# Estimating the health impact of vaccination against 10 pathogens in 98 low and middle income countries from 2000 to 2030

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# Abstract

Background

The last two decades have seen expansion of childhood vaccination programmes in low- and middle-income countries (LMICs). We quantify the health impact of these programmes by estimating the deaths and disability-adjusted life years (DALYs) averted by vaccination against ten pathogens in 98 LMICs between 2000 and 2030.

Methods

Sixteen independent research groups provided model-based disease burden estimates under a range of vaccination coverage scenarios for ten pathogens: hepatitis B (HepB), *Haemophilus influenzae* type b (Hib), human papillomavirus (HPV), Japanese encephalitis (JE), measles, *Neisseria meningitidis* serogroup A (MenA), *Streptococcus pneumoniae*, rotavirus, rubella, yellow fever. Using standardized demographic data and vaccine coverage, the impact of vaccination programmes was determined by comparing model estimates from a no-vaccination counterfactual scenario with those from a reported and projected vaccination scenario. We present deaths/DALYs averted by calendar year, and by annual birth cohort.

Findings

We estimate that vaccination will have averted 69 (2∙5-97∙5% quantile range 52-88) million deaths over the timespan, countries and pathogens considered, 37 (30-48) million of these between 2000-2019. From 2000-2019, this represents a 45% (36-58%) reduction in deaths. Most (95% (92-98%)) of this impact is in under-five age mortality, notably from measles. Over the lifetime of birth cohorts born between 2000 and 2030, we predict that 120 (93-150) million deaths will be averted by vaccination, of which 58 (39-76) and 38 (25-52) million are due to measles and HepB vaccination, respectively. We estimate that recent increases in vaccine coverage and introductions of additional vaccines will result in a 72% (59-81%) reduction in lifetime mortality in the 2019 birth cohort.

Interpretation

Increases in vaccine coverage and the introduction of new vaccines into LMICs have had a major impact in reducing mortality. These public health gains are predicted to increase in coming decades if progress in increasing coverage is sustained.

# Introduction

Vaccines have been responsible for substantial reductions in mortality 1–5 and are among the most cost-effective health interventions 6–8. In addition to direct protection afforded to vaccinated individuals, high levels of vaccination coverage offer indirect protection (herd immunity) to the remaining unvaccinated individuals in a population. Impact is seen on a timescale which is vaccine-dependent: for some childhood diseases (such as measles, rotavirus, pneumococcal disease), impact is seen rapidly, while for human papillomavirus (HPV) and hepatitis B, impacts are commonly seen over a much longer timescale in the reduction of adult morbidity and mortality.

The World Health Organization (WHO) introduced the Expanded Programme on Immunization (EPI) in 1974 9. This programme - supported by UNICEF and global donors - succeeded in delivering substantial increases in coverage of routine childhood vaccines; for instance, global coverage of DTP3 increased from just over 20% in 1980 to over 75% in 1990 10. However, as coverage plateaued in the 1990s, concerns grew around the sustainability of these gains, eventually leading to the formation of Gavi (the Vaccine Alliance) in 1999 11. Gavi’s mission is to sustain and increase coverage and improve access to new vaccines in low- and middle-income countries (LMICs) 12. Since its founding, it has supported immunisation of over 700 million children in LMICs 13 . Global targets for vaccination have also continued to grow in ambition: the Global Vaccine Action Plan (GVAP) framework was launched in 2012 by WHO with the aim of preventing millions of deaths by 2020 through access to vaccines in all countries. This was further reinforced by target 3∙8 of the Sustainable Development Goals calling for access to “vaccines for all” by 2030 14.

Due to the limitations in completeness and quality of death registration and disease surveillance systems in many LMICs, it is often not possible to directly measure the impact of vaccination programmes on mortality and morbidity. Mathematical models are therefore a valuable tool for extrapolating from available disease burden and pathogen surveillance data to generate impact estimates and to generate projections of the impact of future vaccine coverage to inform investment planning.

To improve the quality and coordination of vaccine impact assessment, the Vaccine Impact Modelling Consortium (VIMC) was formed in late 2016 with the support of Gavi and the Bill & Melinda Gates Foundation (BMGF). VIMC currently comprises 18 modelling groups coordinated by a secretariat at Imperial College London, and it models vaccination impact against diseases caused by ten different pathogens across 98 countries (about 69% of the world’s population in 2018), including the 73 countries currently eligible for Gavi support.

This paper presents the first complete set of vaccine impact estimates generated since VIMC was formed, quantifying impact over calendar year and annual birth cohorts between 2000-2030 in terms of deaths and disability adjusted life-years (DALYs) averted. The pathogens included were hepatitis B (HepB), *Haemophilus influenzae* type B (Hib), human papillomavirus (HPV), Japanese encephalitis (JE), measles, *Neisseria meningitidis* serogroup A (MenA), *Streptococcus pneumoniae* (prevented by the pneumococcal conjugate vaccine - PCV), rotavirus (rota), rubella virus and yellow fever virus (YF). VIMC does not currently assess the impacts of diphtheria, tetanus and pertussis (DTP) vaccine 1, cholera vaccine and polio vaccines. VIMC’s vaccine impact estimates are used to support the monitoring of existing vaccination programmes and inform future investment strategy.

# Methods

Modelling groups from different institutions with disease-specific expertise provided the pathogen-specific vaccine impact estimates (Table 1). Twenty mathematical models were used by VIMC to produce the estimates presented here: two models for each pathogen other than HepB, which had three, and yellow fever, which had one. Including multiple models for each pathogen facilitates assessment of structural uncertainty in models. Each model represents the impact of vaccine coverage and efficacy on national level disease burden (and in some cases disease transmission dynamics) to estimate vaccine impact. Model descriptions and the list of 98 LMICs included in the analysis are available in the supplementary information (SI).

Standardised demographic data (live births per year, death rates) based on the United Nations World Population Prospects (UNWPP 2017 15) was used for all countries. Similarly, standardised national level estimates of vaccination coverage for each vaccine considered were provided by the VIMC secretariat to each group. Past coverage in all countries for 1980-2016 was obtained from WHO/UNICEF Estimates of National Immunization Coverage (WUENIC) as published in July 2017 16. Future coverage estimates from 2017 to 2030 were based on Gavi’s operational forecast as of October 2017, for the countries eligible for Gavi support. Gavi’s operational forecasts assume likely dates of vaccine introduction based on non-binding expressions of interest from eligible countries, applications to Gavi for vaccine support, intended introductions as reported to the World Health Organization (WHO), and assessment of country capacity to introduce a specific vaccine in a specific time frame. Following introduction, coverage of new vaccines is typically assumed to reach coverage of a reference vaccine (e.g., coverage of third dose of DTP (DTP3)) within two to three years, after which coverage is assumed to increase 1 percent per year up until a maximum of 90% or 95% depending on the vaccine 1. For the 25 countries considered not supported by Gavi, and for years after 2030 for countries in Gavi’s portfolio, an annual 1% increase in coverage was assumed from 2017 up to a maximum of 90% or the historic high coverage achieved (if >90%). For newly introduced vaccines with only an introduction date and no Gavi coverage forecast, we assumed that coverage would increase to the same coverage as pentavalent (HepB-Hib-DTP3) vaccine in that country in the first three years and subsequently increase by 1% per year. Estimates of numbers of vaccines received per child by year were generated from these coverage estimates and projections assuming independence of coverage between vaccines.

Disease burden was quantified by deaths and DALYs stratified by age. DALYs measure the years of healthy life lost due to premature death and disability from the disease, and are the sum of years of life lost (YLLs) through premature mortality and years lived with disability (YLDs). No discounting or weighting was applied in the calculation of DALYs.

Age-stratified pathogen-specific disease burden estimates (deaths and DALYs) for annual birth cohorts between 2000 to 2030 were generated by each modelling group. Corresponding estimates for the counterfactual scenario, assuming no vaccination had occurred after 2000, were also produced. Supplementary immunisation activities (SIAs), other immunisation campaigns (such as yellow fever reactive campaigns to outbreaks) and second doses were modelled when relevant.

For rubella, only disease burden from congenital rubella syndrome (CRS) 17 was assessed, since rubella only usually causes mild disease in infected persons.

The impact of vaccination was assessed by comparing the counterfactual (‘no vaccination’) scenario with the reported and projected vaccination scenarios. Two forms of aggregation were used to present the results: by calendar year and by year of birth. The former assesses the difference in burden between the reported and projected vaccination and no-vaccination scenarios for a specific year, and gives a cross-sectional view of impact. The latter sums disease burden across every year of life for each yearly birth cohort (born between 2000 and 2030) before again calculating the difference between reported and projected vaccination and no-vaccination scenarios, and therefore gives a lifetime view of vaccine impact.

The population-attributable benefit of vaccination for each pathogen was estimated as the proportion of annual deaths due to each pathogen that would be prevented by vaccination.

We use model averaging to derive impact estimates, with each model for a pathogen given equal weighting. Uncertainty in model estimates was assessed by generating 200 sets of estimates from each model, probabilistically sampling over model parameter uncertainty. The same randomly sampled sets of parameters were used for both vaccination and no-vaccination model runs, allowing uncertainty in vaccine impact to be assessed. Central pathogen-specific estimates presented here represent averages over all such samples from every model available for each pathogen. The 95% (2∙5 and 97∙5% quantiles) credible intervals presented for each pathogen are derived by combining the probabilistic distributions of estimated impact from all the models available for that pathogen.

Estimates involving aggregation across pathogens were generated via a bootstrap approach under the simplifying assumption that the drivers of uncertainty in each model are independent of those in any other model. For each model, a random sample of the statistic of interest was drawn from the 200 probabilistic runs. These model-specific samples were combined by averaging them across models of the same pathogen and then summing the resulting pathogen-specific estimates across pathogens. Means and 2·5 and 97·5% quantiles of 100,000 such bootstrap samples were calculated to derive central estimates and 95% credible intervals.

The main text of this paper focuses on presenting vaccine impacts on mortality; more detailed estimates of mortality impacts and estimates of DALYs averted by vaccination are given in the SI.

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# Results

The average number of vaccines received per child increased across the majority of the 98 countries (Table S1) between 2000 and 2019 (Figure 1A-C). Both increases in coverage of existing vaccines (e.g. measles-containing vaccines) and the introduction of new vaccines (e.g. rotavirus) contribute to this overall trend (Figure 1D). Routine vaccination against JE and rotavirus began to be introduced from 2006, PCV in 2010, HPV in 2014 and MenA in 2016. In addition, coverage increases also reflect the increase in countries eligible for Gavi support (Table S2). The increase in vaccination is also reflected in the proportion of unvaccinated children (Figure S5) for the 2019 cohort. For different assumptions of correlation of vaccine doses within and between different vaccines, the proportion of unvaccinated children in most of the countries is less than 0∙1.

To assess the impact of vaccine use on mortality, we quantify the expected burden of disease in the counterfactual scenario of no vaccination (Figure 2, red curves) and estimate the impact of observed and projected vaccination coverage on that baseline (Figure 2, blue curves). Depending on the pathogen considered, long-term trends in disease prevalence interact with global population growth and aging to result in a variety of projected trends in disease-specific mortality in the counterfactual no-vaccination scenario. However, for all but two pathogens, vaccination between 2000 and 2030 is estimated to cause substantial reductions in the mortality burden in the same time period. The two exceptions are HepB and HPV where most mortality is due to infections that have already occurred, due to the typically long-time delay between infection and severe outcomes for those infections. While HepB vaccination coverage is now relatively high and projected to increase further, most of the impacts of this will only be seen after 2030. For HPV, most countries have yet to introduce vaccination.

The age distribution of mortality varies dramatically across the 10 pathogens as a result of differences in their epidemiology: HepB- and HPV-attributable mortality primarily affects those over 40 years of age, YF, MenA and JE are epidemic diseases which largely affect those under 30 (due to natural immunity acquired with age in older adults), while mortality for all other pathogens is nearly entirely focused in the under-5s. Most of the mortality reduction from measles is attributable to the measles containing vaccine, first dose (MCV1) which is not subject to Gavi funding.

Figure 3 presents the estimated numbers of deaths averted by vaccination in the 98 countries (see also SI Tables 5(a-h)). Two views are given: total deaths averted by calendar year (Figure 3A), and deaths averted over the lifetime of each annual birth cohort (Figure 3B) and for DALYs averted in Figure S2A and S2B, respectively. Estimated numbers of deaths and DALYs averted among the under 5s for calendar and annual birth cohort views are presented in Figure S3(a) and S3(b).

Looking by calendar year, we estimate a total of 69 (52-88) million deaths averted between 2000 and 2030, 37 (30-48) million of which were averted between 2000 and 2019 (Table 2). In the 73 Gavi countries, the corresponding values are 66 (49-83) million deaths averted between 2000-2030, 35 (28-45) million of which were averted between 2000-2019 (Table S4(a)).

Measles vaccination has the largest impact, with 56 (39-74) million deaths averted (54 (37-70) million in the 73 Gavi countries) between 2000-2030.

Considering deaths averted by birth cohort (Figure 3B and Table S3b), the longer-term impact of increasing coverage of HepB vaccination becomes clearer. However, since the majority of HepB deaths (due to liver disease) occur in those over 45 years of age, the impact of vaccination will not be seen in the 2000-2030 time period (Figure 3A) but will start to be seen from 2040 onwards. Similar arguments apply to HPV vaccination (though coverage is substantially lower than for HepB): cervical cancer deaths largely occur in women over 50, leading to a delay of nearly 40 years between vaccination and its direct impact on mortality. Thus, summing vaccination impact over the full lifetimes of the 2000-2030 birth cohorts gives a total of 120 (93-150) million deaths averted in total, 65 (48-83) million of which are in the under-5s. In the 73 Gavi countries, the corresponding values are 100 (78-130) million deaths averted in the 2000-2030 birth cohorts, 62 (46-78) million of which are in the under-5s (Table S4(c)). Table S3(b) summarises deaths averted by pathogen and illustrates that in the 2000-2030 birth cohorts over 53% (45-66%) of deaths averted are in children under 5 years.

The extent to which vaccination reduces overall mortality due to the 10 pathogens varies substantially by country (Figure 3C), largely due to historical variations in vaccination coverage, but also due to variation in the epidemiology of some pathogens by country. We estimate vaccination will prevent 72% (59-81%) of the mortality associated with these 10 pathogens in the 2019 annual birth cohort across the countries we consider. This proportion rises to 76% (54-84%) when we consider only under-5 mortality. In the 73 Gavi countries, the corresponding values are a 72% (57-79%) reduction in all-age mortality, and a 76% (54-84%) reduction in under-5 mortality.

In the period 2000-2019, we estimate that vaccination in the 98 countries reduced overall mortality and under-5 mortality due to these pathogens by 45% (36-58%) and 57% (52-66%), respectively. In the 73 Gavi countries, these reductions were 48% (39-59%) and 57% (53-66%), respectively. For the period 2020-2030, we project these reductions will respectively rise to 60% (33-74%) and 77% (44-86%) in all 98 countries and 64% (35-76%) and 78% (44-86%) in the 73 Gavi countries.

It is informative to place these estimates in their demographic context. Taking the 2019 birth cohort as an example, and using United Nations World Population Prospects (UNWPP) demographic estimates (see Methods), we estimate that under-5 mortality in the 98 countries would be 45% (31-57%) higher in the absence of any vaccination against the ten pathogens. The total number of deaths (occurring at any age) averted in the 2019 birth cohort represent 4∙1% (3∙2-5∙0%) of the live births making up that cohort.

Total impact reflects vaccination coverage as well as underlying disease burden and vaccine effectiveness. We therefore examine the relative impact of each vaccine, by quantifying deaths averted per vaccinated individual for each pathogen (Table 2, Table S3b and SI Tables S6(a-l)). This highlights that while measles, Hib and PCV have the largest relative impact on under-5 mortality, vaccines against HPV, HepB and YF have the largest impact per person vaccinated by year of birth and vaccines against measles and YF have largest impact per person vaccinated by calendar year. YF and HPV vaccination have the largest relative impact of all the vaccines considered, with central estimates for both of over 16 (5-32) deaths averted per 1000 persons vaccinated for the 2000-2019 birth cohorts.

Since most of the pathogens considered (namely Hib, JE, measles, PCV, rota, rubella) result in under-5 mortality, the impact of vaccination on DALYs largely mirrors the impact on mortality (Figure S3). Since HepB- and HPV-related deaths are focused in the over 50s, mortality contributes fewer years of life lost (YLLs) for these pathogens, but morbidity contributes higher years lived with disability (YLDs) for both infections (HepB particularly). Estimates of vaccine impact in DALYs averted are presented in the SI.

# Discussion

This study represents the largest scale study of health impacts of immunisation in LMICs yet undertaken, covering vaccination programs against 10 pathogens and evaluating impact in 98 countries. It represents an advance on past work 1 in its scale (in both antigens and countries considered) and in the emphasis of VIMC on standardising model inputs (vaccine coverage and demography) and outputs (age-specific mortality and DALYs by year of birth cohort and age). Such standardisation allows impacts to be combined across, and compared between, vaccines.

Our analysis highlights where the greatest gains from future investments in improving vaccine coverage are to be made. We predict increasing HPV coverage in girls will avert more deaths per person vaccinated than any other immunisation activity, while increasing PCV coverage will give the largest reductions in under-5 mortality.

We find that immunisation programmes in the 98 countries considered will result in individuals born in 2019 experiencing 72% (59-81%) lower mortality due to those 10 pathogens over their lifetime than they would otherwise. Furthermore, in the absence of vaccination, we estimate that all-cause under-5 mortality would be 45% (31-57%) higher than currently observed. These impacts are a testament to both the public health benefit of vaccines overall and the sustained investment in increasing global vaccination coverage in the last two decades. They also highlight what might be lost if current vaccination programmes are not sustained, and thus provide quantitative evidence supporting both donor and country investments in vaccination programmes.

When compared to mortality estimates from the WHO and IHME global burden of disease study for measles, we find some differences between 2000-2010. These are likely to be driven by differences in source data and model types. For example, the IHME measles estimates are based on static models whereas the two VIMC models are both dynamic. Further comparison is provided in the SI.

Deriving these impact estimates is far from straightforward: cause-specific mortality data in the LMICs considered is limited, making direct observational assessment of impact challenging. However, to inform monitoring and decision-making, countries and international organizations such as Gavi require projections of potential impact under a range of investment scenarios. To fill these gaps, mathematical and statistical models can be used to extrapolate data on levels of current infection (such as case detection from active surveillance) and/or past infection (such as serosurveys) to sites and countries without such data. They can also be used to project future trends given information about vaccine coverage.

In addition, our study has focused on quantifying uncertainty in vaccine impact. Given the limited explicit data on pathogen-specific disease burden available in many of the 98 countries considered, nearly all models need to extrapolate from settings where data are available to those where data are absent. This, together with imperfect knowledge of aspects of the epidemiology of each pathogen (e.g. case fatality ratios, transmissibility, disease progression rates) means that uncertainty in vaccine impact estimates from a single model can be substantial. Here, this uncertainty is quantified probabilistically, with each modelling group providing 200 model runs spanning the range of parametric uncertainty in their models.

A second source of uncertainty is structural: different modelling groups make different subjective choices about how to represent disease epidemiology and may use different data for model parameterisation. In addition, the models within VIMC vary substantially: in their type (static cohort models versus transmission-dynamic models), in their complexity (e.g. in the representation of age effects), and in their approaches to calibration and validation (from formal statistical likelihood approaches to more ad-hoc calibration). VIMC therefore includes at least two models for each pathogen (with the exception of YF) and combines results from different models to derive central estimates of impact and to better quantify underlying uncertainty (see Methods).

A limitation of our current analysis is that we do not currently evaluate uncertainty in demographic estimates and estimates of past and future vaccine coverage. Developing principled approaches to doing so is a topic of current research, but is made challenging by the limited information available on uncertainty in UNWPP demographic estimates and in WUENIC and Gavi operational forecast vaccine coverage estimates.

In addition, our study has only focused on 98 low- and middle- income countries. The countries considered here have the highest burden from the 10 pathogens considered, see table S9 in the SI for relative proportions. Therefore, there has been a greater focus on supporting vaccine introduction and implementation in these countries, mainly through Gavi (the vaccine alliance), see table S8 for a list of countries with introduced vaccines. These 98 countries include the 73 countries1 eligible for gavi support (gavi73-countries) and 25 other countries that are of interest to the funders.

For most vaccines not yet introduced in some countries, we assume that once the vaccine introduced in that country, the coverage would reach the same coverage of a reference vaccine (e.g. DTP3) in 2 to 3 years. However, in some countries, there has been significant delays in implementing the vaccine due to shortages in supply18 and some countries such as India have initially introduced the vaccine in a few states to assess the feasibility of a new oral vaccine into their programme19. Therefore, the use of a reference vaccine for Rota vaccination coverage for countries that have had problems or delays in introduction and scale up might have led to an overestimation of impact.

The majority of models within VIMC adopt a ‘bottom-up’ approach to modelling disease burden and thus the impact of vaccination. These models represent time- and age-varying pathogen-specific infection or disease rates in each country, then model mortality as affecting a fraction of those infected by applying a case fatality ratio (generally estimated from a combination of longitudinal epidemiological studies and surveillance data) to resulting case incidence estimates. As the disease burden attributed to each pathogen is modelled separately, there is a theoretical risk of overestimating deaths due to a failure to account for competing causes of mortality, particularly in the under-5s, where most mortality is concentrated. However, in the 2019 annual birth cohort, UNWPP projections estimate all-cause under-5 mortality at 4∙9% for the 98 countries considered. We estimate the 10 pathogens we consider will cause approximately one seventh of this (0∙7% (0∙48-1∙4%)). With such low absolute proportions, the effect of competing hazards of death on overall mortality estimates is negligible. Conversely, when assessing deaths averted, we consider the counterfactual of no vaccination for each vaccine antigen separately, subsequently summing across all vaccines, since one child’s life can be saved multiple times.

For most pathogens, we currently model infection risk as homogeneous within individual countries (the exceptions being the YF, MenA and JE models). Furthermore, no models in this study account for geographic or socioeconomic clustering of vaccine coverage, or for any potential correlation between access to healthcare (including vaccines) and disease risk. Thus, we may be ignoring disadvantaged sub-populations in countries with lower than average access to vaccines and/or higher than average intrinsic exposure to infection. Subnational stratification of vaccine impact estimates are a priority for future work but require similarly fine-grained estimates of vaccine coverage 20 and disease burden.

Last, in making long-term projections of disease burden and intervention impact, it is necessary to make assumptions about the likely improvements in treatment and disease outcomes in future decades. This is a particular issue for HepB and HPV, where cancer screening and treatment services can make a substantial difference to disease-related mortality 21, or for measles where decreasing background under-five mortality can significantly reduce case-fatality ratios 22. The HPV and HepB models included in VIMC currently make conservative (i.e. relatively pessimistic) assumptions about improvements in cancer screening and treatment in low income countries.

More generally, the estimates provided here should not be viewed as immutable; our understanding of the epidemiology and disease burden caused by all 10 pathogens continues to improve, and models of those diseases should likewise continue to be refined. In addition, future vaccine coverage is unlikely to precisely match the coverage projections used here. Thus, the outputs - whether estimates of the impact of past immunisation activities or projections of future impact - will also change. However, the results in this paper provide the most comprehensive and definitive assessment to date of the impact of the dramatic advances in immunisation coverage in LMICs in the last two decades.

Finally, it is very important to increase vaccine coverage and maintain high overage levels in all countries so as not to allow the coverage gains achieved since 2000 to slip back. This requires continued political commitment, funding, civil society engagement (in promoting benefits and countering hesitancy), improving public trust and confidence in the safety and efficacy of vaccines 23, and strengthening immunisation programmes through education, training and supervision 24.

# Acknowledgements

We thank Gavi, the Vaccine Alliance and the Bill & Melinda Gates Foundation for funding VIMC (BMGF grant number: OPP1157270). We also acknowledge joint Centre funding from the UK Medical Research Council and Department for International Development, which supported aspects of VIMC’s work.

# Authors’ contributions statement

# VIMC secretariat: Xiang Li and CM contributed to study design, data analysis, figures, and writing. ZMC contributed to study design, data analysis, and data interpretation. SEL contributed to data analysis, data interpretation and writing. TG and NF led on study design and writing and contributed to figures, data analysis and data interpretation; HLJ contributed to study design, data collection (input data for models), data interpretation, and writing. NCG reviewed the models for HPV, Rota and Men A and contributed to manuscript revision. WH contributed to figures, data analysis and data curation. KW contributed to writing and data coordination. KAMG contributed to writing and data interpretation. Cambridge MenA model: AK and CLT contributed to the study (model) design, interpretation, and writing; AK also contributed to the study (model) implementation. CDA HepB model: HR, DRS and IG contributed to study design, data analysis, and data interpretation; DRS also contributed to literature search and data collection. Goldstein HepB model: Xi Li contributed to analysing hepatitis B vaccine impact. Harvard HPV model: SR contributed to study design, data analysis, and data interpretation; S Sweet contributed to study design, data analysis, and model design; S Sy contributed to study design and model design. Imperial YF model: KAMG and KJ contributed to data analysis, data interpretation, and critical revision of the draft. Imperial HepB model: MJdV wrote the model description for the paper and contributed to running and design of the model; SN and TBH contributed to design of the model. JHU model for Hib, PCV and rota (LiST): YT ran the analysis to produce impact estimates using the Lives Saved Tool, and contributed to drafting the model descriptions in the supplementary information; EDC supported vaccination impact modeling functionality within the Lives Saved Tool, and contributed to drafting the model descriptions in the supplementary information; NW primarily worked on developing assumptions used in the LiST model, and also worked with the team in setting up the approach used in the models. JHU rubella model: JL, AW and ST contributed to the data collection and data analysis. KPW MenA model: MLJ contributed to study design, data analysis, data interpretation, and critical review of the manuscript. LSHTM models for HPV, measles, Hib, PCV and rotavirus: MJ designed, developed and parameterised HPV and measles models, and contributed to writing of manuscript and description of HPV, measles, PCV, Hib and rotavirus models; AC designed, developed and parameterised PCV, Hib and rotavirus models, and contributed to writing of manuscript and description of PCV, Hib and rotavirus models; KA designed, parameterised and produced results for HPV, PCV and Hib models, and contributed to writing of manuscript and description of measles, HPV, PCV, Hib and rotavirus models; PK coded, designed, parameterised and produced results for measles and rotavirus models, and contributed to writing of manuscript and description of measles and rotavirus models; KvZ coded, parameterised and produced simulations for measles, HPV, PCV, Hib and rotavirus models, and contributed to writing of description of measles, HPV, PCV, Hib and rotavirus models; HT coded, parameterised and produced simulations for measles, PCV, Hib and rotavirus models; CS helped to design and parameterise PCV, Hib and rotavirus models; SV helped to code, design and parameterise measles model; MB helped to design and parameterise HPV model. Notre Dame JE model: SMM contributed to data collection, data analysis, data interpretation, and writing. OUCRU JE model: DMN, QMT and HEC contributed to study design and data interpretation; DMT and QMT also contributed to data analysis; QMT also contributed to literature search; HEC also contributed to writing. PHE rubella model: EV commented on rubella programming, interpreted output, and commented on draft manuscript; TP contributed to programming and running the rubella model, collating and analysing output, commenting on drafts of manuscript. PSU measles model: MJF and KE contributed to data analysis and drafting text on model description. Xiang Li and CM contributed equally, as the VIMC science team throughout 2019. KA, HEC, MJ, HLJ, TP and EV contributed equally, as the writing group. MB, EDC, AC, MJdV, KE, MJF, IG, NCG, TBH, MLJ, KJ, AK, PK, JL, Xi Li, SMM, SN, DMN, HR, DRS, SR, CS, S Sweet, S Sy, YT, HT, QMT, CLT, ST, KvZ, SV, NW, and AW contributed equally, as non-writing group Consortium members.

# Funding statement

VIMC is jointly funded by Gavi, the Vaccine Alliance, and the Bill & Melinda Gates Foundation (BMGF). Funding from Gavi is channelled via VIMC to the Consortium's modelling groups (VIMC-funded institutions represented in this paper: Imperial College London, London School of Hygiene & Tropical Medicine, Oxford University Clinical Research Unit, Public Health England, Johns Hopkins University, The Pennsylvania State University, Center for Disease Analysis Foundation, Kaiser Permanente Washington, University of Cambridge, University of Notre Dame, Harvard University, Conservatoire National des Arts et Métiers). Funding from BMGF was used for salaries of the Consortium secretariat (authors represented here: Professor Hallett, Professor Grassly, Dr Cucunuba, Professor Jit, Dr Xiang Li, Dr Mukandavire, Dr Echeverria-Londono, Ms Woodruff, Professor Ferguson, Dr Garske); and channelled via VIMC for travel and subsistence costs of all Consortium members (all authors). We also acknowledge funding from the Abdul Latif Jameel Institute for Disease and Emergency Analytics (J-IDEA), and joint Centre funding from the UK Medical Research Council and Department for International Development, which supported aspects of VIMC’s work. In addition, the following funding declarations are noted: Mr Gamkrelidze, Dr Razavi and Mr Razavi-Shearer are employees of the Center for Disease Analysis Foundation which had no role in study design, data collection and analysis, interpretation of data, or preparation of the manuscript. Development of LSHTM's models for HPV, measles, PCV, Hib and rotavirus was funded by WHO, Gavi and BMGF under several grants, past and current. BMGF supported the development and maintenance of the Lives Saved Tool.

# Competing interest statement

This publication is authored by members of the Vaccine Impact Modelling Consortium (VIMC, www.vaccineimpact.org). VIMC is jointly funded by Gavi, the Vaccine Alliance, and by the Bill & Melinda Gates Foundation. The views expressed are those of the authors and not necessarily those of the Consortium or its funders. The funders were given the opportunity to review this paper prior to publication, but the final decision on the content of the publication was taken by the authors. Consortium members received funding from Gavi and BMGF via VIMC during the course of the study (see funding statement above). In addition, the following potential conflicts of interest were disclosed: Dr Eilertson and Dr Ferrari report grants from Bill and Melinda Gates Foundation, outside the submitted work. Dr Gamkrelidze, Dr Razavi and Dr Razavi-Shearer report grants from John C Martin Foundation during the conduct of the study; and grants from AbbVie, Gilead, Intercept, Pan American Health Organization, and Association of State and Territorial Health Officials outside the submitted work. Dr Gaythorpe reports personal fees from Wellcome Genome Campus advanced courses and scientific conferences. Dr Hallett reports grants and personal fees from WHO, Pharos, Avenhir Health, outside the submitted work. Dr Nayagam reports Consultancy work for WHO and Pharos Global Health Advisors. Dr Trotter reports personal fees from GSK, outside the submitted work. Professor Ferguson reports grants from UK Medical Research Council during the conduct of the study, and grants from NIH NIGMS, UK National Institute of Health Research, Janssen Pharmaceuticals, outside the submitted work. Dr Garske reports grants from Janssen Pharmaceuticals, outside the submitted work. Dr Verguet reports grants from BMGF and Gavi, outside the submitted work. MJ reports grants from WHO and BMGF.

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# Tables

**Table 1**: Pathogen names, vaccination schedules, modelling groups and model types included in VIMC. Static models only model the direct effect of vaccination on vaccinated cohorts assuming that pathogen transmission intensity is not modified by vaccination coverage. Dynamic models simulate infectious disease transmission dynamics and model both the direct effect of vaccination on vaccinated cohorts and indirect/herd effect of vaccination on unvaccinated populations. See SI model descriptions for more details and citations for each model.

|  |  |  |
| --- | --- | --- |
| **Pathogen/vaccine (short name): *Vaccination schedule*** | **Lead institution for model** | **Model type** |
| Hepatitis B (HepB):  · *Birth dose*  · *Infant 3 doses (< 1 y)* | Center for Disease Analysis | dynamic |
| Imperial College London | dynamic |
| Independent (model developed by Goldstein et al. 25 ) | static |
| Human papillomavirus (HPV):  *- adolescent girls (2 doses)* | Harvard School of Public Health | static |
| London School of Hygiene and Tropical Medicine (LSHTM) | static |
| *Haemophilus influenzae* type B (Hib):  · *Infant 3 doses (< 1 y)* | Johns Hopkins University | static |
| LSHTM | static |
| Japanese encephalitis (JE):  · *Infant dose (< 1 y)* | Oxford University | dynamic |
| University of Notre Dame | dynamic |
| Measles (measles):  *· 1st dose (≤ 1 y)*  *· 2nd dose (< 2 y)* | LSHTM | dynamic |
| Pennsylvania State University | dynamic |
| *Neisseria meningitidis* serogroup A (MenA):  · *Infant dose (< 1 y)* | University of Cambridge | dynamic |
| Kaiser Permanente Washington | dynamic |
| Streptococcus pneumoniae (PCV):  · *Infant 3 doses (< 1 y)* | Johns Hopkins University | static |
| LSHTM | static |
| Rotavirus (rota):  · *Infant 2 doses (< 1 y)* | Johns Hopkins University | static |
| LSHTM | static |
| Rubella (rubella):  *· 1st dose (< 1 y)*  *· 2nd dose (< 2 y)* | Johns Hopkins University | dynamic |
| Public Health England | dynamic |
| Yellow fever (YF):  · *Infant dose (< 1 y)* | Imperial College London | static |

**Table 2**: Estimated total deaths averted (in thousands) by vaccination and deaths averted per thousand individuals vaccinated in different time-period ranges across the 98 countries considered, stratified by pathogen. Both all ages and under-5 deaths averted are shown. Corresponding estimates for DALYs averted are in Table S3a. The values are mean estimates and ranges are the 95% credible intervals (2.5 and 97.5 quantiles).

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Disease** | **Time** | **Deaths averted (1000s)** | **Deaths averted per 1000 vaccinated individuals** | **Deaths averted (1000s), < 5** | **Deaths averted per 1000 vaccinated individuals, <5** |
| HepB | 2000-2019 | 640 (190-1500) | 0.4 (0.1-0.9) | 270 (51-1100) | 0.2 (0-0.6) |
| HepB | 2020-2030 | 1600 (460-2900) | 1 (0.3-1.8) | 230 (59-810) | 0.1 (0-0.5) |
| HepB | 2000-2030 | 2200 (660-3700) | 0.7 (0.2-1.1) | 500 (110-1900) | 0.1 (0-0.5) |
| Hib | 2000-2019 | 1600 (720-2400) | 2.5 (1.1-3.7) | 1600 (720-2400) | 2.5 (1.1-3.7) |
| Hib | 2020-2030 | 2000 (730-3200) | 2.4 (0.9-3.7) | 2000 (730-3200) | 2.4 (0.9-3.7) |
| Hib | 2000-2030 | 3600 (1400-5500) | 2.4 (1-3.7) | 3600 (1400-5500) | 2.4 (1-3.7) |
| HPV | 2000-2019 | 0.013 (0-0.031) | 0 (0-0) | 0 (0-0) | 0 (0-0) |
| HPV | 2020-2030 | 7.4 (1.4-15) | 0 (0-0) | 0 (0-0) | 0 (0-0) |
| HPV | 2000-2030 | 7.4 (1.4-15) | 0 (0-0) | 0 (0-0) | 0 (0-0) |
| JE | 2000-2019 | 75 (6.1-190) | 0.2 (0-0.4) | 52 (4.2-130) | 0.2 (0-0.4) |
| JE | 2020-2030 | 160 (16-420) | 0.4 (0-0.9) | 86 (8.1-230) | 0.2 (0-0.5) |
| JE | 2000-2030 | 240 (22-600) | 0.3 (0-0.6) | 140 (12-350) | 0.2 (0-0.5) |
| Measles | 2000-2019 | 33000 (26000-44000) | 6.9 (5.5-9.2) | 32000 (26000-43000) | 7.9 (6.4-11) |
| Measles | 2020-2030 | 23000 (9400-31000) | 9.1 (3.7-12) | 23000 (10000-31000) | 9 (4-12) |
| Measles | 2000-2030 | 56000 (39000-74000) | 7.7 (5.4-11) | 55000 (40000-73000) | 8.3 (6-11) |
| MenA | 2000-2019 | 73 (12-160) | 0.3 (0-0.6) | 19 (2.4-38) | 0.1 (0-0.3) |
| MenA | 2020-2030 | 140 (52-270) | 0.5 (0.2-1.1) | 33 (11-59) | 0.1 (0-0.2) |
| MenA | 2000-2030 | 210 (130-360) | 0.4 (0.3-0.7) | 52 (32-81) | 0.1 (0.1-0.2) |
| PCV | 2000-2019 | 610 (320-1100) | 2.5 (1.3-4.2) | 610 (320-1100) | 2.5 (1.3-4.2) |
| PCV | 2020-2030 | 1600 (730-2900) | 2.3 (1-4.1) | 1600 (730-2900) | 2.3 (1-4.1) |
| PCV | 2000-2030 | 2200 (1000-4000) | 2.3 (1.1-4.1) | 2200 (1000-4000) | 2.3 (1.1-4.1) |
| Rota | 2000-2019 | 150 (100-200) | 0.8 (0.6-1.1) | 150 (100-200) | 0.8 (0.6-1.1) |
| Rota | 2020-2030 | 590 (370-820) | 0.8 (0.5-1.1) | 590 (370-820) | 0.8 (0.5-1.1) |
| Rota | 2000-2030 | 740 (470-1100) | 0.8 (0.5-1.1) | 740 (470-1100) | 0.8 (0.5-1.1) |
| Rubella | 2000-2019 | 80 (38-200) | 0.1 (0-0.1) | 80 (38-200) | 0.1 (0-0.2) |
| Rubella | 2020-2030 | 260 (130-590) | 0.1 (0.1-0.3) | 260 (130-590) | 0.1 (0.1-0.3) |
| Rubella | 2000-2030 | 340 (180-780) | 0.1 (0-0.2) | 340 (180-780) | 0.1 (0.1-0.2) |
| YF | 2000-2019 | 1300 (450-2800) | 3.5 (1.1-7.1) | 500 (150-1100) | 2.3 (0.7-4.9) |
| YF | 2020-2030 | 2300 (740-4800) | 9 (2.8-19) | 510 (150-1100) | 2 (0.6-4.2) |
| YF | 2000-2030 | 3600 (1100-7500) | 5.7 (1.8-12) | 1000 (310-2200) | 2.1 (0.7-4.5) |
| Total | 2000-2019 | 37000 (30000-48000) | 3.7 (3-4.7) | 36000 (29000-46000) | 4.1 (3.2-5.2) |
| Total | 2020-2030 | 32000 (17000-41000) | 3.2 (1.8-4) | 28000 (15000-36000) | 2.9 (1.6-3.7) |
| Total | 2000-2030 | 69000 (52000-88000) | 3.4 (2.6-4.3) | 64000 (48000-82000) | 3.5 (2.7-4.4) |

# Figures

**Figure 1.** Map of vaccine coverage across the 10 pathogens considered, calculated as mean number of vaccines received per child born in (A) 2000, (B) 2010, (C) 2019. The colour scale shows the expected number of vaccines received per child in each country. (D) Routine vaccine coverage for each pathogen, from 2000 to 2019, averaged across all 98 countries except for JE, MenA and YF which were averaged across the 16, 26 and 32 endemic countries for those pathogens, respectively. The average was obtained by dividing total vaccine doses by the total eligible population.

**Figure 2**: Estimates of disease-specific deaths by calendar year from 2000 to 2030 across all 98 countries, for reported and projected vaccine coverage and counterfactual (no vaccination) coverage. Continuous blue and red lines show estimates of deaths for default and no vaccination coverage scenarios for all ages, respectively. The corresponding shaded areas show the 95% credible region (2.5 and 97.5 quantiles). The grey shaded parts show the area where the 95% credible regions for the counterfactual and reported and projected vaccine coverage estimates overlap.

**Figure 3**: Central estimates of deaths averted in the 98 countries: A) by calendar year (summing across all ages) and pathogen; B) by year of birth (summing across lifetime) and pathogen; C) proportion of lifetime deaths due to the 10 pathogens in the no-vaccination counterfactual that are predicted to be averted by vaccination, by country across 2000-2019 birth cohorts.

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