

Estimates of the health impact of vaccination disaggregated by year of delivery

VIMC

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Background

The Vaccine Impact Modelling Consortium (VIMC) generates estimates of the impact of vaccination for 98 low- and middle-income countries in terms of deaths, cases and disability adjusted life years (DALYs) averted. Using estimates of vaccination coverage at a national level as inputs (coverage data is obtained from WUENIC and Gavi operational forecast), VIMC generates estimates of disease burden for current vaccination levels and for a counterfactual scenario of no vaccination. Impact is then calculated as the difference in burden between these scenarios. Estimates can be temporally disaggregated cross-sectionally (e.g. deaths averted in a specific year) or by year of birth (lifetime impact per birth cohort). The first VIMC paper **Estimating the health impact of vaccination against 10 pathogens in low and middle income countries from 2000 to 2030** (<https://medrxiv.org/cgi/content/short/19004358v1>) presents such estimates.

However funders are naturally interested in evaluating the impact per fully vaccinated person (FVP) - i.e. estimating the future impact of vaccination occurring in a specific year. Therefore, we developed an approach to generating such estimates which takes account of both direct and indirect impacts of vaccination.

This note describes vaccine delivery strategies and the three vaccine impact calculation methods used by VIMC, i.e. impact by calendar year (cross-sectional), by year of birth (lifetime), and by year of vaccination.

Vaccine delivery strategies

For diseases (i.e. hepatitis B (HepB), haemophilus influenzae type B (Hib), pneumococcal disease and rotavirus) where routine vaccination is given as a single dose or several closely separated doses, we estimate disease burden by year and age for two scenarios, with and without vaccination.

However, vaccine delivery methods are more varied for some vaccines. Measles and rubella have first and second doses that are more than a year apart. Many more vaccines are also delivered via preventive campaigns (human papillomavirus (HPV), Japanese encephalitis, meningitis A, rubella, yellow fever), or as catch-up campaigns to target pockets of unvaccinated populations (measles, rubella, yellow fever). Campaigns are one-off events that typically target a specific geographic area and a larger age-range than routine vaccination.

For vaccines that are delivered through a variety of strategies, we estimate the impact for each vaccine delivery strategy separately, by estimating disease burden for several vaccination scenarios. For instance, for measles, there are two doses of routine vaccination, 1st dose (MCV1), given typically at 9 months of age, 2nd dose (MCV2), given at age 2 or 3 years, and a variety of campaigns, or supplementary immunisation activities (SIAs). We therefore evaluate disease burden for the following scenarios:

- No vaccine
- MCV1,
- MCV1 + MCV2,
- MCV1 + MCV2 + SIA

and calculate the incremental impact of each delivery strategy as:

- Impact (MCV1) = burden (no vaccination) - burden (MCV1),

- Impact (MCV2) = burden (MCV1) - burden (MCV1 + MCV2)
- Impact (SIA) = burden (MCV1 + MCV2) - burden (MCV1 + MCV2 + SIA)

Methods of calculating impact

Cross-sectional

This method calculates the difference in annual disease burden between two scenarios (e.g., no vaccine vs MCV1, MCV1 vs MCV1 + MCV2, etc). To make the presentation clear, we use baseline and focal vaccine strategy to denote these two scenarios for impact calculation. For example, taking difference between baseline (no vaccination) and focal (MCV1) vaccine strategy burden estimates derives MCV1 impact estimates. Similarly, the difference between baseline (MCV1) and focal (MCV1 + MCV2) vaccine strategy burden estimates gives MCV2 impact estimates.

Denote $B_b(a, y, c)$ and $B_f(a, y, c)$ as burden estimate for baseline and focal vaccine strategy for age a , in year y and country c , respectively. Vaccine impact $D(a, y, c)$ is evaluated as the difference between baseline and focal vaccine delivery strategy burden estimates, i.e.

$$D(a, y, c) = B_b(a, y, c) - B_f(a, y, c)$$

Cross-sectional impact for country c in year y is reported as

$$D_0(y, c) = \sum_{a \in A} D(a, y, c)$$

where A represents the set of age groups modelled.

While the resulting estimates are intuitively easy to understand, they fail to represent the long-term future impact of vaccination on individual disease risk (e.g. for HepB or HPV). In addition, the impact estimates cannot be linked to specific vaccination activities.

Lifetime

To capture the long-term impact of vaccines we need to aggregate over the lifetime of vaccinated birth cohorts rather than cross-sectionally across ages in any given year. This was the approach adopted by Gavi for evaluating impact its previous strategy period (2012-15). Lifetime impact for country c and cohort k is calculated as

$$D_1(k, c) = \sum_{y-a=k} D(a, y, c).$$

We calculate impact for birth cohorts from 2000 to 2030. Note that VIMC models calculate disease burden up to 2100, so the burden from people older than 70 years in 2100 is not included in our estimates. This will lead to a slight underestimation of impact for diseases with onset later in life, in particular HepB and HPV.

A lifetime or cohort approach to presenting impact is appropriate for capturing the direct effects of vaccination in protecting the immunised individual. However, indirect effects of vaccination (acting via herd immunity) play out across the whole population.

Impact by year of vaccination

Here we describe the approximate approach used by VIMC to estimate vaccine impact by year of vaccination and present the resulting estimates. The method we have adopted is similar to evaluating lifetime by birth cohort but takes a slightly coarser approach to allocation of impact. Due to the nature of the data on vaccination activities considered we use slightly different variants for routine and campaign impact.

For routine vaccination activities we aggregate impact over the lifetime of cohorts born between 2000 and 2030 and followed until 2100. In contrast to the evaluation of lifetime impact for individual birth cohorts,

here we initially aggregate the impact across all birth cohorts of interest, and then distribute this over the years of vaccination proportionally to the number of fully vaccinated persons (FVPs) achieved in any given year. Since we only evaluate disease burden to 2100 we neglect impacts in those who are over 70 in 2100.

Denote FVPs for vaccine v in country c and year y as $FVP_v(y, c)$. We define the impact per FVP as

$$m_v(c) = \frac{\sum_{y-a \in Y-a_r} D(a, y, c)}{\sum_{y \in Y} FVP_v(y, c)}$$

where a_r is routine vaccination age, Y is the vaccination years of interest ($Y = [2000, 2030]$ for VIMC), and $Y - a_r$ represents cohorts receiving vaccinations in years Y .

We then estimate the impact by year of vaccination for routine vaccination v in country c and year y as

$$D_{2v}(y, c) = m_v(c) \times FVP_v(y, c)$$

While we capture the impact that blurs between birth cohorts within the period of interest, there are boundary effects where we do not account for impact generated by indirect effects in cohorts before or after the 2000-2030 range. However, this metric does include indirect effects generated by vaccination outside the period of interest that manifests in birth cohorts within the period of interest.

For campaigns, we aggregate incremental impact over all ages (whether within the 2000-2030 cohort range or not) during the whole period from 2000 to 2100. This is because we do not attempt to predict future campaign coverage past 2030. Therefore, campaign impact on people outside the 2000-2030 cohorts all come from campaign years between 2000 and 2030.

The impact per FVP for vaccine v is defined as

$$m_v(c) = \frac{\sum_{y \in Y_1} \sum_{a \in A} D(a, y, c)}{\sum_{y \in Y_2} FVP_v(y, c)}$$

where A and Y_1 are the set of age groups and calendar years modelled, respectively, and Y_2 is the vaccination years of interest ($Y_2 = [2000, 2030]$ for VIMC).

We then estimate the impact by year of vaccination for campaigns for vaccine v in country c and year y as

$$D_{2v}(y, c) = m_v(c) \times FVP_v(y, c)$$

It should be emphasised that there is no perfect approach to estimating vaccine impact by year of vaccination. Our method has the advantage of distributing indirect effects of vaccination equally between doses across the 2000-2030 birth cohorts. However, by calculating a single estimate of impact per FVP over the period 2000-2100 and then using this ratio to estimate impacts by year of vaccination, we average the effects of any temporal changes in disease incidence in that time period.

Estimates of impact by year of vaccination

Here we present estimates of vaccine impact by year of vaccination and the corresponding values of the cross-sectional and lifetime impacts presented in the first VIMC paper (**Estimating the health impact of vaccination against 10 pathogens in low and middle income countries from 2000 to 2030** <https://medrxiv.org/cgi/content/short/19004358v1>). We also present central estimates for the ‘focal’ model for each disease historically used by Gavi for reporting in its current strategy period. However, VIMC now includes at least two models for each disease, and future impact estimates will use model averages (also presented). It should be noted that these values are based on the Gavi Operational Forecast 15, which is used in the first VIMC paper, and not the Operational Forecast 16 that underpins the impact projections presented in Gavi’s 2021-2025 Investment Opportunity.

Table 1 and Table 2 show estimates of deaths averted and deaths averted per 1000 FVPs across the 73 Gavi-supported countries considered by VIMC over the period 2021-2025, for the three different impact

Table 1: Total deaths averted (in thousands) by vaccination for the period 2021-2025.

disease	Focal model			Model average		
	cross-sectional	lifetime	by year of vaccination	cross-sectional	lifetime	by year of vaccination
HepB	120	3300	3400	390 (110-700)	5200 (3100-8700)	5300 (3200-8600)
Hib	1300	1300	1400	880 (330-1400)	880 (330-1400)	920 (360-1500)
HPV	0.11	2000	1400	0.29 (0-63)	1900 (1600-2100)	1300 (1100-1600)
JE	31	58	70	30 (3-78)	55 (6-150)	64 (6.7-160)
Measles	11000	11000	11000	10000 (5100-13000)	10000 (4300-14000)	11000 (6800-14000)
MenA	74	120	140	60 (3.6-180)	83 (37-150)	88 (36-160)
PCV	900	940	940	670 (310-1200)	690 (310-1300)	700 (320-1300)
Rota	280	300	290	260 (160-360)	270 (160-380)	270 (160-380)
Rubella	150	170	320	100 (52-260)	120 (62-300)	260 (120-650)
YF	880	1900	2800	960 (310-2000)	2100 (680-4200)	3000 (1000-6200)

^a The focal Hib/PCV/Rota model (LiST) updated their model recently. The model now provides higher impact estimates than their original central estimates. For consistency, we now use mean of stochastics to represent focal Hib/PCV/Rota point estimates in this table. For reference, the previous version of the model projected deaths averted by year of vaccination for Hib, PCV and Rota as 990, 700, 200 (in thousands).

^b The focal HepB model has missing pre-2000 cohorts in their central burden estimates. This would cause lower focal cross-sectional impact (110 thousand deaths averted). Therefore, we use mean of stochastics (120 thousand deaths averted) to represent focal HepB cross-sectional impact point estimates in this table.

Table 2: Total death averted per 1000 FVPs of vaccination given for the period 2021-2025.

disease	Focal model			Model average		
	cross-sectional	lifetime	by year of vaccination	cross-sectional	lifetime	by year of vaccination
HepB	0.24	6.6	6.8	0.77 (0.22-1.4)	10 (6.2-18)	10 (6.3-17)
Hib	3.9	3.9	4	2.6 (0.97-4.1)	2.6 (0.96-4.1)	2.7 (1-4.2)
HPV	0.0012	14	16	0.0033 (0-0.71)	13 (11-15)	15 (12-18)
JE	0.18	0.46	0.41	0.17 (0.017-0.45)	0.44 (0.048-1.2)	0.37 (0.039-0.92)
Measles	11	11	9.7	10 (5-13)	10 (4.4-14)	11 (6.8-14)
MenA	0.67	1.1	1.2	0.54 (0.033-1.6)	0.75 (0.33-1.3)	0.8 (0.32-1.4)
PCV	3.3	3.4	3.4	2.4 (1.1-4.4)	2.5 (1.1-4.6)	2.5 (1.1-4.6)
Rota	0.9	0.95	0.94	0.83 (0.53-1.2)	0.86 (0.54-1.3)	0.85 (0.53-1.2)
Rubella	0.16	0.18	0.62	0.1 (0.054-0.26)	0.13 (0.066-0.32)	0.27 (0.12-0.67)
YF	2.8	16	13	3.1 (1-6.5)	18 (5.8-36)	9.9 (3.2-20)

^a The focal Hib/PCV/Rota model (LiST) updated their model recently. The model now provides higher impact metrics than their original central estimates. For consistency, we now use mean of stochastics to represent focal Hib/PCV/Rota point estimates in this table. For reference, the previous version of the model projected deaths averted per 1000 FVPs for Hib, PCV and Rota as 3, 2.6, 0.64 .

^b The focal HepB model has missing pre-2000 cohorts in their central burden estimates. This would cause lower focal cross-sectional impact metric (0.22 deaths averted per 1000 FVPs). Therefore, we use mean of stochastics (0.24 deaths averted per 1000 FVPs) to represent focal HepB cross-sectional impact metric in this table.

aggregation approaches. The period 2021-2025 means calendar years for the cross-sectional view, birth cohorts for the lifetime view, and vaccination years for the year of vaccination view. The estimates in the tables below reflect all immunization activities in Gavi 73 countries, not just those activities supported by Gavi.