

**ECONOMIST
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A global blueprint for cervical cancer elimination: learnings from Sweden



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About this report

A global blueprint for cervical cancer elimination: learnings from Sweden is an Economist Impact report, supported by MSD. It examines the extent to which countries are meeting, and in some instances exceeding, the World Health Organization's (WHO) 90-70-90 goals for cervical cancer elimination within this century. The report describes the exemplary performance of Sweden, which could come close to eliminating cervical cancer before 2030. It also looks at other select countries, across a range of income levels, population health needs and budget constraints, that have prioritised cervical cancer as a key health priority and are now reaping the benefits of their commitment. The report is based on desk research, an in-depth literature review, and insightful interviews with a range of global and national-level experts in the field, including those involved in both upstream and downstream levels of policy, strategy and implementation. Through the synthesis of these success stories, it concludes with a 10-point plan as a baseline of recommendations for other countries to consider in their pursuit of eliminating cervical cancer.

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Executive summary

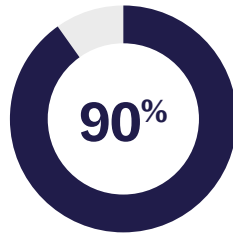
Cervical cancer is a significant global health challenge, affecting over 604,127 women and leading to 342,000 preventable deaths worldwide.¹ In Europe alone, there were 30,447 new cases and 13,437 deaths as a result of cervical cancer.² Unless contained,

and eventually eliminated, the impact of cervical cancer has the potential to destabilise economies and societies, particularly those of low- and middle-income countries (LMICs), where inadequate resourcing remains a key public health challenge that leads to a steady rise in the number of new cases and deaths from cervical cancer.³ Without swift and substantive action, the global cost of cervical cancer is expected to increase to US\$682bn between 2020 and 2050; therefore, the condition does not simply present a public health problem but a sizeable economic one.⁴

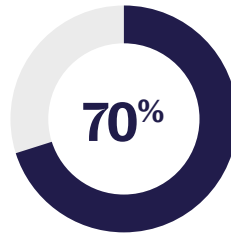
As a result of the remarkable advancements in science and technology, the goal of eliminating cervical cancer is now more viable than ever. This optimistic sentiment has been propagated and amplified through the concerted messaging efforts of multiple stakeholders, including policymakers, patients and patient advocates, bio-pharmaceutical organisations, researchers, and healthcare professionals. However, concrete plans to achieve this ambitious goal are still nascent. Building on from the World Health Organization's (WHO) global strategy for cervical cancer elimination, adopted by the World Health Assembly in August 2020,⁵ many countries have begun developing national and regional strategies in pursuit of this lofty goal. For instance, Europe's Beating Cancer Plan (EBCP), launched by the European Commission in 2021, includes, among its many goals, the elimination of cervical cancer, as well as other cancers caused by human papillomaviruses (HPV).⁶



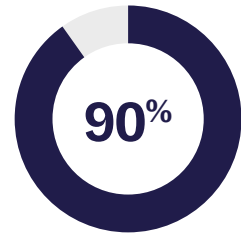
WHO's 90-70-90 targets to achieving cervical cancer elimination:



of girls fully vaccinated with HPV-vaccination by 15 years of age



of women are screened using a high-performance test by 35 years of age and again by 45 years of age

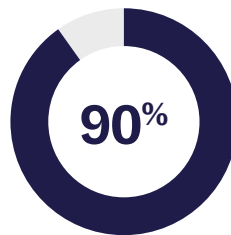


of women identified with cervical disease receive treatment

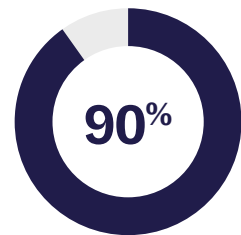
EBCP targets for cervical cancer elimination:



of the European Union's (EU) target population of girls fully vaccinated with HPV-vaccination and the vaccination of boys significantly increased by 2030



of the EU target population offered cervical cancer screening by 2025



of eligible patients have access to Comprehensive Cancer Centres for treatment by 2030

The WHO estimates that investing in interventions to meet the 90-70-90 targets would add \$28 billion to the world's economy and avert 300 000 cervical cancer deaths before 2030, over 14 million by 2070, and over 62 million by 2120.⁸ Progress towards achieving the WHO's 90-70-90 targets is highly variable both between and within countries. Several countries – particularly (but not exclusively) high-income countries (HICs) – are close to meeting, or even surpassing, the targets by 2030. Such countries include Sweden, Australia, Portugal and Rwanda, the last being the exception in the list as the only low-income country. These countries have many lessons to offer the rest of the world, particularly Sweden, which is an exemplar of success, as demonstrated by its development

of world-renowned registries, organised health programmes, evidence-based decision-making, strategies to improve vaccination coverage for both males and females, increasing screening coverage, and most importantly, through high-levels of political commitment within the country. As a result of these organised efforts, Sweden is likely to be the first country to eliminate cervical cancer by 2030.

Based on the insights of experts interviewed, published evidence and learning from countries leading the way towards cervical cancer elimination, Economist Impact recommends a 10-point plan as a baseline for policymakers to consider when developing national strategies aimed at eliminating cervical cancer.

The 10-point plan for cervical cancer elimination



Point 1

Build political commitment and momentum



Point 2

Ensure multi-stakeholder collaboration



Point 3

Prioritise HPV within national cancer policies and vaccination schedules



Point 4

Generate data through the development of robust registries



Point 5

Include screening and vaccination under universal health coverage



Point 6

Understand the target population and design the roll-out of organised and accessible immunisation programmes



Point 7

Ensure equitable vaccination and screening access to the entire population



Point 8

Address the barriers of vaccination hesitancy and misinformation



Point 9

Ensure equitable access to high-quality treatment and optimal care pathways



Point 10

Learn lessons from the Covid-19 pandemic to build system resilience and scale screening and vaccination coverage

Background

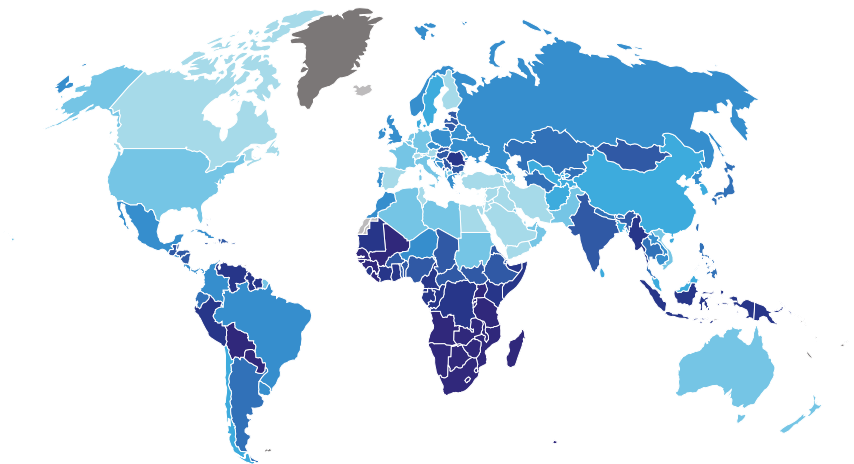
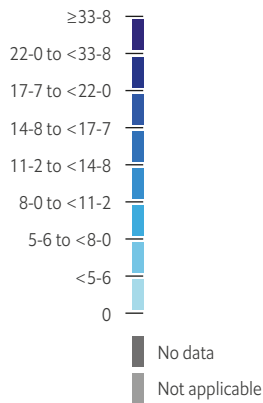
The global burden of cervical cancer

Cervical cancer is a defining global health challenge. It is the fourth most common cancer in the world and accounted for 6.5% of all new cancers diagnosed in women in 2020.¹ According to the latest GLOBOCAN (Global Cancer Incidence, Mortality and Prevalence) data

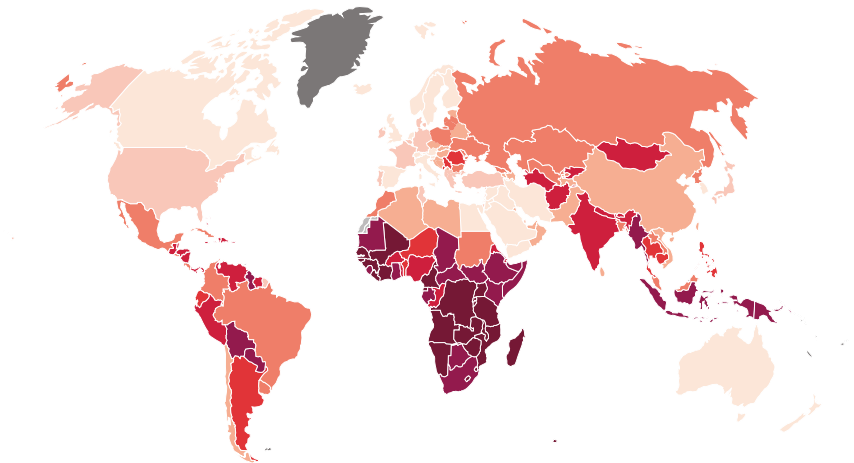
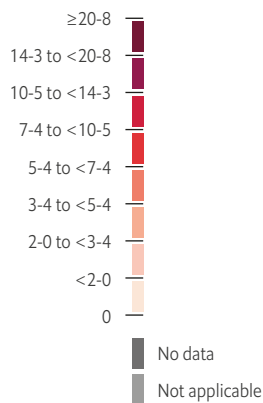
from 2020, 604,127 women were diagnosed with cervical cancer worldwide and 342,000 women died from the disease.¹ In Europe alone, there were 30,447 new cases and 13,437 deaths as a result of cervical cancer.² The vast majority of the global prevalence and mortality is in sub-Saharan Africa, South America and South-East Asia (Figure 1).¹

Figure 1: Global age-standardised incidence and mortality rates (per 100,000 women-years) of cervical cancer in 2020⁷

Age-standardised incidence
(per 100000 women-years)



Age-standardised mortality
(per 100000 women-years)



The global toll of cervical cancer continues to grow substantially over time. An analysis of the Global Burden of Disease (GBD) data showed that over the past two decades (between 1990 and 2019), the incidence of cervical cancer increased by 68.5%, cervical cancer-related deaths rose by 52%, and the number of disability-adjusted life years (DALYs) also grew by 44.99%.³

These numbers are particularly concerning, considering that cervical cancer is in fact highly preventable with the development of a vaccination against human papillomaviruses (HPV). An HPV-infection is the leading cause of cervical cancer; exposure to 14 high-risk HPV subtypes cause more than 95% of cervical cancers, and two of the subtypes (HPV16 and HPV18) alone are responsible for 70% of cases.^{8,9} It should be noted that HPV-related cancers are not limited to the cervix, but also manifest in other areas of the body including the oropharynx (throat), and the male and female genitalia, thereby compounding the burden of HPV-related cancers.⁹

Many countries, across income levels, have made remarkable strides in limiting the growth of cervical cancer cases. This containment has not been achieved through vaccination against HPV alone, but has involved the deployment of several effective and coordinated prevention measures, such as improved health coverage, screening of women, and vaccination of both boys and girls, as well as young women. However, more needs to be done and many countries need to place cervical cancer elimination strategies on the top of their health agendas; without significant intervention, the global incidence of cervical cancer is expected to grow by 700,000 in 2030, potentially resulting in 400,000 preventable deaths.¹⁰ These estimates suggest a 16% rise over the 604,127 cases recorded in 2020, and a 17% rise in deaths relative to the 342,000 deaths in 2020 based on GLOBOCAN data.^{1,10}

The growing burden of cervical cancer profoundly impacts women (primarily those in their early-to-mid-30s), their families and societies, imposing both human and economic costs. Economic modelling estimates that the global cost of cervical cancer is set to increase significantly between 2020 and 2050, amounting to US\$682bn, with the highest costs expected

to occur in several low- and middle-income countries (LMICs), predominantly located in Africa and South America.⁴ Conversely, in high-income countries (HICs), the cost of cervical cancer is lower when compared to the cost of other cancers, possibly because more progress has been made in the prevention, monitoring and early diagnosis of cancers caused by HPV-infections.⁴ Although beyond the scope of this report, it is worth noting that the overall cost of cervical cancer in the United States in 2020 was estimated at a staggering US\$2.3bn, representing 1% of all cancer-related costs. Per patient, annual costs were highest in the end-of-life phase (US\$97,000), followed by initial care (US\$58,700) and continuing care (US\$4,000), highlighting the urgent need for robust prevention efforts.¹⁰⁵

In Europe, there are vast disparities in the prevalence of cervical cancer and its socioeconomic consequences. For instance, the economic burden of cervical cancer is significantly higher in Bulgaria as compared to other European Union (EU) Member States. The direct annual costs of cervical cancer to the Bulgarian health system amounts to €17.68m, mainly driven by drug acquisition, administration costs and inpatient treatment.¹⁰⁶ Investments in cervical cancer prevention, including timely screening, early diagnosis, and higher HPV-vaccination coverage rates, could avert such costs that are relatively high in Bulgaria, as well as in other Eastern European countries, which have the highest share of the cervical cancer burden in Europe. In Sweden, cervical precancerous and cancerous lesions are responsible for most of the economic burden posed by HPV-related cancers. A prevalence-based cost-of-illness study estimated that the total annual direct costs for cervical cancer was €17.8m in 2006, in addition to €7.3m for precancerous cervical lesions. Cervical precancerous and cancerous lesions accounted for 67% of HPV-related outpatient care (n=17,867) and 68% of HPV-related inpatient care (n=1,948). Cervical cancer had the highest indirect costs of all HPV-related cancers, estimated at €40.6m, mainly due to lost productivity, thus driving the Swedish government to take concerted action towards its elimination.¹⁰⁷

Prioritising the elimination of cervical cancer

In 2020, the World Health Assembly adopted the global strategy for cervical cancer elimination, which sets out a vision to meet key targets by 2030 in the pursuit of achieving cervical cancer elimination within the century.⁵ The strategy, developed by the World Health Organization (WHO), is the first of its kind because it declared cervical cancer a public health problem and addressed the health inequities between different countries and within the dimension of gender as the condition only affects women. The WHO's elimination goal is underpinned by three targets (the "90-70-90" targets) to be achieved by 2030, in order to reduce the global incidence of cervical cancer by 2% by 2030, by 42% by 2045, and eventually by 97% by 2120 when the cancer would be eliminated.⁸ Meeting the goal of elimination would require countries to reach and maintain an incidence rate of less than 4 per 100,000 women.

In August 2022, the WHO further published a roadmap to accelerate the elimination of cervical cancer as a public health problem in the European Region between 2022-2030, which is specific to the opportunities and challenges faced in this region.¹² Political action in Europe has demonstrated ambitions to accelerate cervical cancer elimination even beyond the 90-70-90 targets. In February 2021, the European Commission published Europe's Beating Cancer Plan (EBCP), which includes goals and actions to not only eliminate cervical cancer, but also other cancers caused by HPV, through concerted and coordinated efforts across the EU. The plan was developed as a guide for EU Member States to reach the United Nations' (UN) Sustainable Development Goals (SDGs) and the WHO's targets on non-communicable diseases. The EBCP sets a goal of ensuring that cervical screening is offered to 90% of eligible women across Member States by 2025; it currently varies from 25% to 80% between countries. Furthermore, it recommends gender-neutral vaccination, setting a target of at least 90% of girls vaccinated by 2030, while simultaneously increasing vaccination amongst boys.¹³ The plan includes the development of new guidelines and quality assurance schemes for screening, diagnosis, treatment, as well as follow-up and palliative care for cervical cancer, including accreditation and certification programmes.¹³ Investments are prioritised under multiple structures, including the EU4Health programme and other funding initiatives, to support Member States' efforts to broaden the implementation of routine vaccination.¹³



Primary prevention of cervical cancer through HPV-vaccination

Cervical cancer is highly preventable, as HPV causes more than 95% of cervical cancer cases. The virus, transmitted through sexual contact, was first detected in biopsies of cervical cancers in 1983 and became a therapeutic target.¹⁴ HPV-vaccination was first licensed by the US Food and Drug Administration (FDA) in 2006,¹⁵ and clinical trials have showed that vaccination is effective in preventing >90% of infections, precancerous lesions and precancers caused by the HPV subtypes targeted.^{16,17,18}

More recently, the roll-out of school-based vaccination programmes has proved to be an effective approach to achieving high coverage rates. One such school-based HPV-vaccination programme was rolled out in Sweden in 2012, and an evaluation of the programme found that it substantially reduced the risk of invasive cervical cancer at the population-level in the country, lowering the incidence of the disease by half among vaccinated females in comparison to unvaccinated females.¹⁹ Similarly, another study in the United Kingdom found that the cervical cancer risk was reduced by 87% among vaccinated females.²⁰ These trends were also seen in other HICs such as Australia, which first launched its school-based

HPV-vaccination programme for girls in 2007,¹⁹ in tandem with a catch-up programme for older girls and young women.¹⁵

WHO recommendations for HPV-vaccination

The WHO recommends HPV-vaccination targeted at girls aged 9-14 years, before they become sexually active.²¹ HPV-infection in boys is concomitantly reduced when coverage levels for girls reach 80%.²¹

Vaccination of older girls, as well as young women and boys, is recommended by the WHO only "if this is feasible and affordable, and does not divert resources from vaccination of the primary target population or effective cervical cancer screening programmes".²¹

WHO's roadmap for cervical cancer elimination in Europe points out that routine vaccination of boys will provide indirect protection to girls and women, contribute to lowering transmission, and prevent other HPV-related cancers in men. Furthermore, it adds that gender-neutral vaccination programmes may facilitate increased acceptance of HPV-vaccination.¹²

Secondary prevention of cervical cancer through screening

For decades, screening using the Pap smear, which involves a speculum examination of the cervix along with the collection of cells for cytological examination to identify precancerous lesions so they can be treated, has been the mainstream approach against cervical cancer.

Pap smear-based screening programmes have reduced cervical cancer mortality almost five-fold since the 1930s,²² but have their drawbacks – the testing is difficult to implement uniformly, needs to be conducted by trained staff with laboratory support, requires specialised



interventions for abnormal results, and only picks up around half of abnormalities (ie, have a sensitivity of 50%).²³ As a consequence, Pap smear-based programmes have been difficult to implement in LMICs, and where they have been, coverage is generally low.⁸

Visual Inspection under Acetic acid (VIA) screening programmes have been implemented as an alternative in some LMICs. This uses 3% to 5% dilute acetic acid to stain the cervix so abnormalities appear as white areas that can be treated immediately using cryotherapy or thermal ablation. Two studies in India showed that VIA was associated with a 30% to 35% decrease in cervical cancer mortality. However, its sensitivity is modest, ranging between 16% and 82%; it also has a high false positive rate (low specificity) and is less effective in post-menopausal women.²⁴

As 14 high-risk HPV subtypes are responsible for almost all cervical cancer cases,⁸ HPV testing using a nucleic acid amplification test (NAAT) (DNA or mRNA) on a cervical or vaginal sample can be used to detect women who have or are at risk of precancerous lesions.²¹ HPV testing is more sensitive than cytology, meaning fewer cases are likely to be missed, but has lower specificity so more women without these lesions will test positive. However, the use of a triage test such as HPV genotyping for subtypes 16/18, or cervical cytology for women who test positive for HPV, improves specificity.²⁵

Screening through HPV testing has been shown to be better at reducing the incidence of cervical cancer than conventional cytology. Comparative trials in Europe suggest that HPV testing gives 60-70% greater protection against invasive cancer than cytology.²⁶ In particular, the effectiveness of cytology in detecting CIN2 lesions falls after HPV-vaccination whereas HPV

testing is more accurate.²⁷ Use of HPV testing for screening has also been shown to better reduce mortality due to cervical cancer than cytology or VIA.²⁸

In November 2022, the Council of European Union Testing recommended HPV testing using clinically validated assays every five years or so as the preferred screening method for women aged 30 to 65 years in Member States, with ages and intervals adapted to individual risk. It also recommended that Member States consider offering self-sampling kits to non-responders to screening invitations.²⁹

WHO recommendations for screening

The WHO recommends HPV testing using validated HPV DNA NAAT as the preferred method for cervical cancer screening. The HPV screening test may be used with or without triage (a second test such as genotyping, cytology, colposcopy or VIA) before proceeding to treatment in HIV-negative patients. However, triage is recommended routinely before treatment in HIV-positive patients.

Testing may be based on cervical samples collected by health providers or vaginal samples collected by women themselves;²¹ providing women with the option of self-sampling improves acceptability and access to services.⁸

Women aged 30-49 years should be prioritised for screening, which should be performed every 5-10 years; women aged 50-65 years should also be prioritised if they have never been screened before and if resources allow.³⁰ Screening should start earlier, at age 25 years, and be performed more frequently (every 3-5 years) for women with HIV or those who are otherwise immunocompromised.³⁰

Treatment of cervical cancer

There is no treatment for HPV infection, but precancerous lesions, identified via screening, can be treated with thermal ablation or cryotherapy to destroy the abnormal tissue. Where these methods are inappropriate, precancerous lesions can be surgically excised to prevent progression to invasive carcinoma. Without screening, women are unaware of such lesions due to a lack of symptoms.

A diagnosis of invasive cancer must be confirmed by cervical visualisation using colposcopy and a biopsy. Clinical features, plus pathological findings and/or imaging, such as, computed (axial) tomography (CT), magnetic resonance imaging (MRI), positron emission

tomography (PET), may also be used, where resources allow, to provide information on tumour size, status and spread.³¹

Early-stage disease is treated with surgery or radiotherapy, and fertility preserving surgery may be offered to some patients, with hormone replacement therapy (HRT) considered for women aged under 50 years who have lost ovarian function. Locally advanced disease is treated with combined chemotherapy and radiation, while advanced disease that has spread beyond the cervix is typically treated with either combined chemotherapy and radiation or chemotherapy alone. Where there is extensive local or distant metastatic disease, patients should be offered palliative therapy, with the best supportive care and symptom control.

WHO recommendations for treatment

Until HPV-vaccination programmes are implemented universally, and all women have the opportunity to benefit from vaccination, some women previously infected with HPV will continue to be at risk of cervical cancer. As a result, WHO emphasises that improving access to vaccination, screening and the treatment of precancerous lesions must remain a top priority of the global strategy to eliminate cervical cancer.⁸



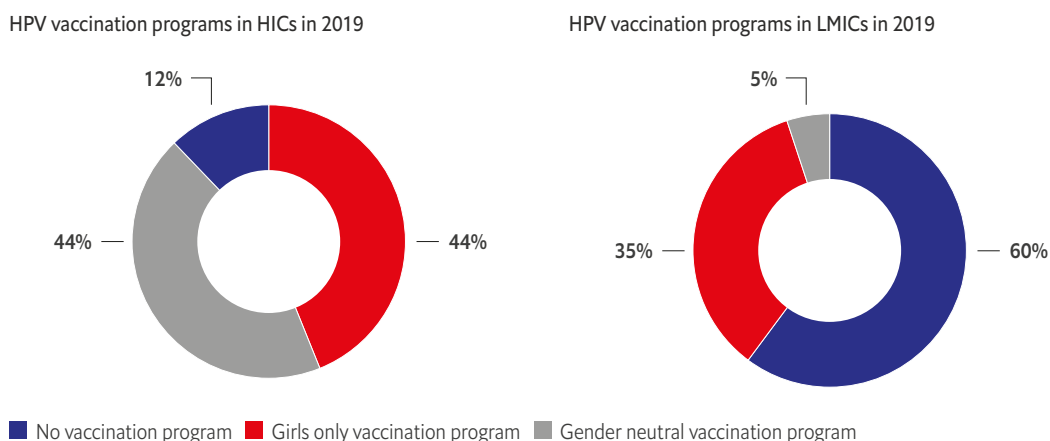
Progress towards elimination of cervical cancer and the WHO targets

Global vaccination coverage remains extremely low with only 13% of eligible girls vaccinated worldwide, far below the WHO's target of 90%. As of July 2022, 117 countries, home to one-third of the world's population of girls aged 9-14 years, have HPV-vaccination programmes.¹¹² However, there are wide disparities in the vaccination coverage. The proportion of HPV-attributable cancers is highest in LMICs and these countries are the least likely to have implemented HPV-vaccination programmes.³⁴ While 85% of HICs had included HPV in their national immunisation schedule as of 2020, less than 25% of low-income, less than 30% of lower middle-income, and less than 60% of upper middle-income countries had these

programmes.⁸ As of June 2020, the Americas and Europe were the regions where most countries had introduced HPV-vaccination – 85% and 77% respectively.³⁵ At that point, GAVI (the Global Alliance for Vaccines and Immunization) support for vaccination had been extended to 19 LMICs (35% of LMICs).³⁵

By 2019, 88% of HICs had introduced HPV-vaccination for girls with half of them (44%) having a gender-neutral vaccination programme. In contrast, only 40% of LMICs had introduced HPV-vaccination for girls and only 5% had gender-neutral vaccination programmes.³⁵ Overall, only 42 countries offer vaccination to boys as of July 2022.³³

Figure 2: A comparison of HPV-vaccination programmes in HICs and LMICs



To this point, Daniel Kelly, Co-Chair of European Cancer Organisation HPV Action Network, says that “There’s been a lot of pushback on boys because of the cost issue, but also some people are not persuaded that the boys are at risk. However, unvaccinated boys put themselves and others at risk of a range of cancers. To me it just makes sense to vaccinate both groups. When you consider the human costs of this disease, and [the fact] that it can be prevented, it still amazes me that governments are still not doing it [vaccinating both girls and boys].”

In 2019, the majority of programmes (59%) delivered HPV-vaccination through schools alone or in a combination of school and facility-based delivery, and in LMICs almost all programmes were school-based or mixed (90%). School-based delivery strategies have been shown to achieve higher coverage than facility-based programmes.³⁵

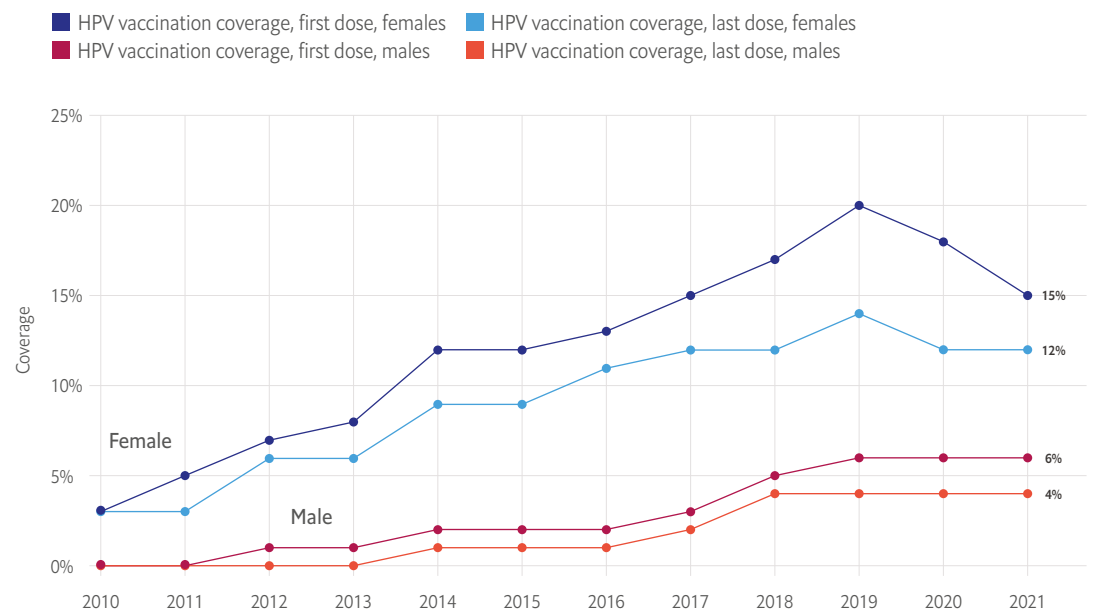
Organised programmes that take the vaccination directly to the target population, such as programmes delivered through schools, are able to achieve higher coverage levels due to better access, in comparison to those that rely on opportunistic delivery mechanisms. Publicly funded school-based programmes are the most

effective because they take away cost barriers.³⁶ Parents often report cost as a barrier to providing their child with HPV-vaccination, along with insufficient information and safety concerns.³⁷ In addition to expanding access to vaccination, publicly funded programmes also increase vaccination uptake indirectly by signalling government and health system endorsement.³⁶

On the other hand, opportunistic HPV-vaccination can help boost coverage among girls who missed or did not complete vaccination through the school programme. It can also be used as a way of reaching older groups who were not offered HPV-vaccination at school because it was not available.³⁸

Coverage for HPV-vaccination fell during the Covid-19 pandemic, particularly in LMICs, but also in some European countries,³⁹ due to school closures, delayed vaccination and difficulties securing vaccination doses. Between 2019 and 2021, the number of girls globally who received a first dose of HPV-vaccination dropped from 20% to 15% – which means 3.5m more girls missed out.^{33,40} The number of girls who did not receive any doses increased in most regions of the world over that period, apart from the EU.³³

Figure 3: global HPV-vaccination coverage³³





An analysis of the progress towards the WHO's target for 70% cervical screening coverage by 2030, based on data collected for 202 countries until February 2021, identified recommendations for screening in 139 countries, covering 88% of HICs and 60% of LMICs.⁴¹ Among these 139 countries, a majority, 109 countries (78%), recommended cytology-based screening, while 48 (35%) recommended primary HPV testing for screening. VIA screening was the most recommended test in resource-limited settings. At least 21 of the 48 countries recommending HPV testing were transitioning from cytology to the HPV test.⁴¹

The 5-year coverage rate for screening of women between 35 and 49 years of age was less than the WHO target of 70% in 32% of HICs, 72% of upper middle-income countries, 94% of LMICs and 100% of low-income countries.⁴¹ Globally, two-thirds of women aged between 20 and 70 years – a total of 1.6bn women – are estimated to have never been screened for cervical cancer.⁴¹

Concurrent chemoradiotherapy followed by brachytherapy (internal radiotherapy) is the treatment recommended for locally advanced cervical cancer, but provision is variable both

across HICs and LMICs. Studies show that up to 50% of patients in HICs such as France, Australia and Japan did not receive treatment that conformed to guidelines for locally advanced cervical cancer, and about 25% did not receive brachytherapy. The presence of significant comorbidities was the main reason cited for non-adherence to treatment guidelines. In addition, under-utilisation of brachytherapy is attributed to inadequate training, time, and logistical challenges, as well as limitations in reimbursement.⁴¹ There is an imminent need to improve access to radiotherapy and brachytherapy, increase the number of trained radiation oncologists to administer treatment, develop guidelines for management of the elderly with comorbidities, and have quality control measures in place to meet the WHO treatment targets for treatment of cervical cancer.

Progress towards meeting WHO's 90-70-90 targets varies markedly between countries. The next section examines how four countries, Sweden, Portugal, Rwanda and Australia, despite their distinct differences (eg, in their population, resources, health systems), are paving the way towards cervical cancer elimination, and provides lessons for other countries who are in pursuit of the same goal.

The first country on the verge of eliminating cervical cancer: Sweden

For most of the world, reaching WHO's 90-70-90 targets by 2030 will be a stretch, but Sweden has surpassed expectations and is striving to become the first country to eliminate cervical cancer before 2030.⁴²

"We've advocated for Sweden to become the first country to eliminate cervical cancer," says Ulrika Årehed Kågström, Secretary General of Cancerfonden (Swedish Cancer Society). "We've worked with our politicians and said that what we really need to do is catch-up vaccination for women who missed out because they were too old for the school-based programme, and help ensure high participation in screening," explains Ms Kågström.

With regards to the WHO's 90-70-90 targets, the country is well on track. As of 2021, 90% of girls had received a single dose of HPV-vaccination by age 15, and 84% the full two doses.^{43,44} Nationally, cervical screening is above 70%, with an estimated 78.5% coverage for women aged 23-70 years, in 2021. Like many other countries, Sweden also faces the challenge of regional inequities, which has led to disparities in screening coverage. The highest screening coverage is seen in Värmland (88.2%) in the Uppsala-Örebro region, whereas the lowest screening coverage rates were seen in Gotland (68.8%), and Stockholm (70.2%), both of which are in the Stockholm region.⁴⁵ Furthermore, for 2,212 women diagnosed with cervical cancer, a population-based study, conducted between 2011 and 2015, found that only 6% of patients did not receive treatment.⁴⁶

As a result of Sweden's efforts towards elimination, the incidence of cervical cancer in Sweden decreased from 24 per 100,000 women in 1965 to 8 per 100,000 women in 2011. While a 20% increase in incidence was noted between 2014 and 2015, the rise was mainly seen in young women who had attended screening and presented with early-stage disease.⁴⁷

The latest data (2021) indicates the incidence rate is at 10.4 per 100,000 women, which is inching close to the 4 per 100,000 women elimination target.⁴⁸ In 2021, 533 new cases of cervical cancer were diagnosed in Sweden, accounting for a mere 1.8% of all cancers; in the same year, there were 149 deaths from cervical cancer, representing 1.3% of all cancer deaths in women.⁴⁹ The number of women living with cervical cancer between 2015 and 2020 was estimated at 2,081.⁵⁰

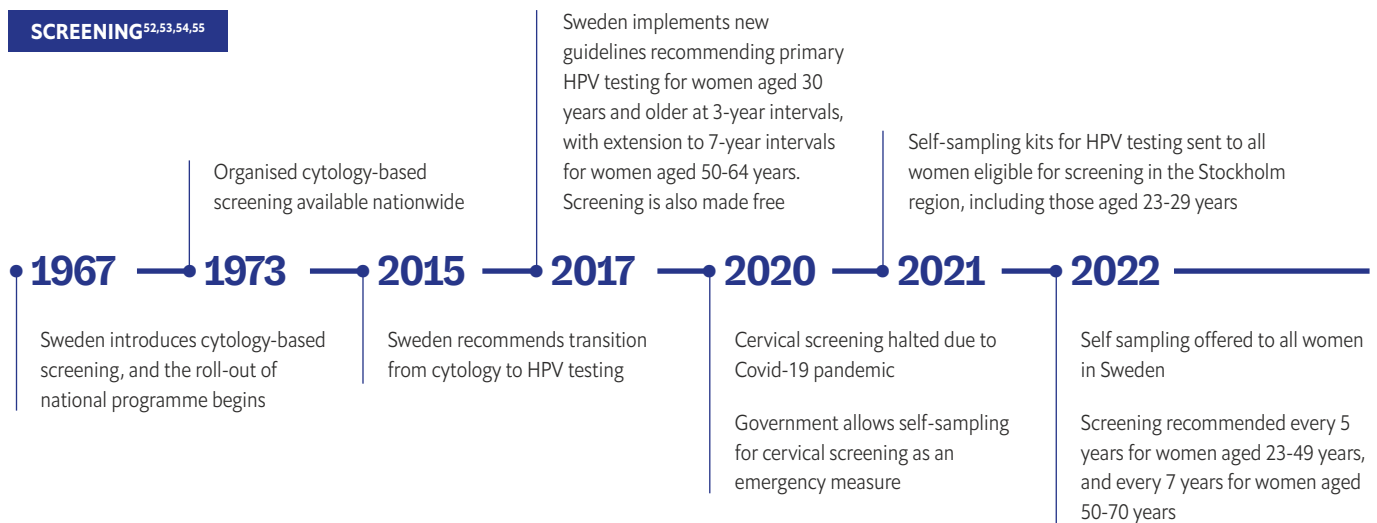
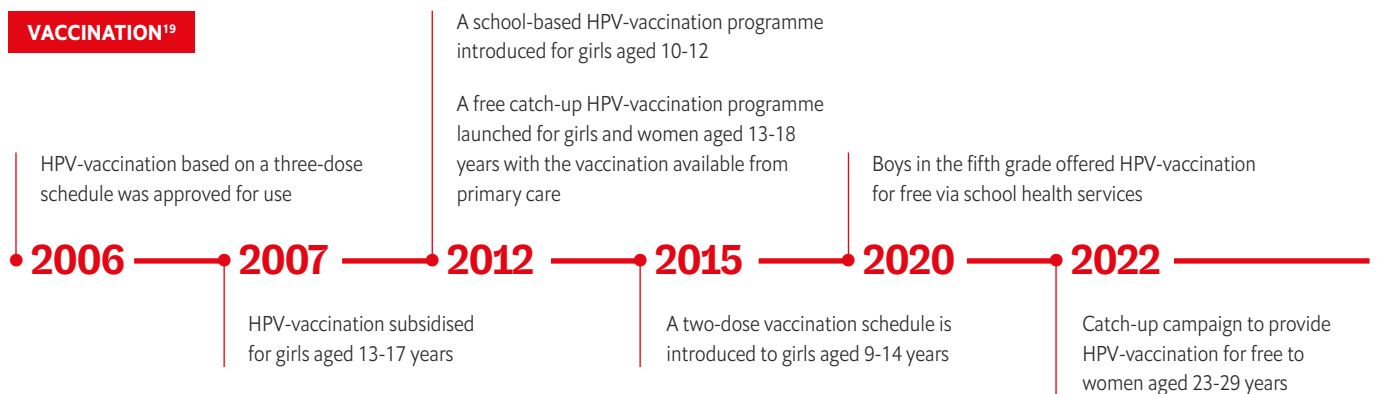
Modelling studies have concluded that primary prevention of cervical cancer through HPV-vaccination for girls or with gender-neutral programmes, based on 80% uptake and with appropriate funding mechanisms in place, is cost-effective in Sweden.⁵¹

"We usually tend to talk about the humanitarian consequences of cancer," says Ms Kågström, "but there is also productivity loss, especially since this is a type of cancer that often affects women when they are most productive, in their prime. Costs for society are very expensive treatments and loss of productivity compared to the very, very small costs for a vaccination programme."

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Ulrika Årehed Kågström, Secretary General, Cancerfonden (Swedish Cancer Society), Sweden

Timeline of vaccination and screening initiatives Sweden



From Sweden's late start to its accelerated path to cervical cancer elimination

Despite the country's significant public health challenges of growing demand for healthcare and finite health budgets, Sweden's unswerving commitment to eliminating cervical cancer has been pivotal to its success. This success does not stem solely from its long-standing national cervical cancer screening programme or its early roll-out of the HPV school-based vaccination programme; many countries were ahead of Sweden to this respect, but a concerted national effort on multiple fronts has ultimately pushed Sweden to the front of the race to elimination.

"I think that we may have been a little bit late in starting the basic vaccination programmes targeting girls and boys in school, and the catch-up programme for girls to 18," says Professor Joakim Dillner, Head of Unit at the Karolinska University Hospital, Center for Cervical Cancer Elimination and director of Research & Development (FoU-chef) at the Medical Diagnostics Karolinska. "Many other countries were faster in implementing those. However, when we actually started, population uptake was quite high. Uptake of the vaccination in girls in Sweden is 90%, which is among the highest globally – not the highest – and the uptake of vaccination among the boys is over 85%." Although Sweden's "tradition of organisation and equity and focus on prevention" has helped achieve these high uptake levels, he says, when there is an effective vaccination to prevent cancer, "it's very easy to explain to people why they should take it – it's obvious."

1. Organised vaccination and screening programmes

While Sweden was later than many to begin tackling cervical cancer, it has since made up for lost time through its use of "organised interventions". Prof Dillner says, "I think this is what we call 'organisation'. The concept is very well described regarding screening. Organised screening means that one starts by identifying the population to be screened, and then invites

everyone to screening at a given time and place. It is well documented that this approach is more effective than trying to have mass media campaigns asking people to book a time because some people will see this information and some will not, and some people will understand the information and some will not. But if everyone is invited, it tends to be that a much larger population comes."

The Nordic countries pioneered this system of "organised interventions" in the 1960s, and it has gradually spread to other countries. In 2021, Sweden surpassed Iceland as the country with the highest cervical cancer screening attendance. Overall, screening attendance is around 85% in Sweden, and, more notably, as high as 92% in women aged 23 to 26 years.

Sweden also offers HPV-vaccination to school children starting as early as the fifth grade, free of charge through the school health services (although parental consent is required).⁵⁶ "The vaccination programme is also 'organised', which means all girls are offered a vaccination," says Prof Dillner. "Of course, they can say no, but there shouldn't be any girl in the country who is not offered a vaccination when we have on-site vaccination at schools."

Sweden also pioneered a catch-up campaign in 2012 to ensure that girls aged 12 to 18 years who were too old to be eligible for the mass vaccination programmes offered through schools were not missed out of the HPV-vaccination drive. This catch-up campaign achieved roughly two-thirds of the coverage of the "organised" school campaign – just shy of 60% – because girls had to seek vaccination within primary care. Vaccination was reimbursed for females up to 26 years of age.¹¹³

2. Advocacy and political buy-in

Sweden may be at the forefront of eliminating cervical cancer now, but the country has had to overcome several hurdles to get here, including, for example, the fact that for many years cervical screening was not free for all women.⁵⁷ After a 2012 EU survey of countries' policies on cervical

screening highlighted that Sweden was only one of four countries in Europe charging for cervical screening, some politicians were upset and started work to change that, Dillner says. In 2012, about 5% of women in Sweden were estimated to have never attended a Pap smear-based screening test.⁵⁸ The Swedish parliament finally made cervical screening free for all eligible women in 2017.

A number of patient advocacy groups have had an important role in raising awareness of cervical cancer and its elimination with policymakers and pushing the government to implement changes, such as the Network Against Gynaecological Cancer. Its Chair, Barbro Sjölander, has been vocal about this public health issue and driving cervical cancer campaigns for almost 10 years. “I had a friend who died of cervical cancer, I didn’t know much about it so that is why I became interested in it,” she explains. The Network Against Gynaecological Cancer has been actively working for HPV-vaccination of girls since 2007, and has also advocated for free cervical screening and the vaccination of boys, and most

recently collaborated with Prof Dillner to push politicians for a catch-up vaccination campaign to accelerate the elimination of cervical cancer. “Over the years, we [have] built a very good reputation. We are well known among politicians and we are well known among people providing care,” says Ms. Sjölander.

Other patient organisations involved in increasing awareness and working to eliminate cervical cancer include GCF Viola, which supports women with gynaecological cancers and their families, as well as acts as an advocacy group to raise awareness of the disease among policymakers.⁵⁹

3. A long track record of evidence-based decision-making

When Pap smear-based screening was introduced in Sweden beginning in the 1960s, for a number of years there was a belief that it could not really fail, explains Dr Karin Sundström, Principal Researcher and epidemiologist at the Karolinska Institutet and Karolinska University Hospital. “But in the 1970s, the community started noticing that there may be some issues with false negatives....and that’s



the start of Swedish cervical cancer screening research. People started publishing on this and trying to systematically see what could be done to improve it.”

Sweden has several attributes that enable robust population-based studies – a publicly-funded health system accessible to the entire population including the vulnerable and hard-to-reach populations, as well as a comprehensive repository of population healthcare data in a variety of registries. “We have population acceptance for traceability through national registers,” says Dr Sundström. “The founding idea is that if as a citizen you use publicly-funded healthcare, you should also contribute back to its improvement with your data. During the 1980s, clinicians and researchers realised that our national cancer registry, which was originally primarily built for cancer monitoring, could also be used for active research.”

The principle upon which these cancer registries are built means that researchers conducting population-based studies do not necessarily have to ask for permission to use patient data. “We have what we would term ‘broad population acceptance’ for this type of research, and we can use something called ‘broad informed consent’ whereby a woman can consent to several studies. If the research can be demonstrated to be for the common good, we can use a principle called ‘opt out’.” explains Dr Sundström. “‘Opt out’ means that when a woman gets invited to cervical screening, she is informed that unless she actively expresses her wish for them not to, her data and samples might be used for research if approved by the Ethical Review Authority.” Dr Sundström adds that it is rare for women to opt out and so results from such studies typically carry very high validity.

Researchers in Sweden have used population studies based on data from the registries to provide evidence to policymakers for the introduction of specific interventions, as well as to analyse the impact of these policies. “One of my

favourite sayings is that if there is controversial debate or uncertainty, the data is not clear enough,” says Prof Dillner. “If the data is really clear then it’s obvious what to do. I find it much more useful to try to obtain better data than to engage in lobbying or something like that.”

4. Comprehensive data in registries

Comprehensive registries are a major advantage in Sweden, other Nordic states, the Netherlands, and the UK, enabling them to conduct wide-scale population studies and ‘organised’ follow-up care for their populations.

Sweden has registries for HPV-vaccination, screening and cancer. A recent study ranked Sweden’s electronic vaccination registry fifth amongst the EU Member States and the UK, based on a number of factors including its level of development, extent and timeliness of information, and integration with other registries and the national health system.⁶⁰

The National Screening Registry captures 100% of the cervical cancer screening data. All screening invitations and laboratory results are linked to this registry using the unique personal ID that is assigned to an individual at birth/naturalisation. Data from the registry is collated at the regional level, and is made available to policymakers to act swiftly and improve screening efforts.⁶¹

“We started building the National Screening Registry in approximately 1995, and it took almost 10 years because there were a lot of issues, such as counties using different IT systems and coding results being different because there was no standardised system,” says Prof Dillner. “We got it to work for the whole country in 2005, and it is immensely useful.”⁶³ It is therefore possible to examine outcomes and other data for all women in Sweden, rather than just a small subset or random sample.

Prof Dillner is expanding the registry to also include biospecimens. This enables obtaining data for both current and candidate screening

tests to quantify how many deaths or other adverse outcomes could have been prevented if the screening test under assessment had been available.

Healthcare professionals are also required to report cases of cancers, suspect cases of cancer, and certain reportable benign and precancerous conditions to the Cancer Register at the National Board of Health and Welfare, which is a record of the incidence of new cancers and trends over time.⁶²

Sweden also has a national care programme for cervical cancer prevention that provides recommendations and guidelines for investigation, diagnosis, treatment, nursing support, rehabilitation, and palliative care for patients, and data for a number of quality indicators are collected.^{64,55} The National Quality Registry for Gynaecological Oncology collects data on the care pathway for specific cancers, including waiting times for management, whether a central assessment is performed, and the outcomes of treatment.^{65,55}

5. Self-sampling for HPV testing – an innovative outcome of the pandemic

In 2020, as a result of the Covid-19 pandemic, Sweden's pursuit of cervical cancer elimination came to a halt; similar to the rest of the world, the country had to divert all its health resources towards containing the pandemic. HPV-vaccination and cervical cancer screening programmes, which normally took place on-site and in-person ceased. However, the country implemented the innovative solution of using self-sampling HPV test kits to continue screening, thereby adapting to the pandemic.

Self-sampling had been recommended in Sweden as a mechanism for reaching non-attenders – those too far away, or too busy to attend a clinic - for almost ten years, but had not been used as a primary screening tool, says Prof Dillner. In 2021 self-sampling HPV kits were sent to all women including those between 23

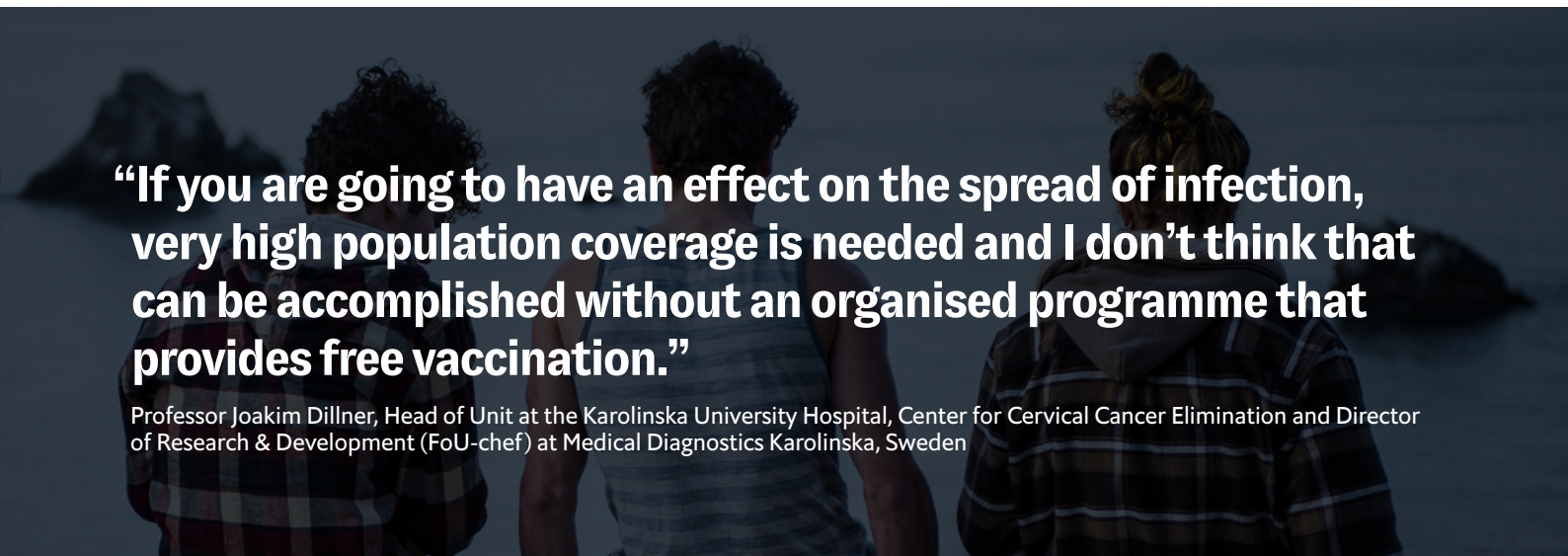
and 29 years of age who had previously been offered a Pap smear. An assessment of cervical cancer screening in the Stockholm region, where 330,000 kits were sent out, showed coverage increased by 5.3% within one year. "Attendance was identical for women who regularly attended screening appointments, but was much higher among those who did not attend regularly," says Prof Dillner, "so the net result was a big increase." Other studies have also shown that self-sampling HPV tests have comparable efficacy to clinician sampling and better acceptability among patients.^{67,68}

Based on the positive evaluation of self-sampling in Stockholm, the Swedish government introduced regulations in 2022 to allow for self-sampling to be routinely used in the screening of cervical cancer in non-emergency situations. The decision followed a study which found that HPV self-sampling tests achieved more screening coverage (34.1%) than pap smear-based screening; the study included a random sample of 10,614 women who had not undergone Pap smear-based cervical screening for at least six years, who received a phone call from a midwife offering the option of a Pap smear or HPV self-sampling test.⁶⁹

Sweden's concerted efforts to find the most effective approach to eliminating cervical cancer are continually evolving based on the evidence. Another population-based study is currently underway in the country to evaluate whether concurrent HPV-vaccination and cervical screening can result in the speedy elimination of cervical cancer.⁷⁰ Such studies have the potential to not only identify the best and fastest course of action, but also help to generate support, through action and investment, among the political class.

6. Catch-up for young women

The cervical cancer community, which includes patients and patient advocates, researchers, bio-pharmaceutical companies, and healthcare professionals, has been pivotal to generating



“If you are going to have an effect on the spread of infection, very high population coverage is needed and I don’t think that can be accomplished without an organised programme that provides free vaccination.”

Professor Joakim Dillner, Head of Unit at the Karolinska University Hospital, Center for Cervical Cancer Elimination and Director of Research & Development (FoU-chef) at Medical Diagnostics Karolinska, Sweden

political momentum for the extended organised efforts that ensure high HPV-vaccination coverage across the eligible population, and in driving the government to invest in catch-up campaigns for young females who missed out on the “organised” school-based vaccination programme. “We wanted them to take advantage of the pandemic and offer HPV-vaccination to women in that [eligible] age group when they got their Covid-19 vaccination,” says Ms Kågström; Stockholm and Gotland began offering these catch-up vaccination programmes first “We thought it was a really positive initiative, and we tried to encourage other counties to do the same, but then the pandemic faded out [so we were unable to adopt this approach].”

Despite Sweden having a decentralised healthcare system across its 21 counties, the approach to eliminating cervical cancer required coordinated, high-level decision-making at the national level. “We calculated that the cost of a national catch-up vaccination campaign wouldn’t be that big, but it’s really challenging to take a decision like that on a national-level since the counties are autonomous, but in the end, parliament took that decision,” says Ms Kågström.

As part of that unusual decision, the Swedish government allocated SKr 25m (or €2.1m) per year for six years for a catch-up campaign to provide HPV-vaccination and concomitant HPV screening for free to women aged 23 to 29 years

(born between 1994 and 1999), says Prof Dillner. Around 85% of this allocation will be used to buy the vaccination, as previously women in this group could only access the vaccination if they paid for it themselves. “If you are going to have an effect on the spread of infection, very high population coverage is needed and I don’t think that can be accomplished without an organised programme that provides free vaccination,” he says.

Sweden’s national vaccination programme is run on the promise of generating vast amounts of real-world data. In exchange for free vaccinations and HPV tests, counties provide healthcare staff to administer the vaccinations, and have agreed to follow the same standards and processes that will enable the outcomes to be evaluated nationally. All girls given vaccination through the programme will also be tested to assess the prevalence of HPV16 and HPV18 in this age group.

Cancerfonden is helping to communicate the importance of vaccination to young women in the target group using influencers on social media, particularly Snapchat and Instagram, says Ms Kågström. “The regions aren’t good at communicating with this age group (young women), and it’s really complicated since they are not all implementing it at the same time. It’s difficult trying to reach this target group. Even if they are informed, they are not ill, they have busy lives, and they have plenty of things to do, so it’s really not on their radar.”

7. Understanding barriers to vaccination and screening

To address the barriers to vaccination and screening in the country, Sweden has dedicated research to identifying and understanding these hurdles. A 2022 survey of 2,000 Swedish women found that one-third reported negative attitudes towards HPV-vaccination expressing some degree of vaccination hesitancy. Hesitancy was correlated with low education, low income, lack of access to reliable information on vaccination, and a general lack of confidence in healthcare institutions.⁷¹

Another nationwide registry-based study conducted between 2013 and 2020, mapped the prevalence of HPV non-vaccination against several variables, including parental place of birth, education level, income, and place of residence (urban/rural). Non-vaccination was more common among people with low education, low income, or of migrant status.⁷² Socioeconomic factors, including education levels, employment status, location of residence and immigrant status have also been linked to other disparities.⁷³

When it comes to screening, there are four main determinants of non-attendance, according to Prof Dillner, with the most important being the region where people live (each region has a different screening programme). “We have not found out exactly what the important difference is between the regional programmes, but we know that some screening programmes are very actively communicating with the population, and have a lot of convenient times to attend.” Other factors are rural domicile, ethnicity and household income.

Looking ahead to a cervical cancer-free Sweden

While Sweden has made impressive strides towards the swift and robust elimination of cervical cancer, there are still some improvements that can be made in the areas of cervical cancer prevention and treatment. A population-based study of 2,212 patients with

a cervical cancer diagnosis between 2011 and 2015 found that only around 6% of patients miss out on treatment;⁴⁶ however, the study also showed that, despite the exclusion of rarer and more aggressive cancer subtypes, the estimated 5-year relative survival for patients studied was lower than expected at 71%. While there was fairly high adherence to evidence-based treatment guidelines and excellent outcomes for early-stage patients treated with surgery, the 5-year survival for advanced disease was poorer than expected, suggesting that there is scope to improve cervical cancer treatment in Sweden.⁴⁶ The study also revealed that 14% of patients with early-stage disease received postoperative adjuvant radiation, which is known to increase morbidity. The researchers concluded that use of postoperative radiation in early-stage disease needed to be reduced and treatment for advanced disease improved.⁴⁶

Lack of adequate infrastructure and healthcare staff shortages may explain the poorer outcomes for those with advanced disease. For instance, the use of radiotherapy in Sweden lags behind other Nordic countries, with the country facing significant shortages of both radiation oncologists and trained nurses. One study identified four clinics in Sweden where at least one radiotherapy machine was either partly or fully closed due to the lack of an operator; furthermore, less equipment is available for radiotherapy in Sweden as compared to other Nordic countries with new technologies spreading at a slower rate. The governments of Denmark and Norway are also more involved in financing radiotherapy than the government of Sweden.⁷⁴

Importantly, overall, not all women in Sweden with cervical abnormalities detected during screening obtain treatment. “It’s not a systemic issue, because [although] in some regions we have zero women with a screening abnormality not being treated, if you look at the WHO goal that at least 90% of the women who have abnormalities should be treated, we are [still] far above that at 95 or 96% [nationally]” says Prof Dillner.

While survival rates for cancer were very high and patients were generally satisfied with treatment in Sweden as compared to several countries, it was generally recognised that the Swedish health care system could reduce waiting times and improve care coordination. In 2015, the Swedish government, therefore, initiated a national reform programme to standardise the patient care pathway and expedite the treatment of cancer. A Standardised Care Pathway (SCP) is a time-bound clinical guideline covering the patient's journey from presentation through diagnosis and referral to treatment.^{75,76} The Swedish National Board of Health and Welfare (NBHW) monitors and evaluates the SCPs and submit annual reports to the Ministry of Health.⁷⁵ The programme has demonstrably improved waiting times and patient satisfaction, but other challenges remain, such as General Practitioners (GPs) misdiagnosing cancer patients who present with multiple comorbidities and nonspecific symptoms, and ethical concerns about side-lining other patients.⁷⁷

Addressing inequities in screening and vaccination coverage

The road to cervical cancer elimination is more viable when the entire eligible population is included within the national efforts. Parents who do not return the consent form for their children to receive HPV-vaccination at school should, if possible, be followed up, says Dr Sundström. "If they say no, they have made an active decision, which is of course to be respected, but there are some parents who perhaps don't fill out the form; and for reasons of equity, ideally they should be contacted in order for this cancer prevention opportunity not to be missed."

Engaging women not attending screening is harder because they have to be found. Women are sent an invitation emphasising that screening is free and offered, in some places, as a self-sampling kit for HPV, and in others, as a midwife-based appointment, explains Dr Sundström. "We say we've reserved a time for you, you don't need to cancel if you don't come, but this is when you should come if you want to come. We think it makes it easy for the woman if she knows

that if she comes at that time, she will definitely receive an examination." This is especially key for women who have been identified as being at higher risk for cervical cancer to ensure that they are actively traced and followed up with for examinations, as well as treatment, if necessary.

In 2020, 93,000 appointments for screening were cancelled because of the pandemic, says Prof Dillner. The switch to self-sampling provided screening to all of these women and also increased participation among non-attending women – for example those from low socioeconomic groups, or with disabilities, mental health issues, busy work lives or previous poor experience of screening.

The screening organisation that Dr Sundström works with checks with the tax registry regularly to identify newly registered immigrant women in order to not overlook any recent new inhabitants. They are sent the same letter as that sent to all Swedish women in the age group eligible for screening, which emphasises the benefits of screening and the fact that it is free. These letters are issued in Swedish but information on screening is available online and in print in several languages.

A new initiative by Cancerfonden (the Swedish Cancer Society) is now also providing new immigrants learning Swedish with information on the Swedish health services, says Ms Kågström. Immigrant students, for example, are given information about HPV-vaccination, cervical screening and other services like mammography so that they understand what the invitations are for, the benefits of participating and that the services are free. In addition, doulas that have the same cultural background and mother tongue as foreign-born women have been engaged to spread awareness of screening, and this has been shown to improve participation.⁷⁸

Overall, Sweden has made tremendous progress in its goal to become the first country to eliminate cervical cancer, and its experience may help other countries to emulate its efforts to improve the delivery and uptake of HPV-vaccination, cervical cancer screening, and cancer treatment.

Implementing a national HPV immunisation programme in a low-income country: Rwanda

Rwanda, defined as a low-income country, became the first African country to implement a national HPV immunisation programme for girls in 2011. On the path to becoming one of the first countries to eliminate cervical cancer, the country is an admirable example of what can be achieved with strong political will and multi-sectoral partnerships, even in an environment with limited resources.

Despite the country's remarkable progress towards cervical cancer elimination, Rwanda has faced its share of challenges. According to Dr Marc Hagenimana, Ag. Director of Cancer Diseases Unit, Rwanda Biomedical Centre, Ministry of Health, "the first challenge is limited funding to scale up the programme especially including capacity building of health care providers to deliver those services". Dr Hagenimana explains how there is lack of awareness and skills to manage cervical cancer in the Rwandan health workforce and this includes insufficient gynae-oncologist specialist. However, Rwanda has been quick to address such challenges through the introduction of a

Gynae-oncologist fellowship programme in the country to strengthen the overall management of cervical cancer.

The vaccination programme was initially supported by a donation from a vaccination manufacturer, and since 2015, vaccination have been procured with support from GAVI, the Vaccine Alliance.⁷⁹ Girls in the sixth grade, rather than a particular age group, are targeted because some girls in rural settings do not know their age.⁸⁰ Rwanda has a high rate of school enrolment, which has allowed a large proportion of girls to be reached at school with the vaccination delivered on school premises on dedicated "Health Days" that occur three times a year. Girls not enrolled in schools, or absent on vaccination days, are traced by a team of community workers so that they can be vaccinated at local health centres.⁸⁰ Two "catch-up" vaccination rounds in the third year of secondary school were held in 2011 to ensure that all girls younger than 15 years were offered the vaccination.⁸⁰

“Awareness and education campaigns have been integrated into the package of community health workers; they [community health workers] have been trained to provide education in the community about cervical cancer prevention and advise them [eligible females] to go to health facilities to receive those services”, explains Dr Hagenimana. Other approaches to bolster awareness has been through the provision of awareness and education campaigns provided via mass media outlets including community radio, articles, social media and mobile network operators, says Dr Hagenimana.

Between 2011 and 2018, 1,156,863 girls received at least their first vaccination, representing 98% of the target population.⁸¹ As schools were closed during the Covid-19 pandemic, some girls missed their first vaccination and coverage decreased from 97% in 2019 to 89% in 2020,⁸² so a catch-up campaign was implemented in 2022 to lift coverage above 90% once again.⁸³

Before the roll-out of the vaccination, the Rwandan ministry of health assembled a technical working group comprising healthcare professionals, representatives from development agencies, private industry, and the community to plan the process. Micro-planning committees were set up to manage specific aspects of the roll-out, including supply chain, logistics and data management. This was followed by broader education of the community through the media, collaboration with religious institutions, and speeches by local and national leaders. Frontline healthcare professionals and teachers also received education and training regarding the vaccination process, benefits and risks.⁸⁴

The success of the vaccination programme has been the direct result of partnerships between the public, the private sector and civil society to organise and deliver the school-based programme,⁸¹ rigorous monitoring of vaccination coverage, and awareness campaigns led by community influencers.

Improving access to high quality cancer treatment: Australia

Australia launched one of the world's first fully funded, school-based HPV-vaccination programmes for girls in 2007, has an organised cervical cancer screening programme, has made huge financial investments in tackling cervical cancer, and supported the development of a National Cervical Cancer Elimination Strategy. It is therefore also well-placed to achieve the elimination of the disease in the near future.⁸⁵

In 2013, the organised vaccination programme for girls aged 12 to 13 years old was expanded to include boys, and by 2020, 87% of girls and 85% of boys younger than 15 years had received their first vaccination; high rates of vaccination coverage, including gender-neutral vaccination, will only improve Australia's efforts directed at cervical cancer elimination.⁸⁶

Since 2017, Australia's organised cervical cancer screening programme uses primary HPV testing every five years for women aged 25 to 69 years, with a final test for women aged 70 to 74 years. However, between 2018 and 2021, only 62% of women aged 25 to 74 years underwent HPV testing. Self-sampling for HPV testing has been provided as an option for all women since July 2022, and is expected to help improve screening rates, particularly among hard-to-reach populations, such as indigenous women and women who belong to ethnic minorities, have experienced sexual violence, are post-menopausal, identify as LGBTQ+, have a disability, or have previously had poor experiences of cervical screening.⁸⁷

In addition to gaps in screening, referrals for colposcopy and biopsy will need to be streamlined to achieve the WHO targets.⁸⁸ Australia has been steadily improving access to

therapeutics for cervical cancer, and there have been corresponding improvements in survival rates. In 2020, 60.9% of patients diagnosed with a high-grade cervical lesion were treated within eight weeks and 85.8% within six months. National level data is not available for treatment of invasive disease, but data from Queensland between 2010 and 2015 shows a 95% treatment rate in metropolitan areas and 90% in remote and rural areas.⁸⁹

Government policy and regulatory efforts have helped push the treatment of cervical cancer and the elimination agenda forward. Cancer Australia, a government agency established in 2006 to improve cancer care, is developing an optimal care pathway for cervical cancer; it is intended as a quick reference guide for physicians to ensure that appropriate multidisciplinary care is provided to patients.⁹⁰ National Cancer Control Indicators are currently being published by Cancer Australia, covering various domains such as prevention, screening, diagnosis, treatment, psychosocial care, research, and outcomes.⁹¹

Australia also has a national population-based cancer registry, and cancer is a notifiable disease in Australia so all cancers, except for basal and squamous cell carcinoma of the skin, have had to be registered in the Australian Cancer Database since 1 January 1982.⁹² The health system in Australia is jointly run by different levels of government – federal, state and territory, and local. Some states have individual cancer control plans,⁹³ and the first nationwide Australian Cancer Plan to develop the country's future approach to cancer care is in development. A public consultation on the draft closed in April 2023, and publication of the final plan is imminent.⁹⁴

Population-based cervical screening using hr-HPV testing and catch-up vaccination programmes: Portugal

Cervical cancer is a rare disease in Portugal. In 2020, 865 new cases and 379 deaths due to cervical cancer were recorded; the age-standardised incidence rate in the same year was estimated to 10.7 per 100,000 and the age-standardised death rate was 3.7 per 100,000 women.¹

Portugal is a very interesting example of a country that is doing well with respect to the WHO targets for cervical cancer elimination because it's not considered a rich country, says Rui Medeiros, Professor of Virology and Molecular Oncology, Head of Molecular Oncology and Viral Pathology GRP, IPO Porto Board Director of NRN-LPCC-Portuguese League Against Cancer President of ECL, Association of European Cancer Leagues, Co-Chair of the European Cancer Organisation's HPV Action Network. "We were rolling out HPV-vaccination before the WHO strategy. Our

national vaccination plan is considered one of the best in the world. Now we have vaccination coverage of over 90% and screening at over 70% in most regions."

The country has a strong history of supporting vaccination, having introduced vaccination against smallpox in the early 19th century and an organised national vaccination system in 1965. "Vaccination is not obligatory," Prof Medeiros adds, "but everyone believes it's necessary and natural to be vaccinated. We have low rates of [vaccination] hesitancy, and those lower rates are due to our culture of accepting public health strategies."

HPV-vaccination was introduced in the national vaccination programme for girls in 2008, and in October 2020, it was expanded to include boys aged 10 years.⁹⁵ By 2021, 96% of girls in the target age group had received at least one dose of HPV-vaccination.⁴⁴

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Cervical cancer screening has been offered opportunistically in Portugal since 1978 and started to become organised after 1990. The organised screening programme, which originally included cytology followed by reflex HPV testing, was progressively implemented in different regions of the country.¹⁰⁸ In 2017, the Portuguese Gynaecology Society changed their recommendations for cervical cancer screening in 25- to 60-year-olds to be performed using “hr-HPV testing”, followed by cytology in positive cases. However, the adoption of HPV DNA testing for cervical cancer screening has been slow.¹⁰⁹

“We have been arguing for 15 years that we should go on the molecular test and only use a Pap smear or biopsy afterwards to confirm the diagnosis,” says Prof Medeiros. “We reviewed what was best for our population, and the decision was that we should have a molecular test that could give us more epidemiological data to evaluate.” HPV DNA-based cervical cancer screening was first implemented in the north of the country where the health system

struggles to cope with the 150,000 [women] who are eligible for a Pap smear every year, he adds.

The geographic coverage has been expanding and in 2022, 342,223 women were invited for screening and 321,888 took part – a 32% rise over the number screened in 2021. However, at the population-level, this number represents only around 61% of eligible women. Typically, family doctors are responsible for inviting women for cervical cancer screening, but invitation rates are low suggesting that awareness needs to be raised among frontline physicians.¹¹⁰

The National Cancer Control plan of Portugal (2021-2030) confirms continued support for the national HPV-vaccination program and sets a goal of 95% population-level coverage by 2030 for cervical cancer screening. This is expected to be achieved by developing and disseminating guidelines for cervical cancer screening, standardising screening procedures, creating indicators for monitoring screening programs, and by assessing the satisfaction of users of the screening program. Improving access to radiotherapy to achieve at least 90% coverage among referred patients and ensuring high-quality therapy conforming to the criteria set by the International Atomic Energy Agency are other objectives of the plan.¹¹¹

Furthermore, after Portugal launched the national immunisation programme in October 2008 for girls aged 13 years,⁹⁵ it quickly ran a universal catch-up vaccination campaign from 2009 to 2011 for girls aged 17 years and older, who were born between 1992 and 1994. Girls aged 10-13 years were covered from 2014 to 2016, and since 2017 only girls aged 10-years were receiving the vaccination. Since 2020, the country has opted for gender-neutral vaccination programmes in which the HPV-vaccination is offered to all 10-year-old children regardless of sex.



Implementing a successful cervical cancer elimination strategy

Implementing a successful cervical cancer elimination strategy essentially involves at least two key pillars. “HPV-vaccination is the first pillar in the cervical cancer elimination strategy and the most effective tool for primary prevention of cervical cancer,” says Dr Nino Berdzuli, Director of the Division of Country Health Programmes, WHO Regional Office for Europe. “When we can prevent the cancer from happening, and have vaccination with an excellent safety and effectiveness profile that can prevent it, it’s unjust actually not to use this vaccination.”

The WHO European region comprises 53 Member States, of which 45 have introduced HPV-vaccination in routine schedules; the middle-income countries are lagging behind. Some countries have reached high HPV-vaccination coverage, moving steadily towards the 2030 target of 90%, but many face challenges with HPV-vaccination uptake or stalled progress. Globally, 126 countries have introduced HPV-vaccination, but 65 are yet to commit. “There is glaring inequity in terms of the access to and uptake of HPV-vaccination,” Dr Berdzuli explains. “This inequity exists between and within countries – within countries, disparities are prominent among vulnerable groups, such as with low socioeconomic refugees and migrants,” she adds.

The second pillar in elimination strategies is screening, and while most countries in Europe offer cervical cytology screening with an HPV test or Pap smear-based test, some countries in Eastern Europe still use an outdated tool from the Soviet era – Romanowsky-Giemsa staining.⁹⁶

“The WHO recommendation is that the HPV DNA test be the preferred method for cervical cancer screening because of its cost effectiveness and higher sensitivity, and also because it offers women the option of self-sampling – a convenience factor that we need to consider, particularly in terms of hard-to-reach women, [and] women who don’t feel comfortable enough or have the time for the various reasons to come to the health system. Despite this evidence for its use, HPV-based screening adoption has been limited outside of HICs” says Dr Berdzuli.

“Coverage also varies and the biggest problem many countries have in reaching the 70% cervical screening target is a lack of organised, well-functioning and quality assured screening programmes. A population-based cancer screening programme followed by adequate diagnosis and management of positive results [are] very important for effective cervical cancer control. If we only have opportunistic cancer screening, it’s going to be very hard to reach the elimination target.”

Across the European region, there is significant disparity in terms of cervical cancer outcomes, Dr Berdzuli says. While mortality rates have significantly decreased in Western Europe, they are three times higher, and rising, in Eastern and Central Europe, the Baltic states, and Central Asian countries.^{97,98} “The disparity is due to the capacity of the health system to be able to diagnose cervical cancer early, and then to treat it properly. The cancer may be diagnosed early, but if the health system does not encompass the full spectrum of cancer

care, the outcomes will not be the same. It's about offering high quality, comprehensive cancer care – surgery, chemotherapy, radiation therapy and palliative care – through a well-functioning cancer care pathway. Cancer is a complex disease and treating cancer requires a well-functioning and coordinated health system, as well as highly trained and qualified healthcare providers.”

While in many cases, coverage for vaccination, screening and treatment is higher in Europe, as compared to other countries, the barriers to uptake and the mechanisms for addressing them are generally the same. It is important to understand why there are gaps in vaccination and screening coverage by using behavioural and cultural research to understand why certain population groups are not coming forward and what drives a late diagnosis. This may be due to cultural factors or health literacy, misinformation and disinformation damaging trust in vaccination efforts, or lower confidence in healthcare institutions; it is therefore vital to tailor efforts to specifically target the various populations and sub-populations that experience these myriad reasons for neglecting screening and vaccination, explains Dr Berdzuli.

“Unless we understand the specifics of these populations, and find the reasons, the factors that contribute to these equity gaps, our policies and strategies for cervical cancer elimination

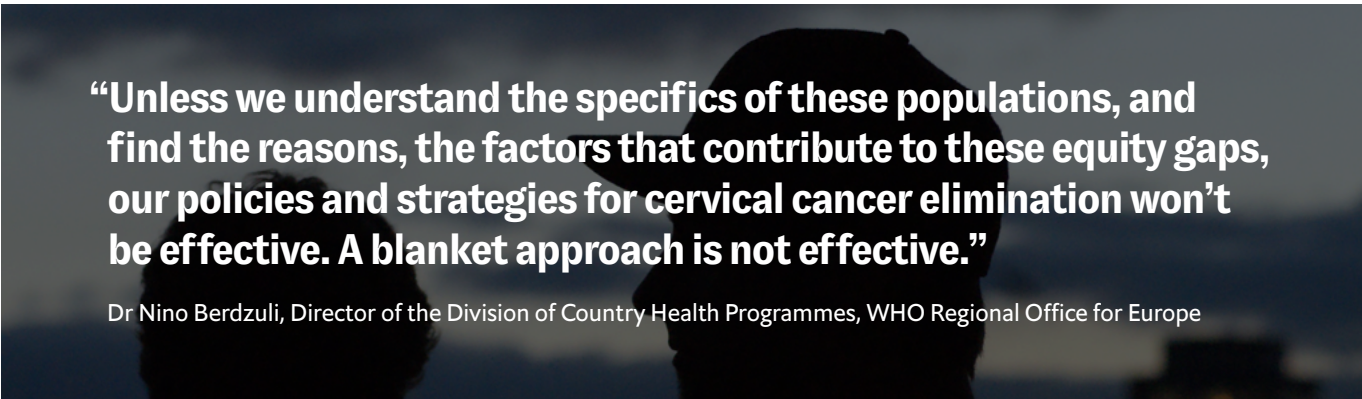
won't be effective. A blanket approach is not effective. It is very important for policymakers to listen to target groups, healthcare workers, parents, girls, and women, to gain insights. Challenges can be local and they require tailored solutions and intervention plans and this is a continuous process,” she adds.

Based on published evidence, insights from the experts interviewed, and lessons from countries leading the way towards cervical cancer elimination, Economist Impact recommends a 10-point baseline plan for policymakers across the world to consider when developing national strategies to eliminate cervical cancer.

1. Build political commitment and momentum

All the countries discussed in this paper, who are leading the way forward in the pursuit of cervical cancer elimination, have at least one thing in common: a high degree of political commitment.

Guidelines and policies from global and regional organisations, such as WHO, have helped focus global attention on cervical cancer, and have helped build political will to implement nation-level policies. Furthermore, political commitment to the elimination of cervical cancer has been fostered through strategies such as the EBCP, which goes a step farther than the WHO targets, by setting benchmarks for EU Member States to achieve by 2030 (as opposed to the end of the



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century). Benchmarks of the plan include a 90% vaccination rate among the target population of girls, while simultaneously supporting the increased vaccination of boys, as well as offering screening to 90% of the qualifying population by 2025, and widening access to effective treatment modalities across borders in the EU to reduce the persistent health inequities within and between countries.⁶ It also brings forward the goal of ensuring that cervical screening is offered to 90% of women eligible within EU Member States by 2025. The plan also supports these goals with funding to help EU Members establish the infrastructure and public health interventions necessary to achieve them.¹³ Setting global and regional benchmarks and targets can also build political accountability and ensure that implementation is followed through.

Advocating for stronger, long-term and sustained political commitment, and ensuring that policy guidance exists for cervical cancer, can greatly improve the rates of screening and treatment. Therefore, having a supportive policy environment is critical to the elimination of cervical cancer.

2. Ensure multi-stakeholder collaboration

Building collaboration between multiple stakeholders, including patients and patient organisations, researchers, healthcare professionals, and bio-pharmaceutical organisations, is one way to encourage political commitment, and has the added benefit of helping scale effective strategies for the management of the condition.

Having targets such as those described above help create a sense of accountability for all stakeholders who are invested in tackling cervical cancer. For instance, the European Cancer Organisation (ECO), established in 2019, set out to influence the EBCP so that every country would incorporate HPV prevention in their national cancer plan – not just for cervical cancer but also other HPV-preventable cancers, says Prof Kelly.

Additionally, healthcare professionals should be consulted in policies aimed at increasing HPV-vaccination and cervical screening coverage to generate awareness and to build trust among the public. Developing innovative collaborations and ensuring multi-stakeholder approaches could help scale and sustain cervical cancer elimination efforts globally.

3. Prioritise HPV within national cancer policies and vaccination schedules

Once political will has been established to eliminate cervical cancer, countries must formalise their commitment within a national cancer plan, if there is one, or establish another similar policy with goals, strategies and funding mechanisms. Including HPV-vaccination in the standard vaccination schedule is also important because it “normalises it” and builds trust in vaccination.

In some countries, the low uptake of HPV-vaccination may be due to it not being mandated by law, unlike other childhood vaccinations. This can create distrust due to contradictory messages from health professionals, governments, and the media, says Prof Medeiros. He adds, “I think it is key to implement HPV-vaccination as a normal vaccination as with the other childhood vaccinations.”

4. Generate data through the development of robust registries

Population-level disease registries provide an accurate picture of the size of the target population and the state of women’s vaccination and screening status to enable policymakers to monitor progress on HPV-vaccination, screening and treatment goals, while serving many other practical and research functions. Registries provide a mechanism for identifying and inviting girls and women for vaccination and screening and following up with them if they do not attend; they also ensure that women with abnormal screening results are followed up and monitored, while enabling researchers to analyse

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Ulrika Årehed Kågström, Secretary General, Cancerfonden (Swedish Cancer Society), Sweden

trends and outcomes and assess new diagnostics and interventions that could improve care for women now and in the future.

5. Include screening and vaccination under universal health coverage

Vaccination and screening programmes achieve higher coverage when they are free because payments exclude women from the lowest socioeconomic groups and deter women who would otherwise participate. “It’s really important that you don’t have to pay for it – you need to make it free, otherwise – you will widen inequity gaps,” cautions Ms Kågström.

6. Understand the target population and design the roll-out of organised and accessible programmes

The WHO’s primary objective is to eliminate cervical cancer as a public health problem globally, so the primary target population for HPV-vaccination is girls aged 9-14 years. The WHO European Roadmap for Cervical Cancer acknowledges the benefits of vaccinating boys, but cervical cancer, which comprises 84% of all HPV-related cancers, should remain the priority for a cervical cancer elimination roadmap. Gender-neutral vaccination should be implemented, where feasible, at the discretion of each member state. Though supporting gender equity and protection of girls and boys through herd immunity would have positive impacts, as Dr Berdzuli emphasises, “Gender-neutral vaccination should not direct resources from the primary targets of the elimination of cervical cancer.”

Once the target population has been identified, an organised programme needs to be developed that takes HPV-vaccination to them. A school-based programme is generally the preferred and most effective delivery mechanism for HPV-vaccination because it reaches all young children in attendance, and is convenient for families. For the healthcare service such vaccination programmes are straightforward, easy to organise and cost-effective. Other strategies may be required in countries where attendance of girls in the target age group is low.

“Sometimes it is said that it is a matter of money to achieve high attendance, but a number of countries that have very low-income levels have managed to achieve very high attendance rates by organising it well by community after community,” says Prof Dillner. “So I think that is an interesting message – that it’s not really about the money but about being well organised.”

7. Ensure equitable access to vaccinations and screening for the entire population

Eliminating cervical cancer means that the entire population must be vaccinated, and this includes marginalised women who often have great barriers to accessing healthcare services. These include women who are caregivers, live in rural areas, come from ethnic minorities, or victims of domestic abuse. Therefore, innovative methods such as self-sampling screening kits could be used as an alternative approach to increasing coverage.

Cervical cancer elimination can be accelerated by widening population coverage through catch-up campaigns. These campaigns can take vaccinations to the girls and young women who were too old to receive when it was introduced, as well as to those who did not receive vaccination at school because they were absent, their parents would not consent or schools were closed due to the Covid-19 pandemic. Additionally, schools should proactively follow up with children who miss out on vaccination because of hesitant

parents, and such parental concerns should be discussed and addressed with the appropriate resources to increase awareness.

Linking delivery of HPV-vaccination to other health interventions such as another vaccination or screening can provide additional opportunities for reaching unvaccinated populations who do not come forward when invited for HPV-vaccination alone. Health services/health professionals should follow up with women who miss out on cervical screening to ensure that they are fully aware of the benefits of vaccination. Any concerns women may have about the procedure can then be addressed.

8. Address the barriers of vaccination hesitancy and misinformation

Attitudes, culture, beliefs and behaviour vary both between and within countries and it is important to really understand a specific population in order to design effective strategies to boost uptake of vaccination and screening.

Research on the drivers of vaccination inequity in Europe highlight poor access and low trust, particularly among those with low socioeconomic states, as key problem areas, and there are many case studies of interventions that have been successful in boosting coverage in some countries which could be implemented and/or adapted to have successful results elsewhere.⁹⁹ Resources have also been developed to help the public tackle myths and misinformation.^{100,101} In 2022, many social media platforms also signed up to a strengthened Code of Practice on Disinformation.¹⁰²

It is important to tackle misinformation and disinformation to prevent “mushrooming”, says Dr Berdzuli. “The only way we can counter this is to increase the trust in the healthcare system and have confident healthcare professionals. This can be achieved by equipping healthcare providers with evidence and facts and by improving their confidence in HPV-vaccination’ effectiveness and safety, and importantly by boosting the capacity

of health authorities to prevent or manage any potential confidence crisis; we work with countries to build these capacities.”

9. Ensure equitable access to high quality treatment and an optimal care pathway

To help provide equitable treatment for women diagnosed with cervical cancer, it is important that the care pathway is standardised throughout the patient journey, from diagnosis to referral to treatment. Health systems should have adequate infrastructure and healthcare staff to reduce waiting times, as well as efficient navigation procedures to expedite the treatment of cancer.

10. Learn lessons from the Covid-19 pandemic to build system resilience and scale screening and vaccination coverage

The Covid-19 pandemic demonstrated that the world is able to design a vaccination and deliver it to populations quickly and at scale. There is much that can be learned from this experience in terms of strengthening supply chains and systems capacity for both vaccination and screening. The pandemic provided opportunities for more efficient, and less wasteful, prevention efforts, such as prioritising women by risk, extended HPV testing using self-collected samples, and by discouraging inefficient policies, such as screening with two tests.¹⁰³

Innovative Covid-19 vaccination delivery methods such as the “vaccine bus” and “drive-through clinics” could increase coverage, and are reportedly favourable amongst young people. A survey of 1,200 young people, between the ages of 16 and 35, in three European countries, France, Germany, and Italy, found that 75.5% of respondents wanted to see the continuation of vaccine buses and drive-through clinics for other vaccinations in the future.¹⁰⁴ Additionally, 55% of respondents were in favour of e-vaccination cards for vaccinations beyond Covid-19 (including HPV) to help keep their health records up to date.

Conclusion



Cervical cancer is a growing public health concern, which threatens the lives of women, their families and societies. The cost of cervical cancer threatens the global economy because early morbidity means that diagnosed women are unable to participate fully at work and early mortality means that they are missing entirely from the labour force. While the political commitment to eliminating cervical cancer within the century has been harboured at the global level through policy reforms such as the WHO's 90-70-90 elimination strategy, the alignment of multi-stakeholder collaboration, including patient advocates, healthcare professionals, researchers, to name a few, has increased political momentum towards the development of regional and national plans. Increased HPV-vaccination and screening coverage are the foundational pillars for eliminating cervical cancer, but these efforts require a sense of organisation to ensure that coverage is truly "universal". Therefore, an increase in funding – while welcome – is not the only solution to eliminating cervical cancer; instead, a step-wise approach is required on multiple fronts to ensure accountability and the effective implementation of measures.

Positively, many countries have made significant gains in their efforts to eliminate cervical cancer, with Sweden set to be the first country to achieve this before 2030, followed by Australia by 2035. But all countries studied in this report have demonstrated that political commitment is the essential foundation for achieving this ambitious goal. This political commitment is often built on evidence-based decision making, which requires actors from the health and science community to take accountability for the generation of data to understand and communicate the true needs of their unique populations. The 10-point plan forms the baseline of actions each country should consider when developing national strategies and implementing measures aimed at the elimination of cervical cancer. The recommendations in this baseline plan will not only alleviate fiscal pressures, but also ensure that women are protected from this highly preventable cancer.

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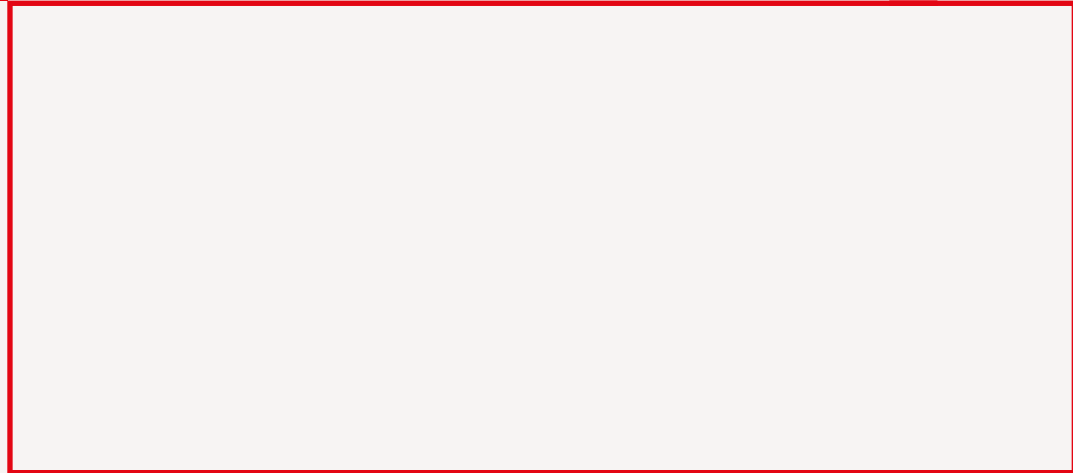
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