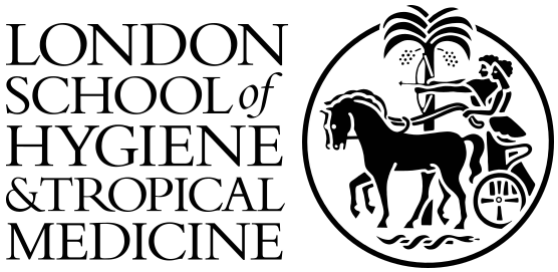

Cost-effectiveness of female human papillomavirus vaccination in 179 countries: a PRIME modelling study

Mark Jit, Marc Brisson, Allison Portnoy*, Raymond Hutubessy*

Summary

Background Introduction of human papillomavirus (HPV) vaccination in settings with the highest burden of HPV is not universal, partly because of the absence of quantitative estimates of country-specific effects on health and economic costs. We aimed to develop and validate a simple generic model of such effects that could be used and understood in a range of settings with little external support.

Methods We developed the Papillomavirus Rapid Interface for Modelling and Economics (PRIME) model to assess cost-effectiveness and health effects of vaccination of girls against HPV before sexual debut in terms of burden of cervical cancer and mortality. PRIME models incidence according to proposed vaccine efficacy against HPV 16/18, vaccine coverage, cervical cancer incidence and mortality, and HPV type distribution. It assumes lifelong vaccine protection and no changes to other screening programmes or vaccine uptake. We validated PRIME against existing reports of HPV vaccination cost-effectiveness, projected outcomes for 179 countries (assuming full vaccination of 12-year-old girls), and outcomes for 71 phase 2 GAVI-eligible countries (using vaccine uptake data from the GAVI Alliance). We assessed differences between countries in terms of cost-effectiveness and health effects.

Findings In validation, PRIME reproduced cost-effectiveness conclusions for 24 of 26 countries from 17 published studies, and for all 72 countries in a published study of GAVI-eligible countries. Vaccination of a cohort of 58 million 12-year-old girls in 179 countries prevented 690 000 cases of cervical cancer and 420 000 deaths during their lifetime (mostly in low-income or middle-income countries), at a net cost of US$4 billion. HPV vaccination was very cost effective (with every disability-adjusted life-year averted costing less than the gross domestic product per head) in 156 (87%) of 179 countries. Introduction of the vaccine in countries without national HPV vaccination at present would prevent substantially more cases of cervical cancer than in countries with such programmes, although the disparity has narrowed since 2012. If 71 phase 2 GAVI-eligible countries adopt vaccination according to forecasts, then in 2070 GAVI Alliance-funded vaccination could prevent 200 000 cases of cervical cancer and 100 000 deaths in some of the highest-burden countries.

Interpretation Large between-country disparities exist for HPV vaccination, with countries with the most to gain yet to introduce national HPV vaccination. Support from the GAVI Alliance could help to reduce such disparities, but a substantial burden will remain even after presently projected vaccine introductions.

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Introduction

Estimates of the possible health and economic effects of human papillomavirus (HPV) vaccination provide vital evidence to support the introduction of the vaccine into national programmes. WHO recommends that cost-effectiveness is considered before introduction of the vaccine,[1] and many high-income countries started such assessments before introduction.[2] In low-income and middle-income countries (LMICs), such assessments are less common, but are equally, if not more, important because of insufficient funding for public health interventions and the need to establish the financial case for vaccination to ministries of finance.[3] For example, the cost of the entire Expanded Programme on Immunization vaccine schedule (Bacillus Calmette-Guérin, diphtheria-tetanus-pertussis, oral polio, and measles) was estimated to be about US$17 per fully vaccinated child.[4] Conversely, the price for three doses of HPV vaccine was estimated to be about $13·50 through GAVI Alliance procurement, $39 at the lowest non-GAVI public sector indicative price, and more than $300 in high-income countries.[5] Some reports have suggested that overinvestment in vaccines for low-burden diseases in LMICs has prevented vaccines against diseases of greater public health concern from being introduced.[6] To avoid misplaced priorities, many

international funders such as the GAVI Alliance are guided by forecasts of the effect of disease and cost-effectiveness to decide which vaccination programmes to fund.[7]

However, assessments of cost-effectiveness of HPV vaccination often use complex models with data and expertise requirements that are prohibitive in many settings. Application of such models to resource-poor settings might require dependence on external consultants, which can sometimes restrict the involvement of local analysts and policy makers and, consequently, the effect that these results have on local decisions.[3] Furthermore, existing analyses have been done with various model types, ranging from simple static models that only consider direct effects, to complex individual-based transmission dynamic models. This variation in model types restricts the comparability of their results,[8–10] because different model types rely on different simplifying assumptions.

To address this knowledge gap and support evidence-based vaccine introduction in countries without reliable economic assessments of HPV vaccination, we aimed to develop a generic model of the health and economic effects of female HPV vaccination that uses straightforward calculations and data requirements and transparent assumptions so that it can be used and understood in a range of settings with little external support.

We also aimed to validate the model against other published HPV models, assess the cost-effectiveness of HPV vaccination in 179 countries with a particular focus on LMICs, and forecast reduction in the global cervical cancer burden and health disparities after HPV vaccination, with different vaccine uptake scenarios including GAVI Alliance strategic demand forecasts.

Methods

Model overview

We developed the Papillomavirus Rapid Interface for Modelling and Economics (PRIME) as a Microsoft Excel-based model that estimates the health and economic effect of vaccination of girls against HPV before sexual debut. We modelled the effect of the vaccine in terms of reduction in age-dependent incidence of cervical cancer and mortality in direct proportion to vaccine efficacy against HPV 16/18, vaccine coverage, and HPV type distribution (appendix p 1). We assumed that no changes to methods of cervical cancer screening or uptake occur during the time horizon of the model—ie, the period during which model results are followed (in most cases, the lifetime of the vaccinated cohort). We further assumed that vaccines provide lifelong protection, as suggested by the absence of vaccine failures in long-term follow-up of vaccinated cohorts, and statistical extrapolation of immunogenicity data.[11] We did not consider indirect effects (herd protection), thus the model provides a conservative lower bound on vaccine effect.

See Online for appendix

Validation

To assess validity of our model, we used PRIME to replicate results of all relevant published cost-effectiveness analyses of HPV vaccination in LMICs, as identified in a recent systematic review.[8] We extracted key parameters (vaccination coverage, vaccine efficacy, vaccination age, cost per vaccinated girl, cost of cervical cancer treatment, discount rate, age-dependent mortality, age-dependent cervical cancer mortality, cervical cancer incidence, and HPV 16/18-dependent fraction of cervical cancers) from every study and used these as input parameters for PRIME. We used Cohen's kappa to test agreement between PRIME and published models about whether vaccination was very cost effective in the countries examined. To further assess validity, we made a separate comparison with results of a cost-effectiveness analysis of HPV vaccination in the GAVI-72 countries (countries that are eligible for GAVI Alliance support in phase 2 of their strategic plan [2006–10]).[12] Appendix pp 2–10 gives further details about study selection and data extraction.

Projections for 179 countries

We parameterised PRIME with data from 179 countries for which UN population estimates are available.[13] Data for size of vaccination cohort, likely vaccine procurement and administration costs, incidence of cervical cancer, treatment costs, all-cause and cervical cancer-specific mortality, gross domestic product (GDP) per head, and proportion of cancers due to HPV16 and HPV18 were obtained from global datasets produced by WHO, the World Bank, the International Agency for Research on Cancer, and other sources (appendix pp 2–10).[13–20]

We estimated the effect of vaccination of the entire cohort (58 million 12-year-old girls) in terms of the number of cases of cervical cancer, deaths, and disability-adjusted life-years (DALYs) averted during their lifetimes. We assumed full vaccination coverage of the relevant cohort for illustrative purposes. We measured cost-effectiveness by comparing the cost per DALY averted (in 2011 US$) with thresholds of GDP per head, which is often used as an indication that an intervention is very cost effective, and three times GDP per head, used to indicate that an intervention is cost effective.[21] We did sensitivity analyses by varying key parameters (vaccine costs, cancer costs, cancer incidence, and cancer mortality) by plus or minus 25%, with cancer incidence and mortality from 2008 estimates (rather than 2012), and setting discount rates to 0% or 6%. We also explored the effect of adjustment of regional cancer costs by country-level variation in GDP per head (in 2011 US$; appendix p 6).

To explore between-country equity of present use of HPV vaccines, we estimated the potential effect of HPV vaccination on reduction of the burden of cervical cancer for countries that had introduced country-wide vaccination by Jan 1, 2012, and by Oct 1, 2013, and countries that are yet to introduce vaccination nationwide. National vaccines introduced by 2012 were determined

from data by Markowitz and colleagues,[22] whereas introductions by October, 2013, were obtained from WHO (Wang S A, WHO, personal communication). We did a similar analysis to explore associations between effect of vaccine and presence of an existing cost-effectiveness evaluation of HPV vaccination, as reported in the four most recent systematic reviews of HPV vaccination.[8,23–25] We included studies focusing only on one country or a small number of countries (fewer than ten in the same publication).

To assess the quality of model parameters, we rated data for cancer incidence, cancer mortality, distribution of HPV type in cancer, and distribution of cancer stage at detection for every country as either "satisfactory" or "unsatisfactory". Ratings were based on whether representative, good quality within-country data were available (appendix pp 6, 7, 25–30).

Projections for GAVI countries

The GAVI Alliance produced HPV vaccination coverage estimates for 2009–12 and strategic demand forecasts to 2032 for 73 countries (the GAVI-72 countries and South Sudan; Johnson H, GAVI Alliance, personal communication). We extrapolated figures (obtained with permission from the GAVI Alliance) for 71 countries (all except South Sudan and Kiribati, for which population projections were not available) by assuming that the proportion of 12-year-old girls who received HPV vaccination remained at the figures for 2032, even though the absolute number of doses would change because of fluctuations in the size of the 12-year-old female population. We then used these forecasts as inputs to PRIME (together with existing inputs for disease burden) to project the effect of vaccine on cervical cancer cases and deaths. We did sensitivity analyses by varying cancer incidence and mortality by plus or minus 25%. We modelled 61 vaccinated cohorts in these 71 GAVI-72 countries (one for every year from 2009–70), and aggregated the projected future effect of vaccination of every cohort to produce results by calendar year. In addition to this base case scenario, we also considered the effect of other scenarios: first, no further vaccine introductions or increases in coverage beyond 2014 (worst case); second, vaccine introductions and increases in coverage in 2012–32 based on GAVI Alliance strategic demand forecasts (middle variant); and third, the entire cohort of 12-year-old girls in every GAVI-72 country is vaccinated every year from 2014 (best case).

Role of the funding source

The funder had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The views expressed are those of the authors and do not necessarily represent the views of WHO. RH is a staff member of WHO. The corresponding author had full access to all data in the study and final responsibility for the decision to submit for publication.

Results

In our validation assessment, PRIME generally provided incremental cost-effectiveness ratios that were very close to those of the original country-based study when the original study parameters were used (figure 1). With a threshold of GDP per head as very cost effective, PRIME reproduced the qualitative conclusions (in terms of vaccination being very cost effective or not) for 24 of 26 countries (k=0·85) in 17 published studies. For the GAVI-72 analysis, both PRIME and Goldie and colleagues[12] produced much the same conclusion for all 72 (k=1) countries: female HPV vaccination would be very cost effective in all countries except Afghanistan and the Democratic Republic of Congo. Appendix pp 17–24 shows the full results.

Vaccination of a cohort of 58 million girls before sexual debut, which represents full coverage in 179 countries of

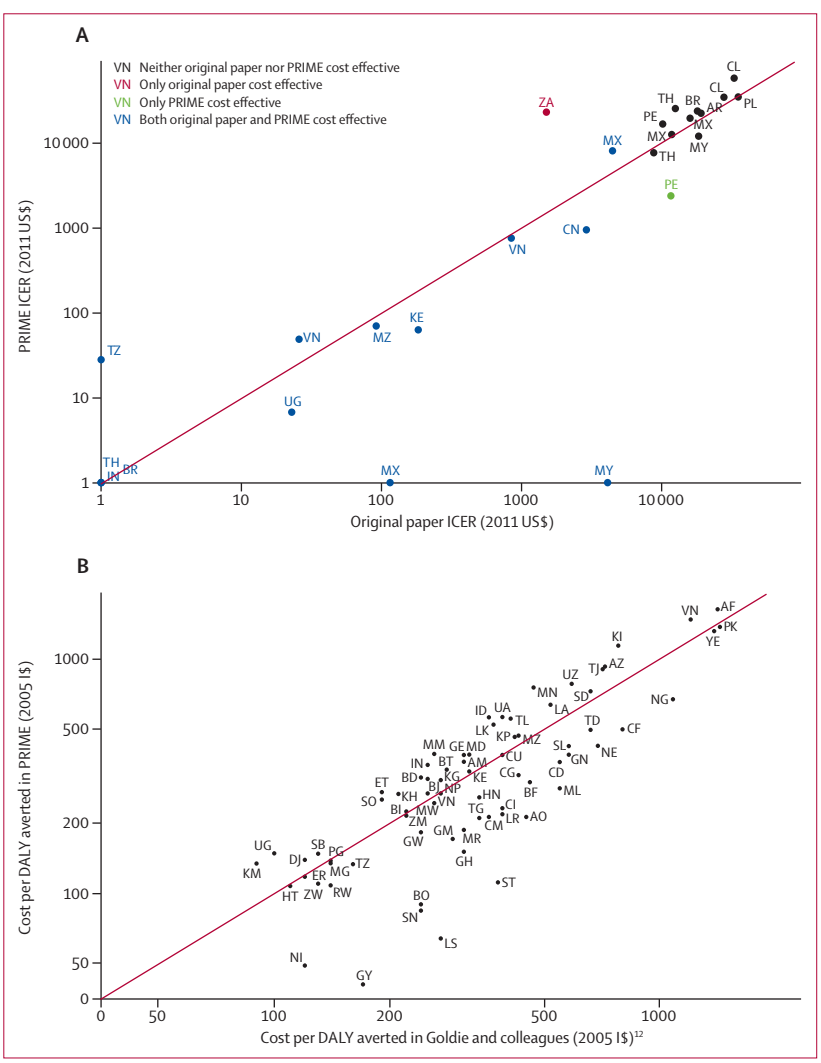

Figure 1: **Comparison of estimated incremental cost-effectiveness ratios (ICERs) between Papillomavirus Rapid Interface for Modelling and Economics (PRIME) and published literature for HPV vaccination of young girls**
(A) In 26 countries with low and middle incomes examined in 17 studies and (B) in GAVI-72 countries examined in Goldie and colleagues.[12] The diagonal line shows perfect agreement between PRIME and original paper ICERs. Appendix pp 11–16 shows defintions of two-letter country abbreviations. DALY=disability-adjusted life year.

	Vaccinated girls (millions)	Vaccine cost (US$, millions)	Net cost (US$, millions)	Cancers prevented (thousands)	Deaths prevented (thousands)	Proportion of all prevented cancers	Proportion of all prevented deaths
World	58·1	4500	4100	690	420	100·0%	100·0%
Southeast Asian Region	17·0	500	390	240	150	35·6%	36·6%
African Region	10·8	300	200	200	130	28·4%	31·6%
Region of the Americas	7·5	1200	1100	110	56	15·5%	13·3%
Western Pacific Region	11·6	990	930	72	42	10·5%	10·0%
European Region	4·9	1100	1100	39	17	5·7%	4·2%
Eastern Mediterranean region	6·2	380	360	29	18	4·2%	4·3%
Low-income countries	9·7	190	130	160	110	23·7%	27·3%
Lower-middle-income countries	24·8	820	670	320	200	46·8%	47·5%
Upper-middle-income countries	17·6	970	830	170	90	24·4%	21·4%
High-income countries	6·1	2500	2500	35	16	5·1%	3·8%

Table 1: **Effect of vaccination of one birth cohort of 12-year-old girls**

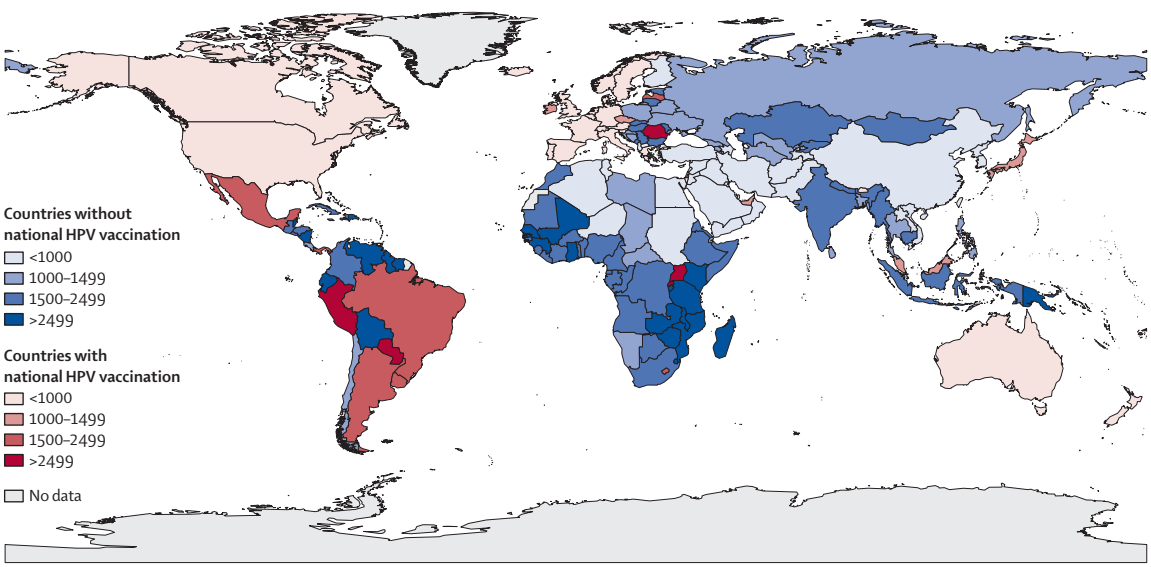

Figure 2: **Estimated number of cervical cancers prevented per 100 000 girls vaccinated against human papillomavirus (HPV) in 186 countries**

12-year-old girls, would prevent 690 000 cases and 420 000 deaths related to cervical cancer during the lifetime of the cohort, at a net cost of US$4 billion (appendix pp 15–24 shows the results by country). Most prevented cancers (480 000 [70%]) and deaths (310 000 [75%]) would occur in countries with low or lower-middle income (table 1).

Figure 2 shows the number of prevented cervical cancers per 100 000 girls vaccinated for countries with and without national HPV vaccination programmes. Of 33 countries where HPV vaccines are likely to have the greatest effect (>2500 cancers prevented per 100 000 girls vaccinated), only four had introduced national vaccination by Jan 1, 2012 (Fiji, Peru, Romania, and Rwanda), and an additional three had between Jan 1, 2012, and Oct 1, 2013 (figure 2). Conversely, of 55 countries where HPV vaccines are likely to have the least effect in comparison (<1000 cancers prevented per 100 000 girls vaccinated; mostly in western Europe and North America), 24 have introduced vaccination.

The number of cancers that could be prevented per 100 000 girls vaccinated was significantly lower (2-sided *t* test p=0·011) in the 46 countries that have introduced national vaccination (2013: median 980, IQR 700–1700) than in the 133 countries that have not (1600, 1000–2300; figure 3). The disparity is seen in every WHO region except the African Region (figure 3). However, worldwide, the disparity narrowed between 2012 and 2013, when the number of cancers that could be prevented per 100 000 girls vaccinated in the 34 countries with national vaccination was lower (median 930, IQR 690–1200) than in 2013. The improvement has mainly been because of new vaccine introductions in the African and Americas regions since 2012.

When parameterised with global data, HPV vaccination

of young girls is cost-effective (less than three times GDP per head) in all but six countries (mostly in the Eastern Mediterranean region) with low reported incidence of cervical cancer compared with other countries with similar income, and very cost-effective (below GDP per head) in 156 (87%) of 179 countries (appendix pp 15–24).

Projections of the quality of data that informs most high-income countries and some middle-income countries (including China, Brazil, Argentina, and South Africa) was judged satisfactory in all categories assessed. However, data quality for most countries in African and Eastern Mediterranean regions and Central Asia was judged unsatisfactory in almost all categories assessed (appendix pp 25–30).

In the sensitivity analyses, our overall results were robust to adjustments to any of the key parameters apart from discount rates (table 2); across all scenarios HPV vaccination was cost-effective in all but three to eight countries. However, discount rates have a large effect; setting discount rates to 0% makes vaccination cost effective in all countries (and very cost effective in all but three countries), whereas setting it to 6% makes vaccination not cost effective in 26 countries (table 2).

In terms of association between vaccine introduction and previous cost-effectiveness assessment, presence of a published economic evaluation of HPV vaccination was strongly associated with having introduced a universal vaccination programme. Only 28 (18%) of 153 countries without published economic evaluations had universal vaccination programmes. These countries mainly had upper-middle incomes or were high income with small populations (such as Greece, New Zealand, Romania, Sweden, and the United Arab Emirates). Only four countries with low and lower-middle income fell into this category (Bhutan, Fiji, the Federated States of Micronesia, and Rwanda). By contrast, 18 (70%) of 26 countries with

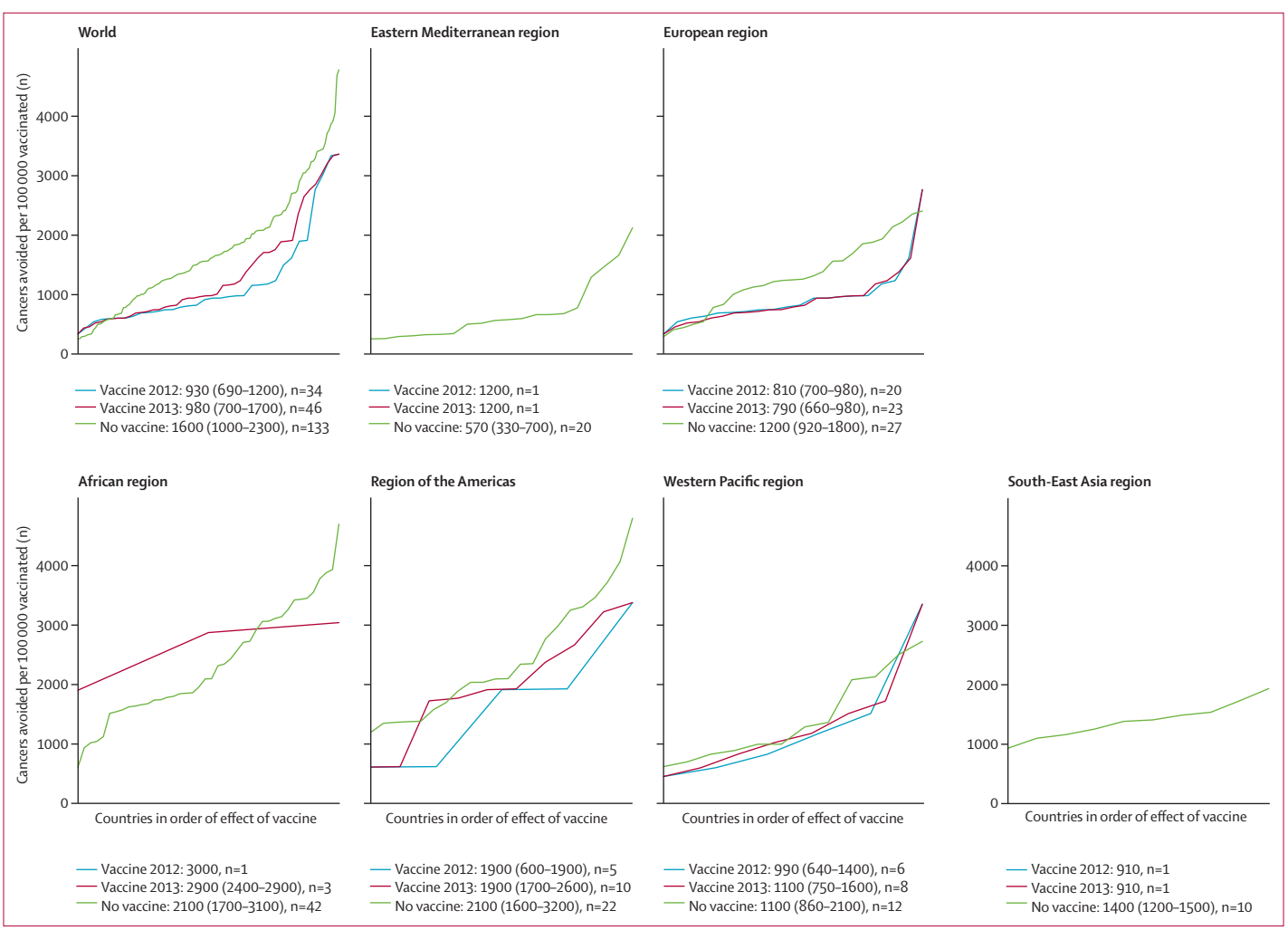

Figure 3: **Effect of vaccine (potential number of cervical cancers prevented per 100 000 girls vaccinated) in countries that have and have not introduced national vaccination (for which there are at least two countries in the relevant category)**

Data show year of vaccine introduction, median cancers avoided per 100 000 vaccinated (IQR), and number of countries. The horizontal axis shows all countries in the relevant category arranged in increasing order of vaccine effect, so a high line shows a high burden of preventable disease.

	Vaccine cost (US$, millions)	Net cost (US$, millions)	Cancers prevented (thousands)	Deaths prevented (thousands)	Not cost effective (n)	Cost effective (n)	Very cost effective (n)
Base case	4500	4100	690	420	6	17	160
Vaccine cost +25%	5600	5200	690	420	7	29	140
Vaccine cost –25%	3400	3000	690	420	5	11	160
Cancer cost GDP-adjusted	4500	4100	690	420	6	17	160
Cancer cost +25%	4500	4000	690	420	6	17	160
Cancer cost –25%	4500	4200	690	420	6	17	160
Cancer incidence +25%	4500	4000	860	420	6	17	160
Cancer incidence –25%	4500	4200	510	420	6	20	150
Cancer incidence 2008 cancer estimates	4500	4000	760	480	3	20	160
Cancer mortality +25%	4500	4100	690	520	5	12	160
Cancer mortality –25%	4500	4100	690	310	8	32	140
Discount rate 6%	4500	4100	690	420	26	55	98
Discount rate 0%	4500	4100	690	420	0	3	180

GDP=gross domestic product per head.

Table 2: **Effect of variations in key parameters of vaccination of an entire 12-year-old cohort**

published economic evaluations had universal vaccination programmes.

Figure 4 shows the projected effect of HPV vaccination in the GAVI-72 countries, assuming that they adopt vaccination on the schedule suggested by GAVI Alliance strategic demand forecasts. According to these forecasts, vaccine demand in GAVI-72 countries is likely to increase sharply in 2015–20; this increase is likely to produce large reductions in incidence and mortality of cervical cancer after 2050 (figure 4). By 2070, vaccination could prevent almost 200 000 cases of cervical cancer and more than 100 000 deaths every year. Equivalent figures for 2030 are 9000 cancers and 3000 deaths prevented, and for 2050 are 40 000 cancers and 20 000 deaths prevented. These projections assume that no related interventions (such as cervical screening or increased access to cancer treatment) are introduced where they did not previously exist. If all GAVI-72 countries are able to adopt HPV vaccination in 2014 with complete coverage, then the maximum effect of global vaccine would be 400 000 fewer cases of cervical cancer and 200 000 fewer deaths every year by 2070. The largest country contributing to the difference is India, which at present is not forecast to introduce HPV vaccination. If no new vaccines are introduced after 2013, then only around 2000 cervical cancer cases and 1000 cancer deaths will be prevented every year after 2070 in GAVI-72 countries.

Discussion

To our knowledge, this study is the first assessment of the likely health and economic effect of female HPV vaccination in 179 countries. By use of a straightforward model, which was validated against existing cost-effectiveness studies in LMICs, we report that HPV vaccination is likely to be very cost effective in most countries and cost-effective in almost every country in the world (panel). Furthermore, cost effectiveness of HPV vaccination could be better than presented, once further benefits not included in our analysis are incorporated such as herd protection, protection against non-cervical cancers and genital warts (in both females and males), and cost savings as a result of reduced need for cervical screening and treatment. Moreover, in high-income countries, which publicly procure HPV vaccines through competitive tenders, vaccine purchase prices could be substantially lower than the US retail price assumed. Hence a country's failure to show cost-effectiveness in this analysis is an indication that cost-effectiveness of HPV vaccination needs to be investigated more closely in that country before introduction of a vaccination programme, rather than as a reason to rule out vaccination.

Only three economic evaluations of HPV vaccination on a multiregional scale have been published.[12,16,26] Two reviews[12,16] were done before GAVI Alliance support for HPV vaccine introduction was announced. Ginsberg and colleagues[16] assessed the cost-effectiveness of female HPV vaccination by WHO subregion using a state transition model, but did not provide assessments of effect or cost-effectiveness at country (rather than regional) level. Goldie and colleagues[12] assessed the cost-effectiveness of HPV vaccination in 72 low-income countries. Both these assessments used more complex models than did ours; however, their results agree with our overall conclusions that HPV vaccination is likely to be very cost effective in most parts of the world. A third global analysis was published more recently,[26] but again this study did not provide country-level assessments. Furthermore, this analysis[26] mainly extrapolated data from high-income and middle-income countries, so its validity in low-income countries where most cervical

cancer burden lies is uncertain. In addition to these multiregional models, a series of regional cost-effectiveness analyses of HPV vaccination have been published for sub-Saharan Africa,[27] the Middle East,[28] North Africa,[28] Central Europe,[29] Eastern Europe,[29] and Central Asia.[29]

Our study is unique in its assessment of the effect and cost-effectiveness of HPV vaccination at country level in almost every country worldwide, with a particular focus on low-income countries and intercountry disparities. One limitation is that we have, out of necessity, relied on global datasets instead of data collected within every country. We note that for many countries (especially in African and Eastern Mediterranean regions) data quality are poor and often extrapolated from other countries in the region. Hence, we might not have comprehensively addressed between-country variations within the same region and income. Consequently, our results should be used mainly to understand between-region variations and not to inform decisions on a national level. For national decisions, PRIME can be used as a technique to guide country-led data collection to inform more contextualised results.

Our validation exercise shows that PRIME provides similar results to those obtained by more complex cost-effectiveness models for evaluation of HPV vaccination of girls before sexual debut. To our knowledge, our model is the first to be validated by quantitative comparison of results with such a broad range of published models. Admittedly, many of the modelling studies in the published work have used the same model or are adaptations of previous models.[8] However, the consistency of our results with almost all literature suggests that the effect and cost-effectiveness of vaccinating girls before sexual debut at high coverage can be reasonably predicted from data for cancer incidence, distribution of HPV type in cancer, and vaccination costs alone.

Our analysis has limitations. PRIME does not model transmission of HPV infection or the natural history of precancerous cervical disease, and many of the parameters we use in this analysis are based on global datasets that extrapolate data from a small number of countries. PRIME also does not model introduction of non-vaccine interventions to reduce cervical cancer burden such as screening. Such interventions are important to consider alongside vaccination as part of a comprehensive strategy to control cervical cancer.[30] Hence, PRIME complements models that have additional features to accurately capture events such as herd (indirect) protection, changes to the prevalence of precancerous neoplasias, and other HPV-related endpoints including non-cervical cancers and anogenital warts. Such events are important to address more complex policy questions such as catch-up and male vaccination, the choice between bivalent and quadrivalent HPV vaccines, and the interaction between vaccination and screening when both are introduced around the same time. The advantage of PRIME is that it is straightforward enough to be used by non-experts and has fairly light data requirements. For example, estimates of population-based HPV prevalence or of cervical neoplasias (which are not available in most countries with a high burden of cervical cancer) are not required.

The potential effect of exclusion of herd immunity is difficult to estimate because published models do not disaggregate direct and indirect effects on outcomes. One review[9] of studies in high-income countries suggested that inclusion of indirect effects decreased cost-effectiveness ratios by 23–44%. A review in LMICs suggested much larger differences, with median cost-effectiveness ratios of I$10 263 for static models and I$650 for dynamic models.[8] However, between-model comparisons need to be treated with caution because models that realistically incorporate indirect effects

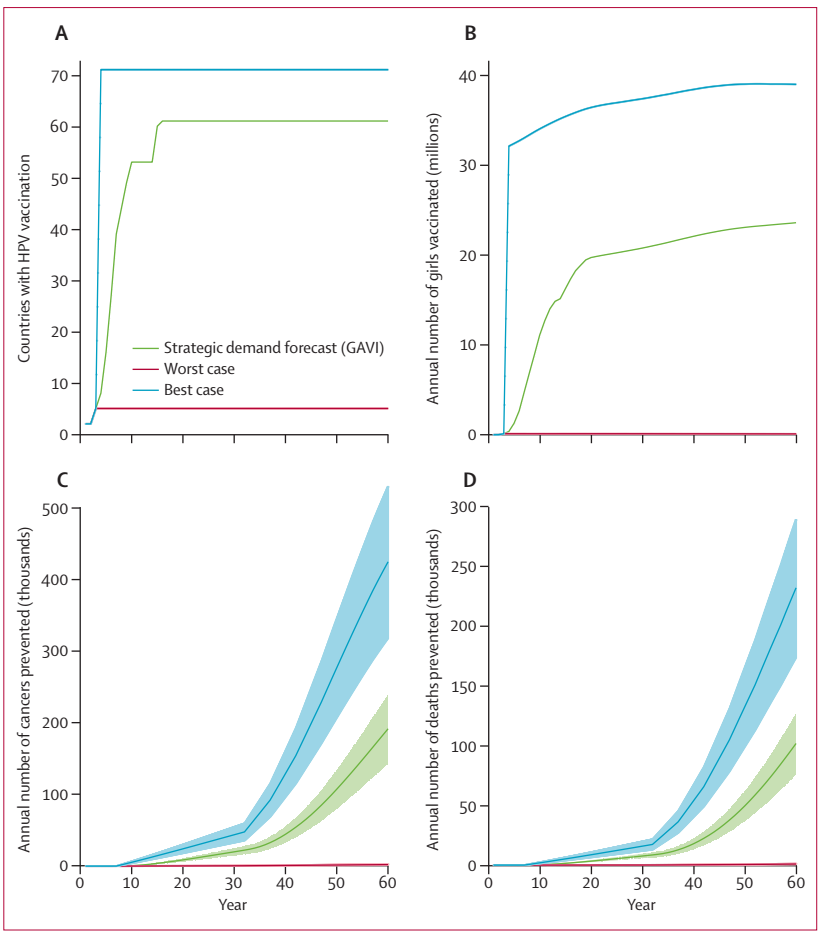

Figure 4: **(A) Number of GAVI-72 countries that have introduced human papillomavirus (HPV) vaccination, (B) annual number of girls vaccinated, (C) annual number of cervical cancers prevented, and (D) annual number of deaths prevented by vaccination in those countries**

Three scenarios are shown: (1) no further vaccine introductions or increases in coverage beyond 2014 (worst case), (2) introductions according to GAVI strategic demand forecasts, and (3) the entire cohort of 12-year olds in every GAVI-72 country is vaccinated every year from 2014 (best case). Shaded regions show the range of results in sensitivity analyses when cancer incidence and mortality are varied by ±25%. A and B have no shaded regions because varying the epidemiological parameters has no effect on the coverage of vaccination.

***Panel:* Research in context**

Systematic review

We recently systematically reviewed all cost-effectiveness analyses of HPV vaccination in low-income and middle-income countries (LMICs) published in PubMed, Embase, and the Cochrane Library published up to April 1, 2012.[8] Our review identified 25 cost-effectiveness evaluations. However, most LMICs only had vaccine projections of vaccine effect and cost-effectiveness from multicountry studies with little involvement of local analysts. Hence, we developed an HPV economic model that was simple enough to be used at a local level for country-led data collection and model parameterisation to support evidence-based decision-making, yet could reasonably reproduce the results of more complex models for the cost-effectiveness of vaccination of girls before sexual debut.

Interpretation

Our model, Papillomavirus Rapid Interface for Modelling and Economics (PRIME), provides similar results to those obtained by more complex cost-effectiveness models, for evaluation of HPV vaccination of girls before sexual debut. A global analysis with PRIME suggests that HPV vaccination is likely to be cost effective in almost every country, and especially low-income countries. However, the potential of vaccination has yet to be realised because countries with the highest vaccine-preventable burden of cervical cancer have largely not introduced country-level programmes. Empowering local decision makers to do their own cost-effectiveness analyses might facilitate vaccine introduction in countries that most need it.

(dynamic models) are largely produced by a small number of modelling groups who might have made other modelling choices (besides inclusion of indirect effects) that differentiate them from other models.

Our analysis suggests that the potential of HPV vaccination has yet to be realised, because if no new GAVI-72 countries introduce HPV vaccination after 2013, only 2000 of more than 400 000 potential vaccine-preventable cancer cases in these countries would be prevented every year. Introduction of vaccines supported by the GAVI Alliance could prevent around half these cases, showing the importance of both GAVI support and access to low vaccine prices for HPV vaccination, but also the magnitude of the challenge remaining even after present projected levels of GAVI support.

Our analysis also emphasises between-country inequalities in vaccine introductions so far, in which most countries with the highest preventable burden of cervical cancer-related HPV vaccination are yet to introduce country-level programmes. The same countries without HPV vaccination programmes are also less likely to have country-specific information from published economic evaluations about the potential health effect, budget implications, and cost-effectiveness of vaccination that decision makers need. PRIME is straightforward enough to be used at a local level to support country-level data collection, model parameterisation, and evidence-based decision-making. This simplicity will enable countries to do their own analyses with local assumptions, data, and expertise, which could enhance the effect that results have on national decision making.

Contributors

MJ, MB, and RH conceived the study. AP compiled the datasets with input from RH and MJ. MJ and MB designed the model structure with input from RH. MJ programmed the model and did the analyses with input from RH and MB. MJ wrote the report with input from all authors. All authors approved the final version of the report.

Declaration of interests

MB has consulted for GlaxoSmithKline (for rotavirus vaccine), and his institution has received unrestricted grants from Merck Frosst. All other authors declare no competing interests.

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