# RESEARCH ARTICLE

Editorial Process: Submission:01/31/2023 Acceptance:05/16/2023

# **HPV Vaccination and Cervical Cancer Screening Policies** and Practices in 18 Countries, Territories and Entities across **Eastern Europe and Central Asia**

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#### Abstract

Background: To assess readiness to achieve the WHO Global Strategy targets for HPV vaccination and cervical screening and to guide capacity building, the current status of these services in 18 Eastern European and Central Asian countries, territories and entities (CTEs) was evaluated. Methods: In order to assess the current status of HPV vaccination and cervical cancer screening in these 18 CTEs, a 30 question survey tool was developed, covering: national policies, strategies and plans for cervical cancer prevention; status of cancer registration; status of HPV vaccination; and current practices for cervical cancer screening and treatment of precancerous lesions. As cervical cancer prevention comes within the mandate of the United Nations Fund for Population Development (UNFPA), the UNFPA offices in the 18 CTEs have regular contact with national experts who are directly involved in cervical cancer prevention actions and are well placed to provide the data required for this survey. Working through the UNFPA offices, the questionnaires were sent to these national experts in April 2021, with data collected from April to July 2021. All CTEs returned completed questionnaires. Results: Only Armenia, Georgia, Moldova, North Macedonia, Turkmenistan and Uzbekistan have implemented national HPV vaccination programmes, with only the last 2 of these reaching the WHO target of 90% of girls fully vaccinated by age 15, while rates in the other 4 range from 8%-40%. Cervical screening is available in all CTEs but only Belarus and Turkmenistan have reached the WHO target of 70% of women screened once by age 35 and again by age 45, while rates elsewhere range from 2%-66%. Only Albania and Turkey follow the WHO recommendation to use a high-performance screening test, while the majority use cervical cytology as the main screening test and Kyrgyzstan, Tajikistan, Turkmenistan and Uzbekistan use visual inspection. No CTEs currently operate systems to coordinate, monitor and quality assure (QA) the entire cervical screening process. Conclusions: Cervical cancer prevention services in this region are very limited. Achieving the WHO Global Strategy targets by 2030 will require substantial investments in capacity building by international development organisations.

Keywords: capacity building- HPV vaccination- cervical screening- Eastern Europe- Central Asia

Asian Pac J Cancer Prev, 24 (5), 1781-1788

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# Introduction

Globally there are more than 570,000 new cases and 311,000 deaths from cervical cancer every year and these numbers are predicted to increase to more 700,000 new cases and 400,000 deaths per year by 2030 (International Agency for Research on Cancer, 2018). Most of this disease and death occurs in low and middle income countries (LMICs) that lack the effective HPV vaccination, cervical screening and cancer treatments that are common in high-income countries (Bray et al., 2018; PATH, 2019; Riley, 2019; Gakidou et al., 2008).

In recognition of this, the World Health Assembly adopted the global strategy to accelerate the elimination of cervical cancer as a public health problem, which specifies that all countries should achieve an incidence rate below 4 per 100,000 women-years (World Health Assembly, 2020). Subsequently, the World Health Organization (WHO) published its Global Strategy to Accelerate the Elimination of Cervical Cancer as a Public Health Problem (WHO, 2020) that focuses on prevention through HPV vaccination and cervical screening with treatment of precancerous cervical lesions, and management of invasive disease through effective treatment and palliative care. The WHO Global Strategy also set targets (the 90-70-90 targets) that all countries should achieve by 2030:

- \* 90% of girls fully vaccinated with HPV vaccine by age 15.
- \* 70% of women screened with a high-performance test (performance similar to or better than a nucleic-acid amplification test for HPV) by age 35 and again by age 45.
- \* 90% of women with cervical disease treated (90% of women with pre-cancer treated; 90% of women with invasive cancer managed).

The UNFPA is the principal UN agency dealing with reproductive rights and health, including cervical cancer prevention. In order to assess readiness to meet the WHO targets and guide capacity building, the policies and practices for HPV vaccination and cervical cancer screening in the 18 CTEs of the UNFPA Eastern Europe and Central Asia region were evaluated.

#### **Materials and Methods**

In order to assess the current status of HPV vaccination and cervical cancer screening in the 18 CTEs included in this study, a 30 question survey tool was developed, covering: national policies, strategies and plans for cervical cancer prevention; status of cancer registration; status of HPV vaccination; and current practices for cervical cancer screening and treatment of precancerous lesions. (A copy of the survey tool is available from the corresponding author). As the UNFPA offices in these 18 CTEs have regular contact with national experts who are directly involved in cervical cancer prevention actions and are well placed to provide the data required for this survey. Working through the UNFPA, the questionnaires were sent to these national experts in April 2021, with data collected from April to July 2021. All CTEs returned completed questionnaires. In BiH, most responsibilities for healthcare have been devolved to the entities: the

Federation of BiH and the Republika Srpska, so an expert was recruited from each.

Statistics are limited to the calculation of percentages using Microsoft Excel (Microsoft Office Home and Business 2016, version 2210).

The data used for this study did not contain any personal identifiers, clinical data, cases reports or cases series and did not involve human or animal subjects. Therefore, neither ethical approval nor informed consent were obtained.

#### Results

HPV vaccination

Fourteen of 18 CTEs have included HPV vaccination in an official strategy or plan. However, only 6 CTEs have implemented national HPV vaccination programs and only 2 of these have reached the WHO coverage target of 90%, with coverage rates in the other 4 ranging from 8% to 40%. In 6 of the other CTEs, HPV vaccination is only available for a fee and in the last 6 CTEs it is not officially available at all (Table 1). Kazakhstan started an HPV vaccination pilot in 2013 but stopped it in 2016 because of the high refusal rate that was attributed to a lack of public awareness about the relevance of HPV vaccination (Kaidarova et al., 2017).

For the 6 CTEs with HPV vaccination programs, 5 have included it in their immunization calendars for age-eligible adolescents/adults, while in Moldova at the time this survey was conducted, it was only a 'recommended' vaccination but has since been included in the vaccination calendar. Three of these CTEs have school-based programs in which HPV vaccination is delivered to children while attending school, together with primary health care (PHC) delivery for children who missed their school vaccination. The other 3 CTEs use only PHC delivery, which requires people to attend their PHC provider to be vaccinated. Only 4 CTEs currently record the identification details of vaccinees in a central electronic registry (Table 1).

# Cervical screening

Seventeen CTEs have included cervical cancer screening (without specifying whether it is organised or opportunistic) in an official strategy or plan, although all 18 CTEs provide some form of cervical cancer screening.

Only 7 CTEs provide the full range of services (screening test, follow-up of screen-positive women by colposcopy with biopsy and treatment of cervical pre-cancer) free to all age-eligible women, while policies elsewhere vary widely (Table 2).

The main screening test in 12 CTEs is cervical cytology with 10 using the Papanicolaou method to stain cervical smears and 2 using Romanowsky method. Four of the 5 Central Asian CTEs use visual inspection with acetic acid/lugol's iodine (VIA/VILI) as their main screening test, and 2 CTEs (Albania and Turkey) have implemented HPV testing as the main cervical screening testr (Table 3).

For the screening age range, there is substantial variation. At the lower limit, Azerbaijan, Belarus and Ukraine start at 18 years of age and there is no upper age

Table 2. State Payments for Cervical Screening Services

											Cervical Cancer Prevention in Eastern Europe and Co
	Cost/dose (\$US)	Central HPV vaccination registry	Delivery platforms	Males	Females	Sexes and ages	Immunization calendar - year	Public sector provision	HPV vaccination included in a national strategy		Table 1. HPV Vaccination Policies and Practices    All ban   iia
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00/	) NA	Yes	PHC	14-45	13-45		Yes 2017	Yes	Yes	Armenia	Practices  Armenia  Armenia  Armenia  Azerbaijan
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J T A	\$35	NA	NA				No	No	Yes	Ukraine	Ilations, scopy is:
2007	NA	No	SCHPHC		9		Yes 2019	Yes	Yes	Uzbekistan	etc; d, State
			HC				119				e jays a a Uzbekistan

PHC, primary health care; SCH, schools; NA, not applicable

Coverage (2020)

No NA 40%

Table 3. Key Aspects of Cervical Screening

a, Screening test: HPV = HPV testing; Cyto = cervical cytology; VIA = visual inspection with acetic acid; b, Cytology stain: Pap = Papanicolaou; Rom = Romanowsky; c, Geographical availability: Nat = entire country, territory or entity; Reg = regional; Mun = municipal; d, Delivery platforms: PHC = Family doctors, women's health clinics, polyclinics etc.; GYN = Gynaecology departments in polyclinics or hospitals; CSC = Cancer screening centres; e, Excluding Brčko District; f, PHC providers in 4 municipalities covering $\approx$ 1/4 of the national target population invite women for screening. Elsewhere, screening is also available but recruitment is opportunistic; g, PHC providers in 18 municipalities covering $\approx$ 1/3 of the national target population invite women for screening and the screening recruitment rate relates to these 18 municipalities. Elsewhere, screening is also available but recruitment is opportunistic; h, VIA is free but cervical cytology and HPV testing are also available for a fee through public sector clinics; NR, no official recommendations	CTE reported recruitment rate, year	Delivery platforms <sup>d</sup>		Geographical availability <sup>c</sup>	Screening interval (years)	Age range (years)	Cytology stain <sup>b</sup>	Screening test <sup>a</sup>		
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icolaou; Rom = Romanowsky; c, Geographical availability: Nat = entire country, territory = Gynaecology departments in polyclinics or hospitals; CSC = Cancer screening centres; e, Elsewhere, screening is also available but recruitment is opportunistic; g, PHC providers ates to these 18 municipalities. Elsewhere, screening is also available but recruitment is all recommendations	22% 2017	PHC GYN		Nat	ω	22-60	Pap	Cyt		North Macedonia
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Table 4. Elements of Organised Screening that have been Implemented

woman screened together with her screening test results and follow-up procedures; v. Provider level recording of ID details for each woman screened together with her screening test results but not monitoring the follow-up/ treatment of screen-positive women; e, Cancer registry: Nat = national; Reg = regional; Imp = implementing; f, Central access to a cancer registry: the central administrative unit has access to a population-based cancer registry well as the interaction between them; i., Colposcopy clinical protocols: protocols describing the management of screen-positive women based on their screening and/or follow-up test results, as well as the clinical procedures that for QA and audit; g, QA system: a centrally managed QA system covering the cervical screening process; h, Screening guidelines: guidelines for the entire screening process describing the roles of all the component services as are required at each step in the process.

Table 5. Cervical Screening Indicators and Targets

Country	Indicator	Target
Albania	Coverage of the target population	90%
	Proportion of screened women receiving a test result within 2 months	96%
	Proportion of screen-positive women who attend colposcopy	90%
Kazakhstan	Coverage of the target population	90%
	Time to complete the entire cervical screening cycle.	60 days
	Cytological precancer (ASC-H, HSIL, AGC, AIS, ?Invasive) detection rate	0.55%
Serbia	Proportion of women invited for screening	100%
	Proportion of women who respond to invitation	75%
	Proportion of women screened	75%

limit in Azerbaijan and Belarus. For the screening interval in the CTEs that use VIA/VILI or cytology, 4 do not have official recommendations, 1 has a 1 year interval and the remaining 11 all have intervals between 3 and 5 years. The 2 CTEs that use HPV testing both have a 5 year screening interval (Table 3).

Ten CTEs make cervical screening available through PHC facilities (family doctors, women's health centres, etc.), 7 use both PHC facilities and gynaecology departments in polyclinics and hospitals, and 1 uses only gynaecology clinics in polyclinics and hospitals. In addition, 3 CTEs also have dedicated cancer screening centres (Table 3).

Only 2 CTEs have reached the WHO target of 70% of women screened by age 35 and again by age 45, with the average screening recruitment rate elsewhere being 32.8% (range 2%-66%) (Table 3). However, only Albania, Georgia and North Macedonia have systems that record the identification of the women who have been screened with rates elsewhere calculated on the basis of the reported number of screening tests delivered or processed (Table 4).

### Cervical screening organisational elements

Eight CTEs reported having a central cervical screening administrative unit (Table 4). However, none of these are currently responsible for identifying and inviting women to be screened (either directly or indirectly through screening providers) or for monitoring screening test results or the follow-up of screen-positive women (Table 4). Of note, Georgia reported that their central administrative unit has recently implemented a cervical screening registry that has access to data from the civil registry, universal health care program and cancer registry that will allow them to coordinate recruitment and recall once sufficient screening history data has been recorded, and monitor women as they move through the entire screening process.

In 10 CTEs, screening recruitment and recall has been delegated to PHC providers who identify women to be screened from lists of their attached populations and in 8 of these, the PHC providers are also officially responsible for monitoring the follow-up of screen-positive women. Two CTEs have mixed systems with PHC providers in 4 and 18 municipalities respectively inviting women to be screened while screening elsewhere is opportunistic. Screening in the remaining 6 CTEs is

entirely opportunistic (Table 4).

Sixteen CTEs have cancer registries covering their entire territories, while Kyrgyzstan has a regional cancer registry (Chuy region) and Armenia is currently implementing a national cancer registry. Of these registries, 11 are members of the International Association of Cancer Registries (IACR) and 4 are also members of the European Network of Cancer Registries (ENCR). Therefore, all of these CTEs have access to the data required to measure the impact of prevention activities on cervical cancer rates, while Georgia has the potential to link screening and cancer registry data to conduct screening program audit (Table 4).

Eleven CTEs reported having cervical screening guidelines, with 9 of these plus 2 other CTEs reporting they have the related clinical protocols. However, the majority of these are more than 5 years old with the oldest published in 2003 and therefore need to be updated (Table 4).

Only 3 CTEs reported that cervical screening is currently subject to active QA monitoring (Table 4), although the range of indicators used in each is very limited (Table 5).

#### Discussion

The results of this survey demonstrate that almost all CTEs in the EECA region have recognised the importance of cervical cancer prevention as indicated by the inclusion of HPV vaccination and/or cervical screening in official strategies or plans. However, implementing effective programs to operationalise these strategies has, in most cases, not yet been achieved.

Only Armenia, Georgia, Moldova, North Macedonia, Turkmenistan and Uzbekistan currently provide HPV vaccination free through public sector programs but only 2 of these CTEs (Turkmenistan and Uzbekistan) have reached the WHO Global Strategy's target of 90% of girls fully vaccinated by age 15 and coverage rates in the remaining 4 CTEs were all ≤40%. Of note, North Macedonia launched its HPV vaccination program in October 2009 and coverage rates have remained between 31%-48% since 2010, which provides an indication of the challenges that need to be faced to achieve the 90% target. A further consideration is that only Armenia, Georgia, North Macedonia and Turkmenistan have implemented

central electronic HPV vaccination registries that would facilitate effective monitoring (Table 1).

Cervical screening is available in all CTEs, although only Belarus and Turkmenistan currently meet the target of 70% of women screened by age 35 and again by age 45, with rates elsewhere ranging from 2% to 66%. Here it should be noted that almost all CTEs calculate screening recruitment on the basis of the number of screening tests delivered or processed without linkage to the identification of the women screened so the rates could be affected by screening women outside the recommended age ranges and/or more frequently than the recommended interval. With regard to the low coverage rates, out of pocket payments have been identified as a barrier to cancer screening uptake (Islam et al., 2017). Therefore, one of the factors that may have influenced coverage rates in the EECA region is that only 7 CTEs (Albania, Armenia, Azerbaijan Belarus, Kosovo, Serbia, Turkey and Uzbekistan) provide the full range of cervical screening services free of charge for all age-eligible women. Elsewhere, one or more of these services are free only for women with health insurance or require co-payment/ full-payment.

Only Albania and Turkey have implemented HPV primary screening and therefore comply with the WHO Global Strategy's recommendation to use a high-performance screening test, with the remaining CTEs all using low-performance screening tests (12 use cervical cytology and 4 use VIA/VILI). However, Georgia, North Macedonia, Turkmenistan and Uzbekistan are now conducting HPV primary screening pilots.

Of particular importance, most CTEs do not appear to have fully appreciated that cervical screening is a process involving multiple health services that need to be carefully coordinated, monitored and subject to robust QA in order to be effective (Bouvard et al., 2021; WHO, 2021). As a result, only 8 CTEs have a central cervical screening administrative unit but none of these are responsible for coordinating or monitoring the entire screening process. Further, only Albania, Georgia and North Macedonia have a central cervical screening registry that records who has been screened together with their screening test results, while only the Georgian registry has the capacity to monitor women as they move through the screening process. Finally, only Albania, Kazakhstan and Serbia reported that cervical screening is subject to active QA monitoring, but the range of indicators used in each case is very limited. Therefore, implementing the organisational elements that are required to ensure the effectiveness and safety of cervical screening must be prioritised.

The WHO has set ambitious targets for cervical cancer prevention through HPV vaccination and cervical screening that should be achieved by 2030. However, achieving these targets in the EECA region will require very substantial investments of money and expertise that most of these resource constrained CTEs will struggle to find. HPV vaccines and HPV tests are expensive technologies and this is likely to have been the principal barrier to their implementation in the EECA region. The cost of these technologies has come down in recent years but they are still very expensive relative to the resources

that are available. In addition, the cost of implementing the organisational elements that are essential for screening programs to be effective will be substantial while the lack of people with the required knowledge and expertise will be an additional barrier. Therefore, while the tasks that need to be accomplished to eliminate cervical cancer as a public health problem are clear, the question of how they will be paid for has yet to be answered.

#### **Author Contribution Statement**

With the exception of the first and last authors, all other authors contributed equally to this publication and their names are listed alphabetically; Davies, Philip. Conception and design; analysis and interpretation of data; drafting and revising; final approval of the published article; Aluloski, Igor. Acquisition of national data; analysis and interpretation of data; reviewing and revising; final approval of the published article; Arifdjanova, Diyora. Acquisition of national data; analysis and interpretation of data; reviewing and revising; final approval of the published article; Brcanski, Jelena. Acquisition of national data; analysis and interpretation of data; reviewing and revising; final approval of the published article; Durdyeva, Akjemal. Acquisition of national data; analysis and interpretation of data; reviewing and revising; final approval of the published article; Ghayrat Umarzoda, Saida. Acquisition of national data; analysis and interpretation of data; reviewing and revising; final approval of the published article; Goshliyev, Kemal. Acquisition of national data; analysis and interpretation of data; reviewing and revising; final approval of the published article; Jovanović, Verica. Acquisition of national data; analysis and interpretation of data; reviewing and revising; final approval of the published article; Jugeli, Levan. Acquisition of national data; analysis and interpretation of data; reviewing and revising; final approval of the published article; Kocinaj-Berisha, Merita. Acquisition of national data; analysis and interpretation of data; reviewing and revising; final approval of the published article; Maistruk, Galina. Acquisition of national data; analysis and interpretation of data; reviewing and revising; final approval of the published article; Naumović, Tamara. Acquisition of national data; analysis and interpretation of data; reviewing and revising; final approval of the published article; Pilav, Aida. Acquisition of national data; analysis and interpretation of data; reviewing and revising; final approval of the published article; Rzayeva, Gulnara. Acquisition of national data; analysis and interpretation of data; reviewing and revising; final approval of the published article; Saribekyan, Karine. Acquisition of national data; analysis and interpretation of data; reviewing and revising; final approval of the published article; Siljak, Sladjana. Acquisition of national data; analysis and interpretation of data; reviewing and revising; final approval of the published article; Ten, Elena. Acquisition of national data; analysis and interpretation of data; reviewing and revising; final approval of the published article; Valuta, Diana. Acquisition of national data; analysis and interpretation of data; reviewing and revising; final approval of the published article; Veljković, Marko. Acquisition of national data; analysis and interpretation of data; reviewing and revising; final approval of the published article; Ylli, Alban. Acquisition of national data; analysis and interpretation of data; reviewing and revising; final approval of the published article; Zhylkaidarova, Alma. Acquisition of national data; analysis and interpretation of data; reviewing and revising; final approval of the published article; Melnic, Eugen. Conception and design; analysis and interpretation of data; drafting and revising; final approval of the published article.

# Acknowledgements

This work was supported by the UNFPA Regional Office for Eastern Europe and Central Asia. However, the views expressed in this article are those of the authors and do not represent an official position of the UNFPA.

Conflict of Interest Statement

All authors confirm that they have no conflicts of interest with the publication of this article.

The authors would like to acknowledge the substantial contributions that have been made by the UNFPA staff at the regional and country levels who are listed below:

Abuova, Gaukhar. SRH Project Officer, UNFPA Kazakhstan; Bergstrand, Louise. SRH Program Analyst, UNFPA EECARO; Berzan, Eugenia. SRH Program Analyst, UNFPA Moldova; Brajovic Grigorijevic, Jovanka. SRH and Youth Programme Analyst, UNFPA North Macedonia; Fuzailova, Nargiza. Reproductive Health Analyst, UNFPA Uzbekistan; Gyulkhasyan, Vahe. SRH Program Analyst, UNFPA Armenia; Huseynov, Ramiz. Program Associate, UNFPA Azerbaijan; Imamović, Enida. SRH and Youth Programme Analyst. UNFPA Bosnia and Herzegovina; Khomasuridze, Tamar. SRH Regional Advisor for Eastern Europe and Central Asia, UNFPA EECARO; Mataradze, George. Program Analyst, UNFPA Georgia; Miftari, Zarife. SRH and Youth Programme Analyst, UNFPA Kosovo; Pidverbetskyv, Bohdan. SRH Project Officer, UNFPA Ukraine; Prepelita, Violeta. Cervical Cancer Prevention in Moldova Project, UNFPA Moldova; Seyidov, Teymur. SRH Program Specialist, UNFPA EECARO; Smankulova, Nurgul. National Program Analyst on SRH, UNFPA Kyrgyzstan; Sovic, Nevena. SRH and Youth Programme Analyst, UNFPA Serbia; Tocaj, Dorina. Reproductive Health and Youth Programme Analyst, UNFPA Albania; Tohirov, Ravshan. RH National Professional Officer, UNFPA Tajikistan

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