Mortality impact of achieving WHO cervical cancer elimination targets: a comparative modelling analysis in 78 low-income and lower-middle-income countries

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Summary

Background WHO is developing a global strategy towards eliminating cervical cancer as a public health problem, which proposes an elimination threshold of four cases per 100 000 women and includes 2030 triple-intervention coverage targets for scale-up of human papillomavirus (HPV) vaccination to 90%, twice-lifetime cervical screening to 70%, and treatment of pre-invasive lesions and invasive cancer to 90%. We assessed the impact of achieving the 90–70–90 triple-intervention targets on cervical cancer mortality and deaths averted over the next century. We also assessed the potential for the elimination initiative to support target 3.4 of the UN Sustainable Development Goals (SDGs)—a one-third reduction in premature mortality from non-communicable diseases by 2030.

Methods The WHO Cervical Cancer Elimination Modelling Consortium (CCEMC) involves three independent, dynamic models of HPV infection, cervical carcinogenesis, screening, and precancer and invasive cancer treatment. Reductions in age-standardised rates of cervical cancer mortality in 78 low-income and lower-middle-income countries (LMICs) were estimated for three core scenarios: girls-only vaccination at age 9 years with catch-up for girls aged 10–14 years; girls-only vaccination plus once-lifetime screening and cancer treatment scale-up; and girls-only vaccination plus twice-lifetime screening and cancer treatment scale-up. Vaccination was assumed to provide 100% lifetime protection against infections with HPV types 16, 18, 31, 33, 45, 52, and 58, and to scale up to 90% coverage in 2020. Cervical screening involved HPV testing at age 35 years, or at ages 35 years and 45 years, with scale-up to 45% coverage by 2023, 70% by 2030, and 90% by 2045, and we assumed that 50% of women with invasive cervical cancer would receive appropriate surgery, radiotherapy, and chemotherapy by 2023, which would increase to 90% by 2030. We summarised results using the median (range) of model predictions.

Findings In 2020, the estimated cervical cancer mortality rate across all 78 LMICs was 13·2 (range 12·9–14·1) per 100 000 women. Compared to the status quo, by 2030, vaccination alone would have minimal impact on cervical cancer mortality, leading to a 0·1% (0·1–0·5) reduction, but additionally scaling up twice-lifetime screening and cancer treatment would reduce mortality by 34·2% (23·3–37·8), averting 300 000 (300 000–400 000) deaths by 2030 (with similar results for once-lifetime screening). By 2070, scaling up vaccination alone would reduce mortality by 61·7% (61·4–66·1), averting 4·8 million (4·1–4·8) deaths. By 2070, additionally scaling up screening and cancer treatment would reduce mortality by 88·9% (84·0–89·3), averting 13·3 million (13·1–13·6) deaths (with once-lifetime screening), or by 92·3% (88·4–93·0), averting 14·6 million (14·1–14·6) deaths (with twice-lifetime screening). By 2120, vaccination alone would reduce mortality by 89·5% (86·6–89·9), averting 45·8 million (44·7–46·4) deaths. By 2120, additionally scaling up screening and cancer treatment would reduce mortality by 97·9% (95·0–98·0), averting 60·8 million (60·2–61·2) deaths (with once-lifetime screening), or by 98·6% (96·5–98·6), averting 62·6 million (62·1–62·8) deaths (with twice-lifetime screening). With the WHO triple-intervention strategy, over the next 10 years, about half (48% [45–55]) of deaths averted would be in sub-Saharan Africa and almost a third (32% [29–34]) would be in South Asia; over the next 100 years, almost 90% of deaths averted would be in these regions. For premature deaths (age 30–69 years), the WHO triple-intervention strategy would result in rate reductions of 33·9% (24·4–37·9) by 2030, 96·2% (94·3–96·8) by 2070, and 98·6% (96·9–98·8) by 2120.

Interpretation These findings emphasise the importance of acting immediately on three fronts to scale up vaccination, screening, and treatment for pre-invasive and invasive cervical cancer. In the next 10 years, a one-third reduction in the rate of premature mortality from cervical cancer in LMICs is possible, contributing to the realisation of the 2030 UN SDGs. Over the next century, successful implementation of the WHO elimination strategy would reduce cervical cancer mortality by almost 99% and save more than 62 million women's lives.

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See Comment page 539

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Introduction

In 2018, an estimated 570 000 cases of cervical cancer were diagnosed, and 311 000 women died from the disease.[1] Although cervical cancer has been relatively well controlled for several decades in many high-income countries, mainly because of cervical screening initiatives and effective cancer treatment services, it remains the most common cause of cancer-related death among women in 42 countries, most of which are low-income and lower-middle-income countries (LMICs).[2]

Prophylactic vaccines against oncogenic human papillomavirus (HPV) have been available in most high-income countries from 2006 onwards. First-generation vaccines directly protect against oncogenic HPV types 16 and 18 in individuals naive for those types, and these HPV types are responsible for approximately 70% of invasive cervical cancers.[3,4] More recently, broader-spectrum protection against the types responsible for up to 90% of cervical cancers has been shown either via direct protection against a larger proportion of types (second-generation 9-valent vaccine) or via cross-protection against non-vaccine included types (bivalent vaccine).[5,6] However, because vaccines are primarily targeted at pre-adolescents or young adolescents, it is expected to take several decades after deployment in a population before their full benefits in terms of cancer prevention are realised, and a substantial impact of vaccines on cervical cancer incidence or mortality outcomes is yet to be observed. To date, vaccine coverage in LMICs has been low overall, with an estimated 3% of the primary targeted population of young girls in less developed regions vaccinated by 2014.[7] By 2016, only 14% of LMICs had established vaccination programmes.[8]

Many high-income countries are transitioning, or considering transitioning, from cervical cytology to primary HPV testing for cervical screening, which is generally a

Research in context

Evidence before this study

Most low-income and lower-middle-income countries (LMICs) do not have access to human papillomavirus (HPV) vaccination, cervical screening programmes are unavailable or poorly implemented, and population-level access to cancer treatment services is variable. WHO, with its partners, is developing a global strategy towards the elimination of cervical cancer as a public health problem. The draft strategy involves triple-intervention targets for scale-up of vaccination, screening, and precancer treatment and invasive cancer treatment and palliative care in all countries; these targets, known as the 90–70–90 WHO triple-intervention strategy, specify 90% coverage of HPV vaccination, 70% coverage of twice-lifetime screening with HPV testing (or a similarly high sensitivity test), and 90% of women having access to cervical precancer and cancer treatment and palliative care services, by 2030. In the accompanying Article published in *The Lancet*, the WHO Cervical Cancer Elimination Modelling Consortium (CCEMC) predicted the impact of various HPV vaccination and screening and precancer treatment strategies on cervical cancer incidence in 78 LMICs. The analysis found that cervical cancer elimination by 2120 at a threshold of four cases per 100 000 women-years was possible in all 78 LMICs if girls-only vaccination was combined with twice-lifetime screening. The results suggested that elimination was consistently achievable, and the number of cervical cancer cases averted maximised, only if vaccination was combined with twice-lifetime cervical screening and with appropriate treatment for women found to have cervical precancer. The CCEMC harnesses three independent, extensively peer-reviewed models: Policy1-Cervix (Cancer Council NSW, Sydney, NSW Australia), Harvard (Harvard University, Boston, MA, USA), and HPV-ADVISE (Laval University, Quebec, QC, Canada). In this analysis, the models projected the reductions in cervical cancer mortality over time by use of standardised scenarios determined via consultations at various WHO technical expert, advisory group, and global stakeholder meetings.

Added value of this study

This analysis of the impact of the WHO triple-intervention cervical cancer elimination strategy on mortality outcomes shows that, in the next 10 years, achieving substantial reductions in mortality will require successful scale-up of cancer diagnostic and treatment services in LMICs, including pathology, surgery, radiotherapy, and chemotherapy; supportive and palliative care services will also need to be scaled up. If this is done, the 2030 UN Sustainable Development Goal of achieving a greater than one-third reduction in premature mortality from non-communicable diseases could be realised for cervical cancer. In the next 50 years, cervical screening and vaccination will both have an important role. The triple-intervention strategy would result in mortality rate reductions of 92% by 2070, increasing to almost 99% over the course of the next century as the full benefits of vaccination of young cohorts are realised over time.

Implications of all the available evidence

Implementing the 90–70–90 WHO triple-intervention strategy to achieve cervical cancer elimination will result in more than 74 million cervical cancer cases averted and more than 62 million women's lives saved over the course of the next century. These findings have informed the draft WHO global strategy for cervical cancer elimination, which will be presented to the WHO Executive Board in February, 2020, and thereafter considered at the World Health Assembly in May, 2020.

more effective and cost-effective approach to screening.[9–11] Initiatives for both HPV vaccination and screening have been introduced in the context of broad access to diagnostic, precancer treatment, cancer treatment, and supportive and palliative care services in high-income countries, and the combination of early detection via screening and effective treatment with surgery, chemotherapy, and radiotherapy has meant that net 5-year survival for cervical cancer is around 60–70% or greater in several high-income countries.[12] However, in LMICs, uptake of cervical screening has been low and inconsistent, and population-level access to cancer care is generally poor. As a consequence of these differentials in access to cervical screening and treatment, the majority of deaths (91%) from cervical cancer currently occur in LMICs and upper-middle-income countries, and 60% of deaths are in LMICs.[1] Access to supportive and palliative care services for people in LMICs is poor,[13] and thus the majority of women dying from cervical cancer do so with little or no supportive care or pain relief.

In May, 2018, the Director-General of WHO announced a call to action to eliminate cervical cancer as a public health problem, and in January, 2019, the WHO Executive Board requested that a draft global strategy to achieve elimination be developed. The draft global strategy being developed by WHO, with its partners, includes triple-intervention targets for scale-up of vaccination, screening, precancer treatment, and invasive cancer treatment in all countries; these targets specify 90% coverage of HPV vaccination, 70% coverage of twice-lifetime screening, and 90% access to cervical precancer and cancer treatment services and palliative care, by 2030.[14] To inform the strategic planning process, the WHO Cervical Cancer Elimination Modelling Consortium (CCEMC) was formed and has done comparative modelling of potential intervention scenarios in all 78 LMICs. In the accompanying Article published in *The Lancet*,[15] CCEMC predictions of the impact of HPV vaccination, screening, and precancer treatment strategies on cervical cancer incidence and cases averted are presented; the analysis found that elimination by 2120 at a threshold of four cases per 100 000 women was possible in all 78 LMICs if girls-only vaccination was combined with twice-lifetime screening. This strategy was predicted to reduce age-standardised incidence across 78 LMICs by 97% and to avert more than 74 million cervical cancer cases over the next century.[15] The analysis concluded that adding screening with high uptake to vaccination will expedite reductions in cervical cancer incidence and the number of cases averted, and will be necessary to eliminate cervical cancer in countries with the highest burden.

The aims of the current analysis were to model cancer treatment scale-up in addition to HPV vaccination and cervical screening and to assess the impact of achieving the 90–70–90 triple-intervention targets on cervical cancer mortality and deaths averted over the next century on the path to elimination. The cervical cancer elimination initiative has been framed within the context of the UN Sustainable Development Goals (SDGs) to support the realisation of SDG target 3.4—a one-third reduction in premature mortality from non-communicable diseases by 2030.[16] Therefore, we also assessed the potential for the cervical cancer elimination strategy to deliver a one-third reduction in premature mortality from cervical cancer by 2030.

For more on the **UN Sustainable Development Goals** see https://sustainabledevelopment.un.org/?menu=1300

Methods

Countries included in the analysis

The 78 LMICs considered were located in six regions according to World Bank definitions: east Asia and Pacific, Europe and central Asia, Latin America and Caribbean, north Africa and the Middle East, South Asia, and sub-Saharan Africa (see the appendix pp 44–45 for the full list of countries within each region and the grouping of countries by income level).

See **Online** for appendix

Description of the WHO CCEMC models

The WHO CCEMC comprised three modelling groups collaborating with WHO and the International Agency for Research on Cancer (IARC). The platforms were independent dynamic models, identified by WHO by use of predefined criteria. The modelling methods have been previously described.[15] In brief, the selected models for the analysis explicitly considered the dynamic transmission of HPV infection (and could thus capture the effects of herd immunity); were capable of projecting the impact of HPV vaccination, cervical screening, and precancer treatment and clinical and screen-detected cancer treatment scale-up at a country level for all 78 LMICs considered; and were independently developed and have been extensively validated and peer reviewed. Three models were selected: Policy1-Cervix (Cancer Council NSW, Sydney, NSW, Australia), Harvard (Harvard University, Boston, MA, USA), and HPV-ADVISE (Laval University, Quebec, QC, Canada). The individual CCEMC models have been previously used to inform national policy on cervical screening and HPV vaccination in Australia, Canada, the UK, and the USA, and at the global level.[10,17–22] The structure of the CCEMC models and the comparative modelling approach were endorsed by the WHO Advisory Committee on Immunization and Vaccines related Implementation Research (IVIR-AC).[23]

HPV transmission and cervical carcinogenesis are modelled for the oncogenic HPV types included in second-generation vaccines (HPV types 16, 18, 31, 33, 45, 52, and 58) and other oncogenic types, and each model simulates the type-specific natural history of cervical cancer from persistent HPV infection to cervical cancer via high-grade precancerous cervical lesions (cervical intraepithelial neoplasia grades 2 [CIN2] and 3 [CIN3]). All models can simulate complex cervical screening and treatment algorithms, and for the current analysis these models were adapted to incorporate country-level assumptions

about the proportion of women receiving cervical cancer treatment and the consequent survival outcomes. Reporting was done according to a consensus-based framework for modelled evaluations of HPV prevention and cervical cancer control: HPV-FRAME.[24] See the appendix (pp 50–56, 74–76) for a detailed description of the model platforms and HPV-FRAME reporting.

Status quo assumptions

The comparator (status quo) S0 scenario assumed no scale-up of vaccination, cervical screening, or cancer treatment. Under the status quo, it was assumed that none of the 78 LMICs had achieved substantial vaccination coverage by 2020, although in practice a few countries, such as Rwanda, have initiated high-coverage vaccination initiatives within the past few years. Thus, our analysis only captures the effect of scaled-up vaccination from 2020 onwards. For cervical screening, modelling groups made different assumptions about whether the impact of limited existing screening coverage was considered in the status quo (see the appendix pp 50–56 for further details).

Treatment for cervical cancer involves stage-appropriate multimodality therapies with radiotherapy and chemotherapy, with surgery (partial or total hysterectomy) being an important option for early-stage disease. Cervical cancer clinical staging was based on the International Federation of Gynaecology and Obstetrics (FIGO) system. Institute for Health Metrics and Evaluation (IHME) sub-regional-level estimates for the stage distribution of invasive cervical cancer at diagnosis, and data on 5-year and 10-year survival rates were derived from systematic reviews done by WHO based on peer-reviewed publications and national reports including cancer control plans, cross-referenced to data from IARC cancer registries. Radiotherapy access, estimated as machine density per 1000 patients with cancer, was used as a surrogate for multimodal treatment delivery. We used 2018 data for radiotherapy access and availability of external beam radiation therapy and personnel (radiation oncologists, medical physicists, and radiation therapy technologists) provided by the International Atomic Energy Agency's Directory of Radiotherapy Centres (DIRAC). Ranges of treatment access rates in each World Bank region encompassed the lowest and the highest treatment access rates of the countries in each region and represented the percentage of the population that could potentially be served with the equipment and workforce available (table 1). These data were then used to derive initial estimates of country-level current status quo stage distributions, treatment access rates, and survival rates (appendix pp 63–70). We used these data as an initial (pre-calibration) input to the models.

Calibration to GLOBOCAN 2018

Global Cancer Observatory (GLOBOCAN) 2018 estimates are based on IARC-certified cancer registry information where available in a country, or on a series of estimation methods if verified registry data are not available.[1,2] Each group incorporated initial country-level stage-specific 5-year and 10-year survival rates, and models were then calibrated to country-specific and age-specific mortality rates from GLOBOCAN 2018 by incorporating a quality factor into the final estimated country-specific and stage-specific survival assumptions. This approach encompasses limitations in the available data on staging, treatment access, uncertainties in actual delivery of treatment, variations in treatment delivery from established protocols and recommendations, equipment and infrastructure maintenance and logistics, and treatment abandonment. The calibrated results for incidence and

	Stage distribution at diagnosis				Overall 5-year (and 10-year) survival rates				Treatment access rate (range)*
	Stage 1	Stage 2	Stage 3–4A	Stage 4B	Stage 1	Stage 2	Stage 3–4A	Stage 4B	
East Asia and Pacific	23%	39%	27%	11%	65% (15%)	51% (13%)	15% (10%)	2% (2%)	17% (0–37)
Europe and central Asia	34%	19%	28%	19%	74% (42%)	62% (37%)	34% (28%)	6% (4%)	48% (18–100)
Latin America and Caribbean	23%	26%	46%	5%	73% (39%)	61% (34%)	32% (26%)	6% (4%)	44% (0–77)
North Africa and Middle East	13%	43%	31%	13%	80% (59%)	69% (52%)	46% (39%)	9% (6%)	67% (0–100)
South Asia	13%	36%	40%	11%	74% (42%)	62% (37%)	34% (28%)	6% (4%)	48% (0–55)
Sub-Saharan Africa	8%	36%	48%	8%	62% (6%)	47% (5%)	9% (4%)	1% (1%)	7% (0–37)

This table provides a regional summary of the data used as an initial (pre-calibration) input to the models; however, each modelling group also applied a quality factor to further adjust survival in the status quo to fit to Global Cancer Observatory (GLOBOCAN) 2018 estimates for cervical cancer mortality by 5-year age group (appendix pp 3–7, 63–70). Detailed country-specific estimates for status quo treatment access rates are provided in the appendix (pp 63–70). Staging is according to International Federation of Gynaecology and Obstetrics (FIGO) staging for carcinoma of cervix (2009 version) and TNM, 7th edition. Data based on a systematic review done by WHO, which obtained information from 43 countries, prioritising countries with population-based cancer registries. Results were derived by the Institute for Health Metrics and Evaluation (IHME) subregions. Regional results shown are weighted on the basis of each country's cancer case burden. *Treatment access rates were estimated on the basis of radiotherapy access and on the most recent availability of external beam radiation therapy and personnel (radiation oncologists, medical physicists, and radiation therapy technologists), which were provided by the Directory of Radiotherapy Centres (DIRAC). Ranges of treatment access rates in each region encompass the lowest and the highest treatment access rates of the countries in each region and represent the percentage of the population that could potentially be serviced on the basis of the equipment and workforce available.

Table 1: **Summary of treatment assumptions by region for status quo scenario: FIGO stage distributions, stage-specific survival rates, and treatment access rates**

mortality are shown for each model in the appendix (pp 3–7), summarised as the results across all 78 LMICs and at the regional level. Calibration results were comparable for all three models and generally demonstrated good fit with GLOBOCAN 2018.

Modelled scenarios

Models projected age-standardised cervical cancer mortality and deaths over time in 78 LMICs for standardised scenarios. The selection of core scenarios was determined after consultation at several WHO technical expert, advisory group, and global stakeholder meetings in 2018 and was based on a multi-step process, as previously described.[15,23] The scenarios were aligned with the scale-up targets articulated in the WHO draft global strategy for elimination.[14] The final fully articulated core scenarios for the mortality impact analysis were ongoing girls-only vaccination at age 9 years with multi-age cohort catch-up in the first year for ages 10–14 years (S1); girls-only vaccination, once-lifetime screening at around age 35 years with precancer treatment, and invasive cancer treatment scale-up (S2); and girls-only vaccination, twice-lifetime screening at around ages 35 years and 45 years with precancer treatment, and invasive cancer treatment scale-up (S3; the WHO triple-intervention strategy). We also considered two supplementary vaccination scenarios: girls-only vaccination with initial extended multi-age cohort catch-up to age 25 years (S4), and vaccination of girls and boys at age 9 years with multi-age cohort catch-up at ages 10–14 years (S5; appendix 57–59).

Vaccination was assumed to scale up to 90% coverage from 2020 with 100% lifetime broad spectrum protection against HPV oncogenic types 16, 18, 31, 33, 45, 52, and 58 in individuals susceptible to the relevant type; the analysis thus applies to a broad-spectrum vaccine that protects against these types either by direct protection (as per a second-generation 9-valent vaccine) or via cross-protection for non-vaccine-included types. We assumed that full efficacy against vaccine types was achieved with two doses for vaccine recipients aged younger than 15 years, and with three doses for older vaccine recipients (although dose delivery was not explicitly modelled). Cervical screening was assumed to involve HPV testing once or twice per lifetime at age 35 years, or at ages 35 years and 45 years, with increasing uptake from 45% in 2023, 70% in 2030, to 90% in 2045 onwards. Sensitivity of HPV testing was assumed to be 90% for CIN2 and 94% for CIN3 or worse, independent of age. We assumed that 90% of HPV screen-positive women received visual assessment and appropriate treatment as required for precancer or cancer (triaging was not explicitly modelled). For successfully delivered precancer treatment, treatment success was assumed to be 100%; CCEMC groups differed in their modelling of post-treatment natural history for whether an elevated risk of recurrence was simulated (appendix pp 50–56). We assumed that 50% of women with invasive cervical cancers would have access to high quality surgery, radiotherapy, and chemotherapy by 2023, and this would increase to 90% by 2030. Once treatment access was scaled up to 90% in 2030, 10-year survival was assumed to increase to 78% for women diagnosed at FIGO Stage 1, 69% at FIGO Stage 2, 52% at FIGO Stages 3–4A, and 8% at FIGO Stage 4B (appendix p 71).

For this analysis we considered two types of intervention packages—vaccination alone or vaccination combined with cervical screening and treatment for precancer and screen-detected cancer, delivered in conjunction with scaled-up treatment services for clinically detected cancer. This approach took into account the feasibility and acceptability of whether interventions could be considered in isolation from each other. Although vaccination can be considered in isolation since it is prophylactic, population-wide implementation of cervical screening leads to screening-related detection of precancer and invasive cervical cancer (with favourable effects on stage-shifting). Referral pathways should be organised so that women with screen-detected invasive cancer are offered prompt and effective treatment (with treatment capacity scaling up as screening expands), since this approach then leads to improved survival outcomes.

Comparative modelling approach and outcomes

Each single-model analysis was done independently at a country level. The coordinating centre for the analysis (Cancer Council NSW, Australia) aggregated all results,

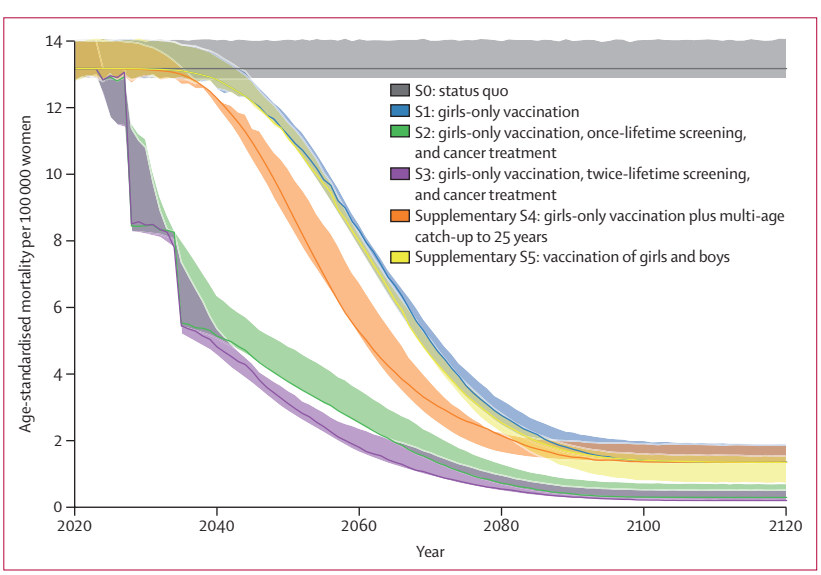

Figure 1: **Age-standardised cervical cancer mortality over time for all 78 LMICs**
The solid lines represent the median outcome of the three models; the shading represents the range of model outputs. HPV=human papillomavirus. LMICs=low-income and lower-middle-income countries. S0=status quo (no scale-up of vaccination, screening or treatment). S1=female-only vaccination at 9 years with multi-age cohort catch-up to age 14 years in 2020. S2=female-only vaccination and once-lifetime HPV testing at age 35 years with cancer treatment scale-up. S3=female-only vaccination and twice-lifetime HPV testing at age 35 years and 45 years with cancer treatment scale-up. Supplementary S4=female-only vaccination at 9 years with extended multi-age cohort catch-up to age 25 years in 2020. Supplementary S5=female and male vaccination at age 9 years with multi-age cohort catch-up to age 14 years in 2020. All scenarios assume the use of a broad-spectrum HPV vaccine with protection against seven oncogenic types.

	S1: girls-only vaccination		S2: girls-only vaccination, once-lifetime screening, and cancer treatment scale-up		S3: girls-only vaccination, twice-lifetime screening, and cancer treatment scale-up		Supplementary S4: girls-only vaccination plus multi-age catch-up to age 25 years		Supplementary S5: vaccination of girls and boys	
	Age-standardised rate	Reduction vs S0 (%)	Age-standardised rate	Reduction vs S0 (%)	Age-standardised rate	Reduction vs S0 (%)	Age-standardised rate	Reduction vs S0 (%)	Age-standardised rate	Reduction vs S0 (%)
Women aged 0–99 years										
2030	13·2 (12·9 to 14·0)	0·1% (0·1 to 0·5)	8·5 (8·2 to 11·1)	34·3% (21·4 to 37·4)	8·5 (8·2 to 10·8)	34·2% (23·3 to 37·8)	13·1 (12·9 to 13·9)	0·2% (–0·3 to 1·5)	13·2 (13·0 to 14·1)	0·1% (–0·7 to 0·2)
2070	5·0 (4·5 to 5·4)	61·7% (61·4 to 66·1)	1·4 (1·4 to 2·2)	88·9% (84·0 to 89·3)	1·0 (0·9 to 1·6)	92·3% (88·4 to 93·0)	3·2 (2·7 to 3·8)	77·5% (70·8 to 79·7)	4·5 (4·5 to 5·0)	65·3% (64·3 to 65·6)
2120	1·3 (1·3 to 1·9)	89·5% (86·6 to 89·9)	0·3 (0·3 to 0·7)	97·9% (95·0 to 98·0)	0·2 (0·2 to 0·5)	98·6% (96·5 to 98·6)	1·3 (1·3 to 1·8)	89·7% (86·9 to 89·9)	1·3 (0·7 to 1·5)	89·9% (89·2 to 94·6)
Women aged 30–69 years* (premature mortality)										
2030	23·7 (23·0 to 25·5)	0·2% (0·0 to 0·5)	15·2 (14·8 to 20·0)	34·2% (22·1 to 37·4)	15·2 (14·7 to 19·4)	33·9% (24·4 to 37·9)	23·6 (23·1 to 25·3)	0·1% (–0·2 to 1·4)	23·7 (23·3 to 25·6)	0·0% (–0·8 to 0·1)
2070	5·5 (5·1 to 6·2)	76·1% (75·7 to 78·5)	1·3 (1·2 to 2·3)	94·4% (91·1 to 94·6)	0·9 (0·8 to 1·4)	96·2% (94·3 to 96·8)	3·3 (3·1 to 3·9)	85·9% (84·9 to 86·8)	5·2 (4·4 to 5·4)	78·9% (77·9 to 81·0)
2120	2·4 (2·1 to 3·4)	89·9% (86·6 to 91·1)	0·5 (0·4 to 1·2)	98·0% (95·5 to 98·3)	0·3 (0·3 to 0·8)	98·6% (96·9 to 98·8)	2·4 (2·0 to 3·4)	89·9% (86·8 to 91·2)	2·4 (0·9 to 2·8)	89·9% (89·2 to 96·2)

Results shown represent age-standardised rates per 100 000 women for a given year, and relative reductions are compared to the status quo (S0) in that year. Results represent the median (range) of estimates across all three models. Detailed results for each decade are provided in the appendix (pp 8–10). S0=status quo (no scale-up of vaccination, screening, or treatment). S1=female-only vaccination and once-lifetime HPV testing at age 35 years and treatment scale-up. S2=female-only vaccination and twice-lifetime HPV testing at age 35 years and 45 years and treatment scale-up. Supplementary S4=female-only vaccination with multi-age cohort catch-up to 25 years in 2020. Supplementary S5=vaccination of girls and boys at age 9 years. All vaccination strategies assume the use of a broad-spectrum HPV vaccine with protection against the seven oncogenic types: 16, 18, 31, 33, 45, 52, and 58. Population projections were obtained from the UN and further projected out to 2120 (appendix pp 46–49). Model methods incorporate randomness and heterogeneity in estimates, which can occasionally, over shorter term timeframes, lead to relative increases rather than decreases in rates compared to the status quo, shown here as negative values. Randomness and heterogeneity can also lead to slight decreases in the percentage reduction in predicted rates even in the first year modelled (2020) and small differences from the expected relative ordering of the impact of different scenarios or the expected relative reductions over time. Caution should be applied in interpreting comparative differences between the values in this table, which represent the median and range across models; any individual median result could represent the findings of any one of the WHO Cervical Cancer Elimination Modelling Consortium (CCEMC) models. *Note that relative reductions in premature mortality are very similar if using the probability of dying between the ages of 30 and 70 years as a measure (appendix pp 8–10).

Table 2: **Projected cervical cancer mortality rates over time, across all 78 low-income and lower-middle-income countries**

applied standard populations and population projections, and estimated the median and range of results. Results are presented across all 78 LMICs, regionally, and by country. Rates were age-standardised by applying the age structure of the 2015 World Female Population aged 0–99 years. Premature mortality from cervical cancer was estimated by applying the 2015 World Female Population for ages 30–69 years, and in sensitivity analysis it was based on the probability of death from cervical cancer from age 30 years to 70 years.[16] For calculation of deaths averted, country-specific and age-specific population projections were based on the UN World Population Prospects: 2017 Revision.[25] Relative reductions over time were compared to the status quo. We summarised results for mortality reductions, and deaths averted were calculated from the beginning of 2020 to the end of 2030, 2070, and 2120, with the median (range) of model predictions for each result. See the appendix (pp 46–49) for more details.

Sensitivity analysis

The analysis was a comparative exercise based on three models with different structural and parameterisation assumptions and a form of sensitivity analysis is built into the reported ranges of results. We reported on key model-specific findings for calibration outcomes and for age-specific mortality rates (appendix pp 3–7, 11–25). We also ran explanatory (but counterfactual) scenarios to understand the sensitivity of the model results to underlying aspects of the impact modelling, including an extreme sensitivity analysis on the impact of cancer treatment scale-up. We also assessed the impact of using alternative population structures for age standardisation on the predicted age-standardised rate and the impact of different underlying fertility assumptions for population projections on the cumulative number of cervical cancer deaths averted.

Role of the funding source

This research was partly funded by WHO, which contributed to study design, data analysis, data interpretation, and writing of the report. Other funders had no role in the design of this analysis or the decision to submit for publication. KC, JJK, and MB had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Predictions from the three models were broadly consistent for all scenarios. Figure 1 shows the summary results across the models for the reduction in age-standardised mortality from 2020 to 2120, table 2 depicts these findings as numerical snapshots of the rates and relative reductions compared to the status quo scenario over time, and the reductions in premature mortality in women aged 30–69 years. Snapshots of the age-specific findings in 2020, 2070, and 2120 for each of the three CCEMC models are shown in the appendix (pp 11–25).

Figure 2A depicts annual cervical cancer deaths over time and figure 2B provides information about the cumulative cervical cancer deaths averted. Table 3 summarises these findings for the cumulative deaths and deaths averted over the periods 2020–2030, 2020–2070, and 2020–2120, for all core and supplementary scenarios.

In 2020, the predicted age-standardised rate for cervical cancer mortality across all 78 LMICs was 13·2 (range 12·9–14·1) per 100 000 women. By 2030, vaccine-only strategies would have minimal impact on cervical cancer mortality, which would remain at 13·2 (12·9–14·0) deaths per 100 000 women, corresponding to a 0·1% (0·1–0·5) reduction, averting a median of 620 deaths across all 78 LMICs by 2030 (rounded to 0·0 million in table 3). However, scaling up twice-lifetime cancer screening and treatment in addition to vaccination would result in a mortality rate of 8·5 (8·2–10·8) by 2030, corresponding to a 34·2% (23·3–37·8) reduction, averting 300 000 (300 000–400 000) deaths, mainly due to the impact of improved access to cancer treatment. In this 10-year timeframe, vaccination plus once-lifetime screening or twice-lifetime screening and treatment scale-up would lead to similar mortality reductions. For further information about the relative contribution of the interventions, see the appendix (pp 33–40).

By 2070, girls-only vaccination would lead to a mortality rate of 5·0 (range 4·5–5·4) per 100 000 women, corresponding to a reduction of 61·7% (61·4–66·1), averting 4·8 million (4·1–4·8) deaths, but scaling up once-lifetime screening and treatment in addition to vaccination would result in a rate of 1·4 (1·4–2·2) per 100 000 women, corresponding to a reduction of 88·9% (84·0–89·3), averting 13·3 million (13·1–13·6) deaths. By 2070, girls-only vaccination, twice-lifetime screening, and treatment would result in a mortality rate of 1·0 (0·9–1·6) per 100 000 women, corresponding to a reduction of 92·3% (88·4–93·0), averting 14·6 million (14·1–14·6) deaths. Compared to girls-only vaccination with catch-up to age 14 years (S1), extended-multi-age cohort vaccination to 25 years (S4) would result in increased intermediate-term mortality benefits, bringing forward the benefits of vaccination by about a decade (figure 1). At the high levels of vaccination coverage for girls assumed in the analysis, additional vaccination of boys at age 9 years (S5) would have minimal additional impact on cervical cancer mortality in women over the next 50 years and would have similar intermediate-term benefits to girls-only vaccination by 2070 (figure 1, figure 3, table 2).

By 2120, girls-only vaccination would result in a mortality rate of 1·3 (range 1·3–1·9) per 100 000 women, corresponding to a mortality reduction of 89·5% (86·6–89·9), averting 45·8 million (44·7–46·4) deaths. By 2120, a mortality rate of 0·2 (0·2–0·5) per 100 000 women, corresponding to a reduction of 98·6% (96·5–98·6), would be achievable with the WHO triple-intervention strategy, averting 62·6 million (62·1–62·8) deaths. If screening were done once per lifetime instead of twice, 60·8 million (60·2–61·2) deaths would be averted over the same period. The specific estimate for the incremental benefit of the twice-lifetime versus once-lifetime screening package over this period was 1·6 million (1·3–2·5) additional deaths averted, with most of these additional deaths averted before 2070. Compared to girls-only vaccination alone, 16·8 million (16·4–17·4) additional deaths would be averted via the triple-intervention strategy by 2120.

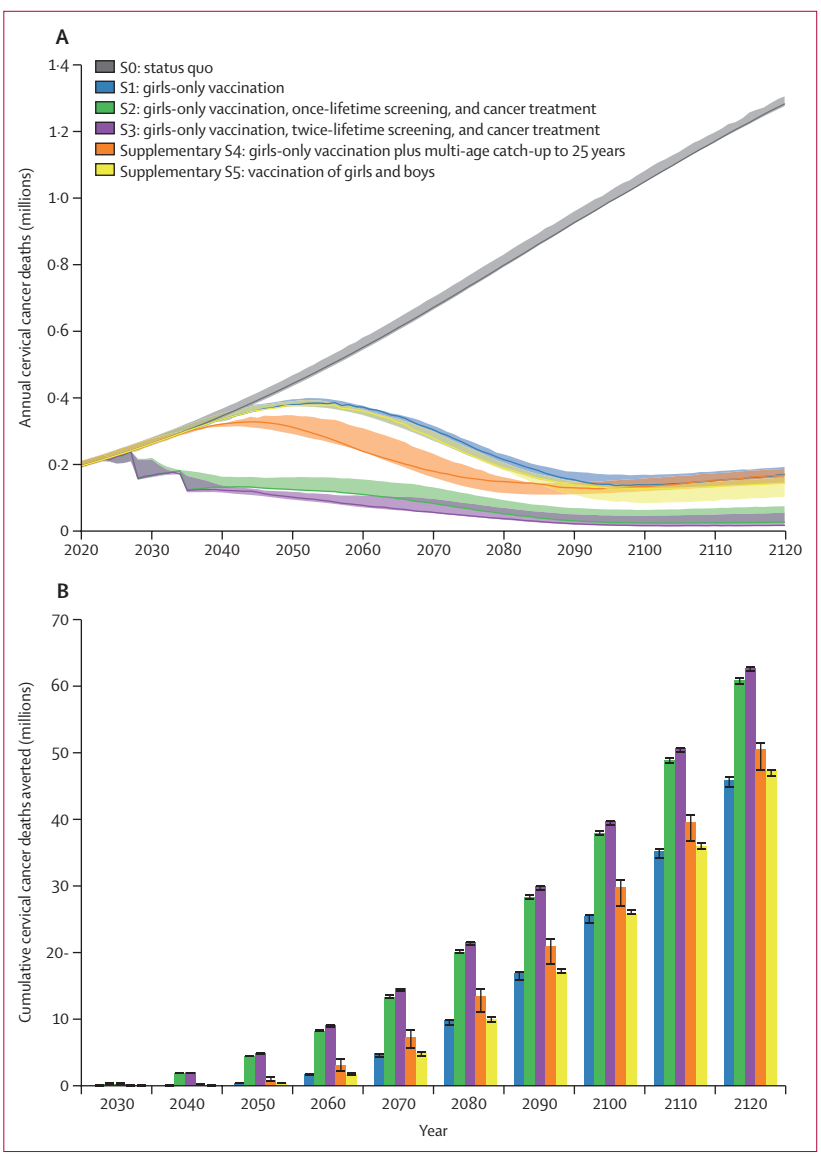

Figure 2: **Projected cervical cancer deaths across all 78 low-income and lower-middle-income countries**
(A) Annual cervical cancer deaths. (B) Cumulative cervical cancer deaths averted. The solid lines in panel A represent the median of the three models and the shading represents the range of the model outputs. In panel B the column height represents the median of the three models and the error bars represent the range of the three models. HPV=human papillomavirus. S0=status quo (no scale-up of vaccination, screening, or treatment). S1=female-only vaccination at age 9 years with multi-age cohort catch-up to age 14 years in 2020. S2=female-only vaccination and once-lifetime HPV testing at age 35 years with cancer treatment scale-up. S3=female-only vaccination and twice-lifetime HPV testing at age 35 years and 45 years with cancer treatment scale-up. Supplementary S4=female-only vaccination at age 9 years with extended multi-age cohort catch-up to age 25 years in 2020. Supplementary S5=female and male vaccination at age 9 years with multi-age cohort catch-up to age 14 years in 2020. All scenarios assume the use of a broad-spectrum HPV vaccine with protection against seven oncogenic types.

	S0: status quo	S1: girls-only vaccination	S2: girls-only vaccination, once-lifetime screening, and cancer treatment scale-up	S3: girls-only vaccination, twice-lifetime screening, and cancer treatment scale-up	Supplementary S4: girls-only vaccination plus multi-age catch-up to age 25 years	Supplementary S5: vaccination of girls and boys
Cumulative deaths by 2030 (2020–2030)	2·5 (2·5–2·7)	2·5 (2·5–2·7)	2·2 (2·2–2·4)	2·2 (2·2–2·4)	2·5 (2·5–2·7)	2·5 (2·5–2·7)
Deaths averted	..	0·0 (0·0–0·0)*	0·3 (0·3–0·3)	0·3 (0·3–0·4)	0·0 (0·0–0·0)	0·0 (0·0–0·0)
Reduction *vs* S0 (%)	..	0% (0–0)*	12% (11–12)	12% (10–13)	0% (0–1)	0% (0–0)
Cumulative deaths by 2070 (2020–2070)	20·7 (20·4–22·0)	16·3 (15·9–17·1)	7·1 (7·1–8·8)	6·4 (6·1–7·4)	13·5 (13·4–14·8)	16·0 (15·9–16·9)
Deaths averted	..	4·8 (4·1–4·8)	13·3 (13·1–13·6)	14·6 (14·1–14·6)	7·3 (5·6–8·5)	4·8 (4·4–5·1)
Reduction *vs* S0 (%)	..	22% (20–23)	65% (60–66)	69% (66–71)	35% (27–39)	23% (22–23)
Cumulative deaths by 2120 (2020–2120)	70·1 (69·7–73·0)	25·1 (23·7–27·1)	8·9 (8·9–12·8)	7·6 (7·3–10·3)	21·5 (19·7–22·5)	23·8 (22·4–25·5)
Deaths averted	..	45·8 (44·7–46·4)	60·8 (60·2–61·2)	62·6 (62·1–62·8)	50·5 (47·2–51·4)	47·3 (46·3–47·5)
Reduction *vs* S0 (%)	..	64% (63–66)	87% (82–87)	89% (86–90)	70% (68–72)	66% (65–68)

Cumulative cervical cancer deaths (in millions) across all 78 low-income and lower-middle-income countries over three time periods are shown. The values show the median (range) of three model outputs. All relative reductions are compared to the status quo (S0) predictions in the same year. HPV=human papillomavirus. S0=status quo (no scale-up of vaccination, screening, or treatment). S1=female-only vaccination at 9 years with multi-age cohort catch-up to 14 years in 2020. S2=female-only vaccination and once-lifetime HPV testing at age 35 years and treatment scale-up. S3=female-only vaccination and twice-lifetime HPV testing at age 35 years and 45 years and treatment scale-up. Supplementary S4=female-only vaccination with multi-age cohort catch-up to 25 years in 2020. Supplementary S5=vaccination of girls and boys at age 9 years, with multi-age catch-up to 14 years in 2020. All vaccination strategies assume the use of a broad-spectrum HPV vaccine with protection against the seven oncogenic types: 16, 18, 31, 33, 45, 52, and 58. Population projections were obtained from the UN and further projected out to 2120 (appendix pp 48–49). The median for deaths is the median of three possible model outputs for a given time period, and might use results from different models at different periods; similarly, the median for deaths averted and percentage reduction versus S0 is the median model for these metrics independently, and might be different to the median model selected for total deaths metric, and might also be different across the different periods. Caution should be applied in interpreting comparative differences between the values in this table, which represent the median and range across models; any individual median result could represent the findings of any one of the Cervical Cancer Elimination Modelling Consortium models. Note that the sum of averted cases and cases predicted for a given strategy might also not be identical to cases predicted for S0 because of rounding. *Note that table entry is zero due to rounding. Actual median and range of estimates for deaths averted: 620 (–1100 to 3600) deaths (model methods incorporate randomness and heterogeneity in estimates, which can occasionally, over shorter-term timeframes, lead to relative increases rather than decreases in rates compared to the status quo, shown here as a negative value).

Table 3: **Estimated cervical cancer deaths and deaths averted (in millions) from 2020 to 2030, 2020 to 2070, and 2020 to 2120**

In terms of premature mortality outcomes (deaths at age 30–69 years), the triple-intervention strategy would result in rate reductions of 33·9% (range 24·4–37·9) by 2030, 96·2% (94·3–96·8) by 2070, and 98·6% (96·9–98·8) by 2120 (table 2).

Figure 3 shows the regional results across the models for the reduction in age-standardised mortality from 2020 to 2120. The highest mortality rates in 2020, at approximately 30 per 100 000 women, are in sub-Saharan Africa, followed by Latin America and the Caribbean (approximately 16 per 100 000 women). These regions are predicted to have the greatest absolute reductions in mortality rates over the next two decades if the triple-intervention strategy can be successfully scaled up; by 2040, cervical cancer mortality in sub-Saharan Africa could be reduced by more than two-thirds to less than ten per 100 000 women, and in Latin America and the Caribbean it could be reduced to approximately six per 100 000 women. Details about the age-specific cervical cancer incidence and mortality rates in 2020, 2070, and 2120 for each region are provided in the appendix (pp 11–25).

With the WHO triple-intervention strategy, over the next 10 years, about half (48% [range 45–55]) of deaths averted would be in sub-Saharan Africa and almost a third (32% [29–34]) would be in South Asia (including India); over the next century, almost 90% of deaths averted would be in these regions (appendix p 26).

The appendix (pp 27–32) provides information at the country level for the predicted impact of the WHO triple-intervention strategy. In all countries, the median estimates of mortality rates by 2120 approach 1 per 100 000 women or lower.

The findings for model-specific, explanatory, and sensitivity analyses are provided in the appendix (pp 11–25, 33–43). Overall, the findings were concordant between models. The only notable difference was in the level of herd immunity predicted at older ages for unvaccinated individuals, which probably relate to underlying differences in assumptions around assortative sexual mixing among different age groups and different behaviour groups; we consider that the model variation in this area provides a useful reflection of true uncertainty in outcomes. The explanatory results demonstrated that the main benefits by 2030 were via cancer treatment scale-up, and that screening would lead to substantial mortality reductions beyond those conferred by vaccination and cancer treatment scale-up from 2030 to 2070–80. The results of the sensitivity analysis show that the choice of standard population is an important driver for rate estimates and also showed that, for deaths averted, differences between individual model estimates were

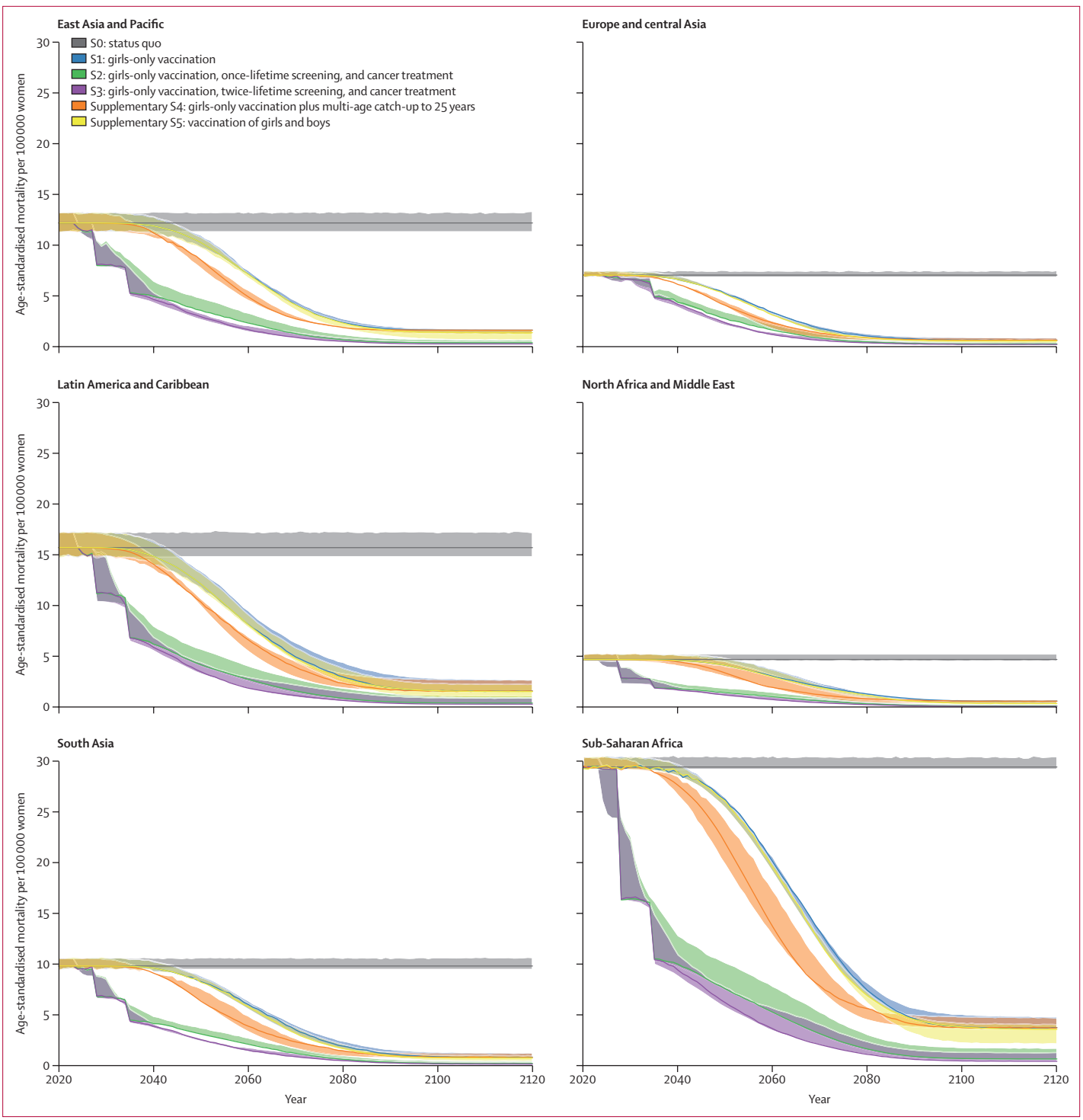

Figure 3: **Age-standardised cervical cancer mortality over time for LMICs in each region**

The solid lines represent the median outcome of the three models; the shading represents the range of model outputs. HPV=human papillomavirus. LMICs=low-income and lower-middle-income countries. S0=status quo (no scale-up of vaccination, screening or treatment). S1=female-only vaccination at 9 years with multi-age cohort catch-up to age 14 years in 2020. S2=female-only vaccination and once-lifetime HPV testing at age 35 years with cancer treatment scale-up. S3=female-only vaccination and twice-lifetime HPV testing at age 35 years and 45 years with cancer treatment scale-up. Supplementary S4=female-only vaccination at 9 years with extended multi-age cohort catch-up to age 25 years in 2020. Supplementary S5=female and male vaccination at age 9 years with multi-age cohort catch-up to age 14 years in 2020. All scenarios assume the use of a broad-spectrum HPV vaccine with protection against seven oncogenic types.

much smaller than the unavoidable uncertainties in future population projections over the next century.

Discussion

In this analysis, we have quantified, for the first time, the number of women's lives that could be saved by the successful implementation of the WHO global strategy for cervical cancer elimination. This report complements our parallel analysis on cervical cancer incidence.[15] Importantly, by extending the analysis to encompass mortality outcomes, we have quantified the impact of scaling up cancer treatment. Taken together, these two modelling analyses show that successful implementation of the WHO 90–70–90 triple-intervention strategy by 2030 would reduce cervical cancer incidence to 0·7 (0·6–1·6) per 100 000 women[15] and mortality to 0·2 (0·2–0·5) per 100 000 women across all 78 LMICs by 2120. This outcome, which is only achievable through a multi-sectoral and integrated approach across the continuum of cancer care, would represent extraordinary reductions in cervical cancer incidence (97% reduction) and mortality (99% reduction). Consequently, around 74·1 million cervical cancer cases and 62·6 million deaths would be averted, representing an enormous gain in terms of both quality of life and lives saved.

A major strength of this study is that we used a comparative approach involving well established model platforms that have been previously validated with data from multiple countries and that have jointly informed many national vaccination and cervical screening policy decisions. Predictions from the three models were broadly consistent for all scenarios, even over a century-long projection period. Our results for vaccination-only strategies are generally consistent with a recent analysis of the shorter-term impact on likely radiotherapy demand in LMICs,[26] which estimated that bivalent HPV vaccination of girls aged 12 years would only result in a 3·9% reduction in incident cervical cancer cases from 2015 to 2035. In line with our findings, the analysis found that incremental scale-up of radiotherapy in LMICs in the shorter term (up to 2035) would yield substantial health gains. Our sensitivity analysis demonstrated that for deaths averted, the variations generated by the differences in models were much smaller than uncertainties due to population size and structure over the next century. The sensitivity analysis also demonstrated that rates are somewhat sensitive to the choice of standard population used; this emphasises the importance of using the 2015 World Female Population for calculating cervical cancer incidence and mortality rates for comparability with our findings and across countries.

There were also some limitations to our analysis. The quality and availability of data about access to cancer treatment services, effective delivery of treatment, stage-distribution at diagnosis, and survival are variable for LMICs. Our modelling of survival was based on the latest data from major WHO reviews and we used updated DIRAC radiotherapy machine density as a surrogate for radiotherapy capacity and treatment access; this approach is reflective of the importance of radiotherapy as a cornerstone of effective treatment for cervical cancer and in line with the approach used by recently published models and the 2015 *Lancet Oncology* Commission on expanding global access to radiotherapy.[26,27] Furthermore, each modelling group independently did country-level model calibration of stage-specific survival to the best available mortality estimates from GLOBOCAN 2018. We incorporated a calibrated quality factor into the final estimated country-specific and stage-specific survival assumptions, which encompasses data limitations in treatment delivery information as well as variations in treatment delivery from established protocols and recommendations, equipment and infrastructure maintenance and logistics, and treatment abandonment due to financial stress or for other reasons. We did not take into account treatment improvements over time, assuming that mortality benefits resulting from cancer treatment scale-up by 2030 will be only due to the delivery of existing, effective treatment modalities, and not to emerging or hypothetical improvements in treatment beyond what is proven to be effective on a large scale in health services in high-income countries today.

Another limitation is that we did not explicitly model HPV infection, precancer and cervical cancer in women living with HIV. Increased progression to precancer and invasive cancer and reduced clearance of HPV is known to occur in women living with HIV, and this group is at increased risk of developing invasive cervical cancer, although this risk might now be partly or largely countered by the beneficial effects of antiretroviral therapy in many settings.[28,29] A separate collaborative group sponsored and coordinated by WHO is analysing the effects of HIV burden on estimates of cervical cancer elimination timing in selected countries. Current WHO cervical screening recommendations specify more frequent screening in women living with HIV,[30] and thus the mortality benefits we predicted are likely to depend on successful implementation of more intensive strategies for screening in high HIV-burden settings.

We did not include vaccination of boys or adult women in our core scenarios, because neither strategy has been found to be universally cost-effective even in high-income countries, and neither approach is recommended as part of the draft WHO elimination strategy. WHO's Strategic Advisory Group of Experts on Immunisation (SAGE) has recommended that vaccinating boys or older women should be delayed until current vaccine supply constraints are alleviated.[31] Priority should be given to vaccination of young girls since this strategy will generate the greatest health benefits overall; boys will derive protection via herd immunity if high-coverage vaccination can be achieved in girls, and older women will be offered protection via scale-up of screening and treatment services. In this analysis,

we did not explicitly consider cost-effectiveness, although previous work has shown the cost-effectiveness of combined vaccination and cervical screening approaches in various upper-middle-income countries and LMICs.[32,33] Cost-effectiveness will be required to weigh the trade-offs of the different strategies assessed here, including the incremental costs and benefits of vaccinating boys and doing two cervical screening tests instead of one in a lifetime. We found that the additional benefit of twice-lifetime versus once-lifetime screening was 1·6 million more deaths averted over a century, but the differences in cases averted is much higher.[15] Thus, the incremental improvement in quality of life from including a second screen is likely to be substantial. Furthermore, our findings for screening are in the context of rapid and effective scale-up of cancer treatment. If cancer treatment is not as broadly available as we assumed, the incremental benefits of additional cancer prevention via increasing screening to two tests in a lifetime would be larger. Finally, the incremental benefits of a second screen are higher when considered over the next 50 years rather than 100 years, because if vaccination is scaled up successfully then screening will provide the most benefit in the next 50–60 years. In the future, it will be important to assess the potential for future de-intensification of cervical screening, since our findings suggest that this could be considered in some countries after about 2070–80, when the full benefits of vaccination for mortality outcomes are becoming realised. The ongoing work of the CCEMC is focused on more detailed analysis of the incremental benefits of the strategies and on quantifying cost-effectiveness for the 78 LMICs; we are also analysing a larger number of more nuanced alternative scenarios at a country level, including optimal triage policy. In general terms, more detailed country-level analyses, taking into account specific local factors important for the effective delivery of vaccination and screening interventions, will continue to be required, and should be viewed as an important complement to the current large-scale analysis.

The WHO scale-up targets for elimination can be considered aspirational. Many challenges will need to be overcome, including vaccine and screening test supply and delivery challenges, and the infrastructure challenges associated with scale-up of invasive cancer diagnostics, treatment, and supportive and palliative care services. If scale-up is achieved more slowly than we have assumed, then reductions in mortality will be correspondingly delayed. With respect to HPV vaccination, the assumed scaled up 90% coverage rate is broadly in line with data suggesting that global coverage of other vaccines in LMICs (including measles, poliomyelitis, hepatitis B and diphtheria-tetanus-pertussis) is 84–90%.[34] Our analysis for screening broadly applies to a wide range of clinically validated HPV tests that can achieve benchmark sensitivity and specificity. Testing could be done either at a central laboratory or in a point of care environment, with clinician-collected or self-collected samples; the sensitivity of PCR-based self-collected tests has been shown to be comparable to that of clinician-collected samples.[35] In principle, our findings also apply to any future screening test with similar performance to that of primary HPV testing. For example, machine learning approaches for analysing digitised cervical images hold promise in some settings.[36] Our modelling of screening assumed that the majority (90%) of HPV-positive women were treated, with visual assessment for treatment done only to exclude the possibility of a frank cancer or a large precancerous lesion (which would require referral). Therefore, our findings for the impact of the cervical screening and referral pathway are likely to represent the maximum attainable benefit. In practice, resource-stratified guidelines recommend different approaches in different settings and, where possible, women are triaged to treatment to minimise the potential harms, which include psychosocial impact, potential overtreatment, and a possible impact on obstetric outcomes. WHO is revising its guidelines for cervical screening and has already revised its guidelines for precancer treatment to take into account the latest evidence and the elimination strategy.[30,37]

One of our main findings is that although achieving cervical cancer elimination per se will take many decades, the benefits of scaling up to the WHO elimination coverage targets will start to be realised within a decade. Key to this insight is an understanding of the timing of the effects of each intervention. Over the next 10–20 years, scaling up cancer treatment services will have the greatest impact because thousands of women in LMICs are being diagnosed every year with cervical cancer but have no access to adequate treatment. With appropriate treatment, survival prospects for early-stage and locally advanced cervical cancer are high. As a linked issue, offering appropriate palliative care to women who require it is an ethical and moral imperative. Over the intermediate term (the next 50–60 years), cervical screening will make an important contribution to outcomes, and over the longer term the full benefits of vaccination will be realised. The realisation of the major benefits of screening and vaccination over the intermediate and longer term will, however, require immediate action to implement these initiatives.

Scaling up to national vaccination, screening, and cancer treatment services in LMICs will be greatly facilitated by the successful realisation of universal health coverage in countries (SDG target 3.8). The 2019 Political Declaration of the UN high-level meeting on universal health coverage reaffirmed that health is a precondition for, and an outcome and indicator of, all dimensions of sustainable development, and countries strongly recommitted to achieving universal health coverage by 2030.[38] Building resilient and sustainable health systems could also be facilitated by the cervical cancer elimination initiative.[39] For example, cervical screening initiatives might be able to support or build on

HIV services, since women receiving antiretroviral therapy return for refills regularly. Opportunities exist to link screening with sexual and reproductive health services, potentially increasing both uptake of screening and of contraception services. The elimination initiative could assist with building cancer literacy and addressing stigma in communities, and scaling up treatment as well as supportive and palliative care services for cervical cancer should have positive implications for various other tumour types. Access to universal health coverage will be a key underlying factor for the achievement of SDG goal 3.4, to reduce premature mortality from non-communicable diseases by a third by 2030. We have shown that, when considered at a level across all 78 LMICs, the cervical cancer elimination initiative will specifically support efforts to achieve this target. More broadly, the elimination agenda will support a reduction in poverty (SGD1), an increase in gender equality (SDG5), and reduction in inequalities (SDG10). Thus, successful implementation of the elimination initiative will have both nearer-term and enduring positive consequences, not only for women but also for their families and broader society.

In conclusion, these findings emphasise the importance of acting now on three fronts to scale up HPV vaccination, screening, and treatment for cervical cancer. In the next 10 years, achieving substantial reductions in cervical cancer mortality will depend on successful scale-up of cancer treatment services in LMICs, and supportive and palliative care will need to be scaled up alongside such services. Implementing the WHO strategy towards cervical cancer elimination will result in large-scale mortality reductions and more than 62 million women's lives saved over the next century in LMICs. These findings have informed the draft WHO global strategy for cervical cancer elimination, which will be presented to the WHO Executive Board in February, 2020, and thereafter considered at the World Health Assembly in May, 2020.

Contributors

KC, JJK, and MB co-designed the study and co-led overall data interpretation. KC led the Policy1-Cervix analysis, JJK led the Harvard analysis, and MB led the HPV-ADVISE analysis. AK, KTS, MC, EAB, JT, FB, NB, and RH also participated in study design. AI, DT, EF, NB, and RH led the systematic review and analysis of cancer treatment access and survival in LMICs. KC, JJK, MB, MC, AK, DTNN, KTS, EAB, CR, SS, MD, GG, DM, EB, J-FL, AI, DT, EF, and FB participated in data collection. KC, JJK, MB, AK, KTS, MC, EAB, DM, DTNN, EB, SS, CR, MD, GG, J-FL, MAS, EF, DT, AI, and FB participated in data analysis. MC, AK, DTNN, KTS, and KC produced the tables and figures. KC, JJK, and MB drafted the Article and RH coordinated the CCEMC. All authors interpreted the results and critically revised the manuscript for scientific content. All authors approved the final version of the Article.

Declaration of interests

KC, AK, KTS, MC, DTNN, and MAS report grants from the National Health and Medical Research Council Australia during the conduct of the study. KC and MC are investigators of an investigator-initiated trial of cervical screening in Australia (Compass; ACTRN12613001207707 and NCT02328872), which is conducted and funded by the VCS Foundation, a government-funded health promotion charity; the VCS Foundation received equipment and a funding contribution from Roche Molecular Systems and Ventana USA but KC and MC (or their institution on their behalf) do not receive direct funding from industry for this trial or any other project. MAS also reports grants from Cancer Institute NSW during the conduct of the study. JJK, MB, EAB, MD, GG, DM, EB, J-FL, SS, and CR report grants from WHO during the conduct of the study. JT, EF, DT, FB, AI, NB, and RH declare no competing interests.

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