# ABSTRACT

of the Thesis Work of Alima Rinatkyzy Satanova on the topic " **Analysis of the effectiveness of vaccination against human papillomavirus in the Republic of Kazakhstan",** submitted for the degree of Doctor of Philosophy (PhD) in the specialty 8D10103 – "Medicine"

## Relevance of the Problem

According to the International Agency for Research on Cancer (IARC), cervical cancer (CC) remains one of the leading causes of cancer-related mortality among women of reproductive age worldwide. In 2022, over 600,000 new cases and more than 300,000 deaths were recorded, underscoring the global public health significance of this disease. Particular concern arises in low- and middle-income countries, where coverage with preventive measures, including human papillomavirus (HPV) vaccination—a key factor in cervical carcinogenesis—remains insufficient. More than 200 HPV genotypes have been identified, of which 14 are considered high-risk oncogenic types, especially types 16 and 18, which account for up to 70% of all cervical cancer cases. Modern prevention strategies include the implementation of HPV vaccines, which have demonstrated high efficacy in preventing infection with oncogenic HPV types and the development of precancerous cervical lesions. The World Health Organization (WHO) considers vaccination of girls prior to the onset of sexual activity the most effective measure of primary prevention. In the Republic of Kazakhstan, despite the implementation of a national cervical cancer screening program since 2008, epidemiological indicators remain consistently high. According to the National Oncological Registry, the incidence of cervical cancer is 18.9 per 100,000 women, and the mortality rate is 5.7 per 100,000. Low vaccination coverage, limited health education, vaccine hesitancy, and the absence of differentiated screening strategies for vaccinated women hinder effective disease prevention. To date, Kazakhstan has not conducted comprehensive studies evaluating the long-term outcomes of HPV vaccination administered within the 2013–2015 pilot program, nor its impact on cytological indicators and public awareness levels. The absence of evidence-based data hampers adjustments to screening protocols. In this context, an epidemiological and clinical assessment of HPV vaccine effectiveness is particularly timely and relevant. Thus, this study addresses key public health priorities in Kazakhstan aimed at reducing cancer incidence and mortality, and represents a significant contribution to the development of evidence-based approaches to cervical cancer prevention at the national level.

## Purpose of the Study

To assess the effectiveness of HPV vaccination in the Republic of Kazakhstan.

**Study Objectives:**

1. Analyze cervical cancer incidence and mortality in Kazakhstan from 2014 to 2023.
2. Investigate public awareness and perceptions of HPV vaccination across different population groups in Kazakhstan.
3. Evaluate the cervical status of HPV-vaccinated women using cytological examination and PCR testing.
4. Determine HPV status among vaccinated and unvaccinated women to assess vaccine effectiveness.
5. Develop and propose a cervical cancer screening model tailored to both vaccinated and unvaccinated populations.

**Study Methods**

This study employed information-analytical, epidemiological, clinical, laboratory-diagnostic, instrumental, and statistical methods.

A bilingual questionnaire was used to survey 889 unvaccinated and 1121 vaccinated women, collecting data on menstrual function, gynecological history, sexual activity, contraceptive use, chronic diseases, and awareness of cervical cancer prevention methods, including screening and HPV vaccination.

Epidemiological analysis included calculating incidence and mortality rates using Poisson and log-linear models. Clinical examinations included gynecological assessment, bimanual examination, and sample collection.

Laboratory and instrumental diagnostics included PCR-based HPV testing using the validated Cobas® 4800 HPV system (Roche, Germany), and cytological smear evaluation using the 2014 Bethesda system and conventional Papanicolaou staining.

Statistical analysis was conducted to identify risk factors for precancerous lesions and invasive cervical cancer.

**Object of the Study**

For the epidemiological component, data were obtained from Electronic Registry of Oncological Patients, and cervical cancer screening results from 2014–2023.

The clinical component included 889 conditionally healthy unvaccinated women living in Almaty, and 1121 vaccinated women (vaccinated between 2013–2015) from Almaty, Astana, Pavlodar, and Atyrau.

**Subject of the Study**

Effectiveness of HPV vaccination among women and adolescents in Kazakhstan, including its impact on high-risk HPV infection rates, prevalence of cervical precancerous conditions, public awareness of screening and prevention, and the development of an optimized screening model for vaccinated and unvaccinated populations.

**The Main Provisions to be Defended:**

1. A comprehensive analysis of 10-year epidemiological data confirms a persistent increase in incidence and mortality, along with significant regional disparities necessitating targeted prevention strategies.
2. The study demonstrates low public awareness of HPV vaccination and high refusal rates, highlighting the need for intensified health education initiatives.
3. HPV vaccination has shown proven efficacy in reducing high-risk HPV infection rates and the occurrence of precancerous cervical lesions among vaccinated women.
4. A tailored screening model for vaccinated populations has been developed, incorporating age-specific and risk-based adjustments to optimize preventive interventions.

**The Main Results of the Study:**

The study found that between 2014–2023, Kazakhstan maintained a consistently high cervical cancer incidence and mortality rate—18.9 and 5.7 per 100,000 women, respectively. Epidemiological analysis revealed marked regional disparities correlated with differences in screening and vaccination coverage.

Survey results showed higher awareness among vaccinated women—88.3% were aware of HPV, compared to 39.6% of unvaccinated respondents. Awareness of HPV vaccination was reported by 92.1% of vaccinated women and only 31.2% of unvaccinated women ($p<0.001$).

HPV prevalence was 0.8% among vaccinated women and 14.5% among unvaccinated ($p<0.001$). The vaccine significantly reduced high-risk HPV infections, including types 16 and 18. Cytological analysis revealed normal findings (NILM) in 96.2% of vaccinated women, compared to 78.4% of unvaccinated. High-grade lesions (HSIL) were found only among unvaccinated women.

Based on these findings, a differentiated screening model was proposed, incorporating epidemiological, clinical, sexual history, vaccination status, HPV testing, and cytology results. This model aims to optimize prevention programs and healthcare resource allocation.

**Scientific Novelty**

1. For the first time, a detailed study of cervical cancer trends in Kazakhstan over the past decade was conducted, identifying key epidemiological trends and regional features.
2. Public awareness and perception of HPV vaccination were assessed for the first time, identifying key barriers to effective vaccine uptake.

3. For the first time in Kazakhstan, a comprehensive assessment of the effectiveness of the human papillomavirus (HPV) vaccination program was conducted, demonstrating a significant reduction in high-risk HPV infection and a decrease in the prevalence of precancerous cervical conditions among vaccinated women ten years after immunization.

4. For the first time, a study was conducted to assess the prevalence of human papillomavirus (HPV) among women of reproductive age. This made it possible to identify key infection trends within this critical population group, which is of great importance for developing effective prevention strategies and increasing vaccination coverage among young women.

**Practical Significance**

The results confirm the high effectiveness of HPV vaccines in reducing infection rates with high-risk types 16 and 18, providing a basis for expanding national vaccination programs to reduce cervical cancer burden in Kazakhstan.

Findings on HPV prevalence across groups support improvements in screening and prevention, facilitating risk-based interventions and efficient use of healthcare resources. Regional incidence and mortality comparisons offer critical insights for designing region-specific preventive strategies.

The study provides an evidence base for health policy initiatives aimed at cervical cancer elimination. Promoting the effectiveness of HPV vaccination and regular screening may enhance public awareness and increase vaccine uptake, reducing HPV-related diseases.

The findings may also contribute to international collaboration in cervical cancer and HPV prevention efforts.

**Personal Contribution of the Doctoral Student:**

The author was actively involved in developing the research concept, organizing the collection and analysis of data related to cervical cancer incidence and mortality in Kazakhstan, as well as coordinating and conducting the collection of samples for cytology and HPV PCR testing. In addition, the author performed statistical data analysis, formulated key conclusions, and proposed recommendations for optimizing the HPV vaccination program. A significant component of the work also included the preparation of scientific publications and the presentation of research findings at academic conferences.

**Conclusions**

1. Between 2014 and 2023, the Republic of Kazakhstan maintained a high incidence and mortality rate of cervical cancer. The average incidence was 18.9 cases per 100,000 female population, while the mortality rate was 5.7 per 100,000.

2. The survey results showed that vaccinated women were significantly more informed about human papillomavirus and its prevention. Specifically, 88.3% of vaccinated respondents had heard of HPV, compared to only 39.6% among unvaccinated women. Awareness of the availability of vaccination was reported by 92.1% of vaccinated women, while only 31.2% of unvaccinated women were aware of it. These differences are statistically significant ($p<0.001$) and indicate a higher level of awareness in the immunized group.

3. Among vaccinated women, a high proportion of normal cytological findings was observed (NILM — 96.2%). The detection rate of LSIL was 1.8%, while no cases of HSIL were recorded. PCR diagnostics revealed high-risk HPV in 0.8% of vaccinated women, compared to 14.5% among unvaccinated women. HPV types 16 and 18 were predominantly detected in the unvaccinated group, indicating the high effectiveness of HPV vaccination.

4. The prevalence of high-risk HPV infection among unvaccinated women was 14.5%, compared to 0.8% among vaccinated women. The rate of cytological abnormalities (ASCUS, LSIL, HSIL) was 21.6% in the unvaccinated group and less than 4% in the vaccinated group. These findings confirm a reduction in both HPV infection and precancerous conditions among vaccinated women.

5. A differentiated screening model was proposed: for vaccinated women—primary HPV testing and cytology every 5 years starting at age 25; for unvaccinated—annual cytology with optional PCR and colposcopy in case of abnormalities.

**Approbation of the Thesis Results:**

The main findings and results of the dissertation were presented at the following conferences:

1. IGCS Annual Global Meeting, Digital (poster presentation), September 10–13, 2020
2. ASCO Annual Meeting, Virtual, May 29–30, 2020
3. IGCS Annual Global Meeting, Digital (poster presentation), August 30 – September 2, 2021
4. ASCO Annual Meeting, Virtual, June 4–8, 2021
5. VIII Congress of Oncologists and Radiologists of Kazakhstan, Turkestan, October 14–16, 2021 (oral presentation)
6. XIII Congress of Oncologists and Radiologists of CIS and Eurasian Countries, April 27–29, 2022, Almaty, Kazakhstan (oral presentation)
7. 23rd European Congress on Gynecological Oncology, October 27–30, 2022, Berlin, Germany (poster presentation)

8. ASCO Annual Meeting 2022, June 3–7, 2022, Chicago, USA (poster presentation)
9. The 24th European Congress on Gynaecological Oncology, October 28 – November 1, 2023, Istanbul, Türkiye (poster presentation)
10. "Implementation of HPV Vaccination in the Republic of Kazakhstan", August 20, 2024, Shymkent, Kazakhstan (oral presentation)
11. 2024 IGCS Annual Global Meeting, October 16–18, Dublin, Ireland (poster presentation)
12. Extended meeting of the S.N. Nugmanov Department of Oncology, Asfendiyarov Kazakh National Medical University, Protocol No. 9, April 16, 2025

**Publications**

A total of 17 papers were published, including one in a Scopus-indexed journal (APJCP), five in national peer-reviewed journals, eight in conference proceedings indexed in Scopus and WoS, one in a multidisciplinary journal, and two guideline manuals.

I. Indexed in Scopus:

1. Vaccination Effectiveness against Human Papillomavirus in Kazakhstan. *Asian Pacific Journal of Cancer Prevention*, Volume 25, Issue 2, February 2024.
   DOI: 10.31557/APJCP.2024.25.2.681
   (Scopus – 39%, WoS – Q3 at the time of publication)
   Authors: Raikhan Bolatbekova, Yerlan Kukubassov, Saniya Ossikbayeva, Dilyara Kaidarova

II. Articles published in journals included in the List of Publications Recommended by the Committee for Quality Assurance in the Sphere of Education and Science , Ministry of Science and Higher Education of the Republic of Kazakhstan:

1. The Role of HPV Vaccination in the Elimination of Cervical Cancer: Literature Review
   Oncology and Radiology of Kazakhstan – 2022, No. 2 (64), pp. 79–83
2. Global Prevalence of Human Papillomavirus Causing Cervical Cancer: A Literature Review
   Oncology and Radiology of Kazakhstan – 2022, No. 3 (65), pp. 42–46
3. Assessment of Cervical Cancer Risk Factors and Awareness Among Young Women in Almaty
   Oncology and Radiology of Kazakhstan – 2023, No. 1 (67), pp. 14–18
4. Cervical Cancer Incidence and Mortality in Almaty (2005–2022)
   Oncology and Radiology of Kazakhstan – 2023, No. 2 (68), pp. 9–14

5. Assessment of Reproductive Health in Girls Vaccinated Against HPV in the Republic of Kazakhstan
   Oncology and Radiology of Kazakhstan – 2024, No. 2 (72), pp. 4–7

III. Abstracts and Scientific Contributions in International Conference Proceedings:

1. Evaluation of Changes in Indicators of Oncological Services for Cervical Cancer in Kazakhstan
   IGCS Annual Global Meeting, Digital, September 10–13, 2020
   International Journal of Gynecologic Cancer, 2020; 30:A42
   DOI: 10.1136/ijgc-2020-IGCS.74
   (Scopus – 51%, WoS – Q2)
2. Opportunities and Challenges in the Cervical Cancer Screening Program in Kazakhstan: Results after imPACT Review
   ASCO Annual Meeting, Virtual, May 29–30, 2020
   Journal of Clinical Oncology, Volume 38, Number 15_suppl
   DOI: 10.1200/JCO.2020.38.15_suppl.e18020
   (Scopus – 98%, WoS – Q1)
3. Overall Survival and Time Trends in Cervical Cancer in Almaty, Kazakhstan
   IGCS Annual Global Meeting, Digital, August 30 – September 2, 2021
   International Journal of Gynecologic Cancer, 2021; 31(Suppl 4): A1–A153
   DOI: 10.1136/ijgc-2021-IGCS.156
   (Scopus – 51%, WoS – Q2)
4. Cervical Cancer Screening: Twelve Years of Experience with the National Screening Program in Kazakhstan
   ASCO Annual Meeting, Virtual, June 4–8, 2021
   Journal of Clinical Oncology, 39(15_suppl): e17520
   DOI: 10.1200/JCO.2021.39.15_suppl.e17520
   (Scopus – 98%, WoS – Q1)
5. Prevalence of HPV Infection Among Young Women in Almaty, Kazakhstan
   23rd European Congress on Gynecological Oncology, October 27–30, 2022, Berlin, Germany
   International Journal of Gynecologic Cancer, 32(Suppl 2): A376.1–A376
   DOI: 10.1136/ijgc-2022-ESGO.806
   (Scopus – 51%, WoS – Q2)
6. Prevalence of HPV and Cytological Abnormalities in Young Women in Almaty, Kazakhstan
   ASCO Annual Meeting 2022, June 3–7, 2022, Chicago, USA
   Journal of Clinical Oncology, Volume 40, Number 16_suppl
   DOI: 10.1200/JCO.2022.40.16_suppl.e2250
   (Scopus – 98%, WoS – Q1)
7. Informing the Assessment of Risk Factors for Cervical Cancer Among Young Women in Almaty

The 24th European Congress on Gynaecological Oncology, October 28 – November 1, 2023, Istanbul, Türkiye
International Journal of Gynecologic Cancer, 2023; 33(Suppl 3): A61.2–A62
DOI: 10.1136/ijgc-2023-ESGO.123
(Scopus – 51%, WoS – Q2)

8. Attitudes and Perceptions Towards HPV Vaccination Among Women in Kazakhstan
   2024 IGCS Annual Global Meeting, October 16–18, Dublin, Ireland
   International Journal of Gynecologic Cancer, 2024; 34(Suppl 3): A1–A391
   DOI: 10.1136/ijgc-2024-IGCS.315
   (Scopus – 51%, WoS – Q2)

IV. Other Scientific Publications:

1. Cervical Cancer Elimination Program
   Interdisciplinary Approaches to Medicine, 2021, 2(1), pp. 19–21

V. Guidelines and Methodological Recommendations:

1. Early Diagnosis of Cervical Cancer
   Methodological Guidelines
   ISBN 978-601-7548-22-3
2. Communication in the HPV Vaccination Program in the Republic of Kazakhstan
   Methodological Guidelines
   ISBN 978-601-7548-31-5

**Structure and Scope of the Dissertation**

The dissertation comprises 106 pages and includes an introduction, three main chapters, a conclusion with key findings and practical recommendations, and a list of 196 references. It also contains 10 tables and 26 figures.