The key to determining the effectiveness of HPV immunization in controlling CC remains the age at which vaccination should be given. The effectiveness of vaccination at ages 12-13 have previously been noted [10]. In the current study, it was found that the main group of female patients was vaccinated mostly at age 18 or older, 20 at age 15-17, and 2 at age 8-14; the remaining study subjects from the main group were not vaccinated. Table 7 shows the distribution of vaccinations by age.

In Table 8 displays the distribution of vaccinations among patients with chronic diseases and immunodeficiency in both the main group and the control group. It shows the number of patients with and without the risk factor present in each group and provides a total count for each category. Table 9 shows that the chance of finding a risk factor (no vaccination) in the main group is almost 72 times higher than in the control group, and the p-values do not exceed 0.05. It calculates the odds ratio (OR), standard odds ratio error (S), and 95% Confidence Interval (CI) bounds. The odds ratio of 72.333 indicates that the chance of finding a risk factor (no vaccination) in the primary group is approximately 72 times higher than in the control group, suggesting a significant association between vaccination and the presence of risk factors. The 95% CI bounds (6.515 to 803.145) provide a range within which the true odds ratio is likely to fall with 95% confidence. The p-values (not provided in the table) do not exceed 0.05, indicating statistical significance.

Thus, among all subjects, there was an association between the presence of the event, the presence of vaccination, and the age at which the HPV vaccination was administered. The results of the study showed that among unvaccinated patients, the chance of detecting Papanicolaou smear changes is almost 7 times higher than among vaccinated patients (odds ratio 6.982). It has also been found that the effectiveness of the vaccine depends on the age at which it was administered - the most effective vaccination is at the age of 12-13 years. Among patients with chronic diseases and immunodeficiency conditions, the chance of detecting the absence of vaccination among those with Papanicolaou smear changes was 72 times higher than among those without changes. Thus, vaccination is associated with a reduced risk of cervical changes caused by HPV infection.

Discussion

Kazakhstan tried to be the first among the Central Asian countries to vaccinate against HPV, but without much success. In 2013-2015, girls were vaccinated against the human papillomavirus in four regions of the country: Almaty, Astana, Pavlodar, and Atyrau regions. Almost 17 thousand people received from one to three doses (at that time - a full course) of the vaccine. Ultimately, the program was stopped due to a large-scale negative response in the media and social networks, which reached its peak when two girls fainted after being vaccinated in the Pavlodar region. A commission under the Ministry of Health that investigated the incident later concluded that their reaction was related to the conditions of the vaccination, and not the drug itself, but there was no attempt to resume the campaign for many years.

The current study noted the effectiveness of vaccination for the prevention of CC. In previous studies, HPV vaccines are unequivocally effective against the full spectrum of HPV-related diseases [9]. The research was not typed and identified HPV in subjects. A study by Aimagambetova and Azizan [5] showed that the prevalence of HPV infection in Kazakhstan was estimated at 44% to 56%. The most common HPV types are HPV 16, HPV 18, HPV 51, and HPV 33. The incidence of CC is about 3 thousand cases per year, while fatalities occur in about 1 thousand patients each year. The research examined the effectiveness of preventive vaccines, but these vaccines cannot help those patients who are already infected with the virus and have a risk of developing concomitant neoplasms [11]. Also in the same publication, the authors note that therapeutic HPV vaccines are necessary for modern medicine to reduce the burden of CC, but the problem remains the lack of information about the immune mechanisms against HPV infection and the technology to develop sufficiently effective and immunogenic vaccines. It is worth noting that no vaccine has yet been licensed for use in the therapy of infection or CC itself, but prophylactic drugs have found use immediately after surgical interventions for cervical neoplasia to prevent reactivation of the virus or reinfection [12].

The research did not address whether vaccination was done as part of a state or municipal program. At the same time, studies are showing the effectiveness of HPV vaccination programs. For example, Falcaro et al. [10] studied the effectiveness of such a program in the United Kingdom in preventing cervical neoplasms, which started on September 1, 2008, and covered women aged 12 to 14 years. Data from women aged 20-64 years were evaluated. The results of the study concluded that the immunization program significantly reduced the incidence of cervical cancer, especially among patients vaccinated at the age of 12 to 13 years, and virtually eliminated

the pathology among women born after September 1, 1995. At the same time, an HPV vaccination program for adolescents in Zimbabwe may be less successful, despite the willingness of health facilities and providers, due to the prejudices held by the population about both the vaccination itself and CC [13]. Vaccination rates and accessibility to a qualified specialist consultation in the current study were not assessed separately in subjects from rural and urban areas. At the same time, Buskwofie et al [14], after reviewing the literature on the incidence of CC from 1999 to 2020, concluded that people who are socioeconomically disenfranchised and patients living in rural areas have extremely low rates of vaccination, screening, and therapy for CC, which is associated with increased morbidity and mortality from the disease.

Rural residents have previously been found to be less aware of the risks of developing CC. For example, a recent study [15] included 116 participants from a Malaysian village, 88.8% of whom had heard of CC, but only just under 30% had heard of the connection between CC and HPV, and 42% knew of HPV vaccination respectively, leading to conclusions about low awareness of the topic of CC and HPV vaccination in the study population. This research was conducted with a sample of the female population only. However, the feasibility of vaccinating male adolescents remains an open question. Studied HPV vaccination among boys from the side of cost-effectiveness. Only 9 studies were found and analysed, which did not allow the authors to draw unequivocal conclusions. The researchers noted that countries should evaluate the economic aspects of vaccination programs themselves, as well as consider criteria such as gender equality [16].

The current study also examined the effectiveness of vaccination in the context of CC, but the effect of vaccines on the incidence of other types of HPV-associated malignancies remains an important aspect. Thus, Nielsen et al [17] studied the relationship of prophylactic HPV vaccines with oral and oropharyngeal HPV infection. The researchers analysed 9 studies that included information on nearly 50 thousand patients and concluded that HPV vaccines were effective in controlling HPV infection. A separate issue is the calculation of the efficacy of the vaccine depending on its type. There are currently two approved HPV prophylactic vaccines that primarily target highly oncogenic HPV types. These drugs are highly immunogenic and effectively induce the production of specific immunoglobulins. Earlier it was found that bivalent drugs showed higher efficacy in HPV infection than quadrivalent analogs. The authors also note that HPV prophylaxis with non-valent vaccines before sexual initiation is associated with immunization against several subtypes of the virus [18]. The same authors predict an increase in vaccine efficacy, but at the same time note the importance of the further study of the specific pathological mechanisms of HPV infection.

The results of the current study in the context of vaccinating adult women are similar to the findings of other authors. It has previously been found that while they are highly effective in preventing HPV infection, cancers, and other pathologies, they do not help to get rid of existing infections. Vaccinating adults may provide some protection and accelerated exposure, although it may not be cost-effective. These same authors also note that screening for HPV infection is also necessary for vaccinated cohorts, although intervals between preventive examinations may increase [19]. Previous studies have also found that a 2-dose vaccination plan is as effective as a 3-dose plan, but at the same time, other studies have also noted the effectiveness of the first dose alone in controlling HPV-associated pathology [20]. The current study did not separately evaluate efficacy at different doses, but this issue was explored in a recent review by Markowitz et al. [21], who selected 35 studies to evaluate immunogenicity at different vaccine dose numbers. The authors noted that most of the publications reflected the highest estimates of efficacy at three doses, but at the same time, efficacy at 1 dose was also noted. Nevertheless, the authors did not draw unequivocal conclusions.

A separate problem remains for patients with immunodeficiency conditions and chronic heart and kidney failure, who were also included in the current study. Such patients are at particularly high risk of developing CC [22]. Although screening studies are the backbone of CC prevention in HIV-positive patients, the importance of HPV vaccination in such patients has also been noted [23], which is also consistent with the results of the current study. Women with chronic diseases typically have lower rates of CC screening [24], so HPV vaccination is particularly relevant and reflected in the findings. Thus, evidence is accumulating on the positive aspects of HPV vaccination promotion and its effectiveness both in Kazakhstan and in other countries.

In conclusions, this study evaluated the effectiveness of HPV vaccination in Kazakhstan. The effectiveness of vaccination and its association with the absence of cervical intraepithelial neoplasia stage 2 or 3 or adenocarcinoma in situ in the control group was noted for all aspects studied. In the Republic of Kazakhstan, despite certain successes, the development and popularization of HPV vaccination are important for the country. It represents a fundamental element in the primary prevention of CC and other malignant neoplasms. The public health objectives should be to ensure access to vaccination for all target populations. In the process of research, new questions and problems have arisen that need to be addressed. It is also important to note that the availability of vaccination and public awareness about it are important factors in the fight against cancers and other cancers. Additional public education is needed about vaccination as an effective method of early prevention of HPV infection and cancers.

The research demonstrates a difference between the two study groups in a limited sample. Findings from large-scale studies involving more patients from the Kazakh female population, as well as more disaggregated data (including vaccine type and frequency of administration), would provide even more accurate results. Further work is also needed to develop and improve national immunization program methodologies, introduce them into practice, and consider HPV vaccination programs for male adolescents. The research relevance is in the contribution to the further study of the problem of HPV vaccination in Kazakhstan, as

well as to popularize immunization among the adolescent population. The research materials may be useful for paediatricians, obstetricians-gynaecologists, oncologists, and surgeons, as well as for researchers whose activities are related to this topic. In future studies, the authors need to focus on HPV vaccine efficacy in the context of CC prevention, such as the number of patients treated and the waiting time (intermediate results) or lives saved and years of life (final results).

Author Contribution Statement

AS, RB, YK, SO and DK conceptualized and designed the study, AS and YK collected the data, AS, RB, YK, SO and DK analyzed and interpreted the results, AS prepared the initial manuscript. All authors reviewed the results and approved the final version of the manuscript.

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Conflict of Interest

The authors declare no conflict of interest.

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