

**SPECIAL REPORT**

The European response to the WHO call to eliminate cervical cancer as a public health problem

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Abstract

The age-standardised incidence of cervical cancer in Europe varies widely by country (between 3 and 25/100000 women-years) in 2018. Human papillomavirus (HPV) vaccine coverage is low in countries with the highest incidence and screening performance is heterogeneous among European countries. A broad group of delegates of scientific professional societies and cancer organisations endorse the principles of the WHO call to eliminate cervical cancer as a public health problem, also in Europe. All European nations should, by 2030, reach at least 90% HPV vaccine coverage among girls by the age of 15 years and also boys, if cost-effective; they should introduce organised population-based HPV-based screening and achieve 70% of screening

Abbreviations: ECCO, European Cancer Organisation; EFC, European Federation for Colposcopy; ESGO, European Society of Gynaecological Oncology; EU, European Union; HPV, human papillomavirus; IARC, International Agency for Research on Cancer; WHO, World Health Organisation

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coverage in the target age group, providing also HPV testing on self-samples for non-screened or underscreened women; and to manage 90% of screen-positive women. To guide member states, a group of scientific professional societies and cancer organisations engage to assist in the rollout of a series of concerted evidence-based actions. European health authorities are requested to mandate a group of experts to develop the third edition of European Guidelines for Quality Assurance of Cervical Cancer prevention based on integrated HPV vaccination and screening and to monitor the progress towards the elimination goal. The occurrence of the COVID-19 pandemic, having interrupted prevention activities temporarily, should not deviate stakeholders from this ambition. In the immediate postepidemic phase, health professionals should focus on high-risk women and adhere to cost-effective policies including self-sampling.

KEYWORDS

cervical cancer screening, COVID-19, elimination of cervical cancer, Europe, HPV vaccination, WHO

1 | CURRENT BURDEN OF CERVICAL CANCER

According to the International Agency for Research on Cancer (IARC) estimates of the cancer burden in Europe, approximately 33 000 women were diagnosed with cervical cancer and 15 000 died from the disease in 2018.¹ These estimates concern the European region as defined by the United Nations. The incidence rates vary widely within Europe, with age-standardised incidence rates (ASIR) ranging from less than 5/100000 in Malta (3.5), Switzerland (3.8) and Finland (4.7) to ASIRs over 20/100000 in Latvia (25.0), Bosnia Herzegovina (23.9), Estonia (22.5), Moldova (21.4), Serbia (20.3) and Bulgaria (20.3) (see Figure 1; Table 1).

There is a clear Western to Eastern Europe trend with ASIRs lower than 10/100000 and age-standardised mortality rates (ASMR) lower than 3/100000 in Northern, Southern and Western Europe, compared with ASIR of 16/100000 and ASMR of 6/100000 in Central-Eastern Europe. In the 28 member states of the European Union (EU) (as defined in 2018, still including the United Kingdom), the average age-standardised incidence and mortality rates are 10.0 and 3.1 per 100 000 women-years, respectively. For a more detailed assessment of the burden of cervical cancer in Europe vs other continents and on the methodology of estimation, we refer to a recent publication in *Lancet Global Health*¹ and the description of the sources and methods used in developing the GLOBOCAN estimates.^{2,3}

2 | PREVENTION OF CERVICAL CANCER

Historically, screening by detection and treatment of cervical precancer lesions identified through cytological examination of Pap smears has resulted in a significant reduction in cervical cancer incidence and mortality.⁴⁻⁶ The implementation of the European Guidelines for Quality

What's new?

Cervical cancer incidence, human papillomavirus (HPV) vaccination coverage, and screening performance vary widely across Europe. This report addresses for the first time the issue of how Europe should respond to the ambitious call from the World Health Organization to reduce the incidence of cervical cancer to less than 4/100,000/year. To meet this target, all European countries should put in place programs to reach 90% and 70% of HPV vaccination and screening coverage, respectively, and manage 90% of screen-positive women by 2030. Despite the temporary interruptions of prevention activities caused by COVID-19, the pandemic should not deviate stakeholders from this ambition.

Assurance of Cervical Cancer Screening has played a pivotal role in achieving this result.⁷ However, recent trend analyses indicate that even in countries with well-organised cytology-based screening programmes, cervical cancer incidence rates have stopped decreasing or are even increasing.^{1,8-10} This phenomenon might be explained by an increased exposure to oncogenic types of the human papillomavirus (HPV), lower screening coverage rates, particularly among young women, and the limitations of cytology-based screening.¹

Therefore, new effective preventive tools, which have become available in the last decade, should be implemented without delay.

Strong evidence has accumulated, indicating that primary prevention by vaccination against the main carcinogenic HPV types is safe and protects well against future HPV infection and associated anogenital precancer in young females and males.¹¹⁻¹⁵ However, current HPV

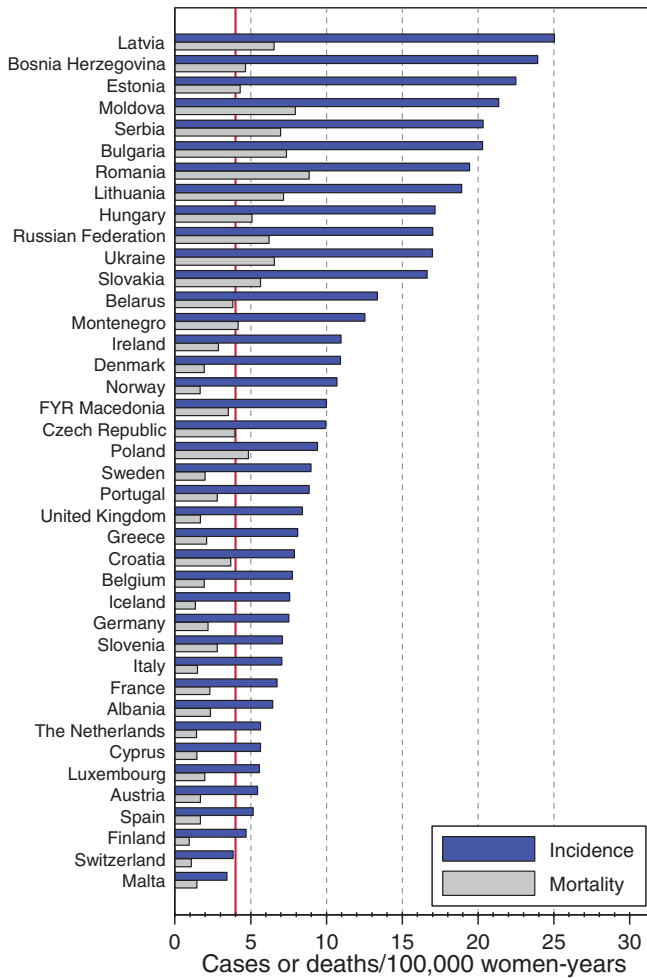


FIGURE 1 World-age-standardised rates of incidence of and mortality from cervical cancer (/100 000 women-years), in Europe, estimates for 2018, by country and ranked in descending order of incidence. The red line corresponds with the WHO elimination target (4/100000/year). Source: IARC GLOBOCAN¹ [Color figure can be viewed at wileyonlinelibrary.com]

vaccine coverage estimates show very large discrepancies among countries (Table 2). The European Centre for Disease Control and Prevention in its recently released guidance on HPV vaccination in EU countries stated that a gender neutral vaccination becomes increasingly cost-effective in the presence of persistently suboptimal coverage of females with reducing vaccine price.¹⁶ However, in countries with HPV vaccination coverage of 80% or higher among girls, boys are already well protected by herd-immunity, which renders gender-neutral vaccination less cost-effective. Interventions to increase vaccination coverage among girls where it is low might be more cost-effective than adding vaccination of boys.¹⁷ Intervention research aiming to identify effective strategies to increase HPV vaccination uptake and implementation of such strategies should be promoted.

Regarding secondary prevention, randomised population-based trials have demonstrated that HPV-based screening is more performant in protecting against incident cervical precancer and cancer than cytology.^{18,19} In addition, screening with validated polymerase

TABLE 1 Burden of cervical cancer in the member states of the European Union in 2018

Member state	Nb cases	ASIR	Nb deaths	ASMR
Austria	390	5.5	163	1.7
Belgium	640	7.8	235	2.0
Bulgaria	1080	20.3	475	7.4
Croatia	266	7.9	175	3.7
Cyprus	45	5.7	18	1.5
Czech Republic	813	9.9	435	4.0
Denmark	415	10.9	131	2.0
Estonia	230	22.5	60	4.3
Finland	182	4.7	64	0.9
France	3067	6.7	1472	2.3
Germany	4608	7.5	2011	2.2
Greece	696	8.1	271	2.1
Hungary	1312	17.2	499	5.1
Ireland	340	11.0	107	2.9
Italy	3105	7.1	986	1.5
Latvia	339	25.0	134	6.5
Lithuania	431	18.9	209	7.2
Luxembourg	25	5.6	11	2.0
Malta	11	3.5	7	1.4
Poland	3220	9.4	1947	4.9
Portugal	750	8.9	340	2.8
Romania	3308	19.5	1743	8.9
Slovakia	692	16.6	281	5.7
Slovenia	110	7.1	65	2.8
Spain	1942	5.2	825	1.7
Sweden	558	9.0	222	2.0
The Netherlands	670	5.7	250	1.4
UK ^a	3430	8.4	1033	1.7
Whole EU	32 675	10.0	14 169	3.1

Note: Source: IARC GLOBOCAN.¹

Abbreviations: ASIR, age-standardised incidence rate (cases of cervical cancer per 100 000 women-year); ASMR, age-standardised mortality rate (deaths from cervical cancer per 100 000 women-year), computed by using the standard world population as reference; EU, European Union; Nb, number; UK, United Kingdom.

^aUK still was member of the EU in 2018.

chain reaction-based HPV assays offers the advantage that it can be performed on a specimen collected by the woman herself. The offer of self-sampling devices has been shown to be performant in reaching underscreened populations.^{20,21} Neither the World Health Organisation (WHO) nor EU guidelines recommend screening by cotesting with HPV and cytology.^{22,23}

HPV infection is mainly sexually transmitted and this fact entails sensitive and tailored communications, including appropriate health education, to the general public as well as to individual women needing counselling in order to reduce stigma, shame and worry, by taking into account the particular social and cultural background.^{24,25}

TABLE 2 Estimations for 2018 of the vaccine coverage in European HPV vaccination programmes (aggregated by country)

28 member countries of the EU ^a		
Country	Coverage (%)	Comment
Austria	-	Estimate not available. No data reported
Belgium	67	Estimate extrapolated from 2016. Estimate based on weighted average of survey data from regions (Flanders 89.5% and Wallonia-Brussels 36.1%)
Bulgaria	5	
Croatia	-	Estimate not available. No data reported
Cyprus	64	Estimations for the Government Controlled Area
Czech Republic	-	Estimate not available. No data reported
Denmark	54	
Estonia	44	
Finland	62	Estimate based on reported coverage from the national vaccination registry
France	24	
Germany	31	Data not reported. Estimate extrapolated from 2017
Greece	-	Estimate not available. No data reported
Hungary	71	
Ireland	62	
Italy	40	
Latvia	53	
Lithuania	46	
Luxembourg	14	Estimate extrapolated from 2015
Malta	81	
Netherlands	45	Estimate based on reported coverage data for the 14th year cohort from the national vaccination registry
Portugal	80	Estimate based on reported official coverage
Romania	-	HPV vaccination not introduced
Slovakia	-	HPV vaccination not introduced
Slovenia	45	
Spain	69	
Sweden	75	Estimate based on reported official coverage
UK ^a	81	
Other European countries		
Country	Coverage (%)	Comment
Andorra	-	Estimate not available. No data reported
Armenia	2	
Azerbaijan	-	Vaccine not introduced
Belarus	-	Vaccine not introduced
Georgia	-	
Iceland	85	
Liechtenstein		
Moldova	-	Vaccine not introduced
Macedonia	40	
Monaco	-	Estimate not available. No data reported
Norway	86	
Russia	-	Vaccine not introduced. Only in some regions
San Marino	16	
Switzerland	57	Estimate based on national survey. Females who were 16 years of age at the interview.
Ukraine	-	Vaccine not introduced

Note: Source: ICO WHO 2018 Estimates (http://www.who.int/immunization/monitoring_surveillance/data/HPV_estimates.xls).

^aIn 2018, the UK still was member of the European Union.

3 | WHO CALL FOR THE ELIMINATION OF CERVICAL CANCER

Recognising that cervical cancer affects many women at an age when they have important economic and familial responsibilities, and acknowledging its high level of preventability, has motivated the WHO Director General to launch an appeal to all countries of the world to eliminate this disease as a public health problem.²⁶ It is estimated that by vaccinating 90% of girls before they reach the age of 15 years, by screening 70% of women at least twice in the age-range 30 to 40 years, and by treating at least 90% of screen-detected cervical precancer lesions, by 2030, the incidence of cervical cancer could be reduced to the level of a very rare disease (≤ 4 per 100 000/year) by the end of the current century.^{22,27} Europe as a whole (with most countries belonging to the group with very high human development index [HDI]) could reach this goal sooner by 2055 to 2059.²⁷

4 | PROPOSAL FOR EUROPEAN ACTIONS

Implementation of HPV-based screening as recommended in EU guidelines, including offering nonscreened women the choice of self-sampling, in combination with HPV vaccination of girls, and vaccination of boys if resources permit, could achieve the WHO goal in European countries by 2050 to 2065 depending on the current burden and the chosen strategies (see red line in Figure 1).²⁷ On the initiative of the European CanCer Organisation (ECCO) and the European Society of Gynaecological Oncology (ESGO), a resolution was adopted proposing as a series of goals and actions to be taken to support the achievement of the WHO goal in Europe (<https://www.eccosummit.eu/Resolutions/HPV>, see Boxes 1-5). The following organisations have endorsed this proposal for European actions: ESGO, ECCO and European Federation for Colposcopy. Upon the initiative of ESGO, the resolution was widened to a platform of experts and

BOX 1 Action on HPV vaccination

- All European country cancer plans should include actions towards achieving population-based HPV vaccination of girls, and also vaccination of boys if cost-effective.
- Vaccination programmes against HPV infection should be in place in all European countries.
- The target vaccination rate by 2030 in all European countries should be at least 90% of adolescents, preferentially for both genders, by the age of 15 years.
- In support of vaccination goals, global cooperation should be fostered to resolve vaccine supply issues to ensure sufficient vaccine doses for the vaccination programmes of all countries.

BOX 2 Actions on HPV vaccination and screening

Guidelines on integrated HPV vaccination and cervical cancer screening should be regularly updated. A third edition of evidence-based EU Guidelines for Quality Assurance in Cervical Cancer Prevention should be developed, which should include recommendations on how to screen vaccinated populations.

BOX 3 Actions on screening and early diagnosis

- By 2030, at least 70% of women in Europe, belonging to the target age group, should have been screened for cervical cancer with a clinically validated HPV test within the last 5 years. This coverage should be reached as part of an organised programme. HPV screening programmes should take into consideration innovations such as self-sampling in order to reach women who may not participate in the regular screening programme.
- Future European guidelines should include recommendations on how to communicate the results of HPV testing and how to counsel women and their partners to avoid stigma and shame.

BOX 4 Actions on treatment

- Across all European countries, 90% of women with Grade III cervical intraepithelial neoplasia should be treated within 3 months. All women with diagnosed cervical cancer should have access to appropriate oncological services including palliative care for incurable cases.
- All European country cancer plans should include actions towards achieving these treatment goals.
- Guidelines on HPV vaccination and cervical cancer screening should also review the relevance of ablation (cryotherapy, thermal ablation) as a simple, safe and efficacious technique to treat cervical precancers, especially in younger women in Europe.

representatives from other involved societies, and cancer institutions and agencies.

The series of actions enumerated earlier contributing to the elimination of cervical cancer were compiled before the outbreak of the COVID-19 pandemic. The control measures against the spread of

BOX 5 Other actions to support the elimination goal

HPV awareness

All European country cancer plans should include actions towards increasing public, patient and healthcare professional understanding and awareness of HPV. This awareness should include the range of HPV-related cancers and diseases, their symptoms and forms of prevention. Furthermore, this communication effort should elaborate to the public, patients and healthcare professionals on the strategies being pursued to achieve the goal of cervical cancer elimination, and the role of the public, patients and healthcare professionals play in achieving the elimination goal. Awareness levels of the public, patients and healthcare professionals on HPV should be monitored and enhanced where necessary.

Public confidence in HPV vaccination and actions against fake news

- Health authorities and stakeholders should invest in effective communication about the effectiveness and safety of HPV vaccines to generate a basis for confidence.
- Cancer societies, patient and healthcare professional associations, and other stakeholders, should publish recommendations to combat the impacts on HPV vaccination uptake posed by deliberate misinformation, spread via traditional news media (print and broadcast) or social media, on ineffectiveness or risks associated with HPV vaccination.
- All major social media platforms operating in Europe should have developed and implemented strategies to improve health literacy and reduce the spread of fake news on vaccination.
- All national cancer plans in Europe should include actions to combat the deterrence effects of fake news upon HPV vaccination rates, as part of a broader campaign to reduce the negative impact of vaccination hesitancy on all vaccination programmes.

Improving data and monitoring

- By 2025, all European countries should have population-based registries in place to track and report upon HPV vaccination, HPV screening and cancer incidence and mortality data.
- Monitoring should include reporting of harms associated with HPV vaccinations, screening and treatment of screen detected lesions.
- European countries should evaluate cervical cancer screening programmes using the key performance indicators harmonised through the second European Screening

Report (2017) and such evaluation reports should be published.

Training

Health professionals (general practitioners, nurses, specialists, care givers and field workers) involved in education, cervical cancer prevention and treatment of precancer should be aware of the principles of cervical cancer control and be adequately trained for their specific contributions. Training should include objective and tailored communication of the benefits and harms from primary and secondary prevention.

EU Cancer Mission

- The EU Cancer Mission should have clear elements within its programme that are supportive to the WHO global call for the elimination of cervical cancer as a public health problem. This should include supporting research priorities such as development and evaluation of new vaccine and screening technologies, triage of screen-positive women using accurate markers, as well as care and treatment techniques. Research on interventions that optimise population coverage and adherence to follow-up, risk-based management as well as implementation of science research focusing on transforming research findings to public health benefits should also be promoted.
- EU Cancer Mission goals, such as on prevention and treatment of HPV-related disease, should be complemented by an EU Cancer Masterplan that supports achievement in respect to nonresearch-related matters. This might include facilitating greater use of EU Structural Funds to achieve EU and WHO common goals pertaining to HPV vaccination, cervical cancer screening, treatment of screen-detected lesions, and treatment of invasive cancer, as well as HPV awareness and education.

Monitoring of EU Member State Cancer Plans

As part of the coordination role that the EU should play in assisting member states to combat cancer, a public monitoring and reporting system should be established with respect to EU member state cancer plan items, similar to "the State of Health in the EU." This should include monitoring of actions towards international goals on HPV-related cancer control.

SARS-CoV-2 have interrupted the implementation of current preventive programmes and delayed new activities planned in Europe and elsewhere.²⁸ Concerns related to cervical cancer control amidst the COVID-19 pandemic and the period thereafter are addressed in Box 6.

BOX 6 Limiting the impact the COVID-19 pandemic on cervical cancer prevention activities

European public health authorities, organisers of preventive health programmes, in general, and HPV vaccination and cervical cancer screening organisations, in particular, should safeguard allocation of resources and communicate clearly how prevention activities will resume after the control measures against the COVID-19 pandemic are relaxed.

Given budgetary constraints, stakeholders and health professionals are invited to adhere strictly to evidence-based and cost-effective prevention policies. Guidelines should be developed on safe collection of specimens, specimen handling, colposcopy, biopsy taking and treatment of precancer lesions in the immediate postepidemic phase, prioritising high-risk groups.³⁰ Offering self-sampling kits might be anticipated.

5 | CONCLUSIONS

Previous editions of the European Guidelines for Quality Assurance in Cervical Cancer Screening, mandated by the European Commission, were pivotal in introducing the implementation of organised secondary prevention of this malignancy in EU member states.^{23,29} Today, new generations of vaccinated women are entering the target age group for screening and this new situation requires updated guidance. The authors of this article underline the need for a new third edition of EU guidelines for integrated primary and secondary prevention of cervical cancer. Although waiting for an official mandate from the EU Commission, a large group of professional societies and cancer organisations are engaged and willing to assist the WHO and European health authorities to achieve the laudable goal of eliminating cervical cancer.

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DISCLAIMER

Where authors are identified as personnel of the International Agency for Research on Cancer or WHO, the authors alone are responsible for the views expressed in this article and they do not necessarily represent the decisions, policy or views of the International Agency for Research on Cancer or WHO.

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