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## Methodology for key projections in Gavi’s Investment Opportunity 2026–2030

Gavi’s Investment Opportunity 2026–2030 (Gavi 6.0 strategic period) presents projections of the expected number of children countries will immunise with Gavi support and the associated health and economic impacts. This technical appendix summarises the methodology used to derive these projections and other key pieces of evidence.

### Underlying assumptions and forecasts

There are two key components underlying the impact projections. The first is how Gavi defines the support it provides to countries. The second is the set of assumptions used to produce forecasts of future immunisation coverage for vaccines in the Gavi portfolio. The following section describes these in more detail.

### Gavi support

Like other institutional investment cases in the health space, Gavi takes a contribution perspective to reflect the impact of immunisation activities undertaken by countries with the support of the Vaccine Alliance. However, historically and for this investment opportunity, Gavi ‘support’ is defined narrowly to only count the impact of the new vaccines that Gavi has helped each country introduce and scale up, as opposed to counting the total impact of all immunisation activity across Gavi-supported countries.<sup>1</sup>

Effectively, Gavi counts the impact of vaccinations for which it provides direct financial support or catalytic support. The former includes financing to eligible countries for new vaccines (regardless of country transition phase and co-financing requirements), while the latter is counted during the five-year period immediately following a country’s transition out of Gavi direct support for a particular vaccine and is limited to the following cases:

- countries that introduce a vaccine with Gavi support and continue to finance routine delivery after Gavi support concludes;
- countries that self-finance routine delivery of a vaccine after Gavi finances the launch of the vaccine through a catch-up campaign; and
- countries that self-finance a vaccine but have access to Gavi-negotiated prices – e.g. pneumococcal conjugate vaccine (PCV) and human papillomavirus (HPV) vaccine.

In the 2026–2030 strategic period, approximately 90% of future deaths averted are expected to result from Gavi’s direct support, compared to 93% of future deaths averted in the 2021–2025 strategic period.

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<sup>1</sup> Gavi ‘support’ excludes the impact of vaccines that Gavi funds but did not help a country introduce, for example first dose of measles component of the measles-rubella vaccine.

The Investment Opportunity 2026–2030 numbers immunised and impact projections include supported vaccines delivered through routine systems and preventive campaigns, as follows: pentavalent; hexavalent; yellow fever; inactivated polio vaccine (IPV); pneumococcal conjugate vaccine (PCV); rotavirus; second dose of measles-containing vaccine (MCV2); measles-rubella; human papillomavirus (HPV); meningitis A (menA); multivalent meningococcal conjugate vaccine (MMCV); Japanese encephalitis (JE); typhoid conjugate vaccine (TCV); diphtheria, tetanus and pertussis (DTP)-containing boosters; hepatitis B birth dose; and oral cholera vaccine (OCV). New vaccines for which forecasts are not yet available, namely respiratory syncytial virus (RSV) and rabies, are not included – nor are vaccines newly approved for Gavi support under Gavi’s Vaccine Investment Strategy (VIS) 2024: dengue, tuberculosis and group B streptococcus. The numbers immunised and impact projections also exclude outbreak response vaccination (e.g. from use of stockpiles).

### Vaccine coverage forecasts

A key input to Gavi impact modelling is immunisation coverage estimates, which come mainly from the WHO/UNICEF Estimates of National Immunization Coverage (WUENIC);<sup>2</sup> countries’ administrative coverage estimates submitted through the WHO/UNICEF electronic Joint Reporting Form (eJRF) for historical values; and Gavi’s operational forecast for future values.

Future coverage of vaccines in the Gavi portfolio is based on analyses that are linked to Gavi’s financial forecasts. These projections – known as operational forecasts (OP) – forecast dose requirements for countries based on their historical trend of consumption of existing vaccines. This forecast of dose requirements is translated into the number of people immunised and is updated on an annual basis. Gavi 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. Coverage is then derived at the antigen level from the vaccine-level operational forecast. Following introduction, coverage of new vaccines is typically assumed to reach coverage of a reference vaccine (e.g. DTP3) within two to three years or longer for large countries, after which coverage is assumed to increase one percentage point per year up to a maximum of 90% or 95%, depending on the vaccine.

Since Gavi ultimately reports on progress on increasing routine immunisation coverage using WUENIC, the implied routine immunisation coverage in the forecast was adjusted so that the coverage in 2023 is consistent with historical coverage in 2022 as reported in the July 2023 update of WUENIC. This adjustment was not made for vaccines without WUENIC estimates, which include future new vaccine introductions, HPV vaccine, malaria vaccine, several VIS vaccines and vaccination campaigns.

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<sup>2</sup> WHO/UNICEF Estimates of National Immunization Coverage, <https://www.who.int/teams/immunization-vaccines-and-biologicals/immunization-analysis-and-insights/global-monitoring/immunization-coverage/who-unicef-estimates-of-national-immunization-coverage>

Target populations were standardised based on targeted age groups using population estimates from the United Nations Department of Economic and Social Affairs Population Division World Population Prospects (WPP) 2022.<sup>3</sup> It should be noted that the UNPD WPP estimates will be updated in July 2024 (WPP 2024), and as such the next iterations of WUENIC (July 2024) and the Gavi operational forecast (OPv22) will use the WPP 2024 estimates.

The future number of individuals expected to be immunised with different vaccines as presented in the Investment Opportunity is based on an updated version of Gavi's latest operational forecast (OPv21), released in November 2023.<sup>4</sup> To support Gavi Board discussions between December 2023 and June 2024 on the design of Gavi's 2026–2030 strategy, the OPv21 forecast was updated to examine the costs and benefits of different options, reflect Board priorities, and incorporate any additional information on supply and country demand. This version is referred to as OPv21.1. The final vaccine coverage and impact figures that underpin Gavi's 2026–2030 strategy (approved by the Gavi Board at its 6–7 June 2024 meeting) – and the figures in the Investment Opportunity across Gavi 5.0/5.1 and 6.0 – are based on the OPv21 for 2023–2025 and the OPv21.1 for 2026–2030, with adjustments made to the OPv21 to account for implications from introductions and campaigns in the OPv21.1.

Additional points to note on the projected numbers immunised in Figure 7 of the Investment Opportunity:

- For HPV vaccine, number immunised is based on either the first or the second dose depending on the country schedule in a given year; most Gavi-supported HPV vaccine programmes are expected to use a one-dose schedule in Gavi 6.0.
- For malaria vaccine, number immunised is defined as the number of individuals reached with the fourth dose of malaria vaccine.
- For oral cholera vaccine (OCV) preventive campaigns, number immunised is defined as the number of individuals who were targeted for a second preventive OCV dose.
- For hexavalent, number immunised represents the third dose; the number immunised with fourth dose is projected to be 747,000 in Gavi 5.0/5.1 and 23 million in Gavi 6.0.
- For DTP-containing boosters, numbers immunised include all three boosters (standalone for ages 2 years, 5–6 years, 10–11 years). Gavi vaccine support is available only for the first booster (second year of life); Vaccine Introduction Grant (VIG) support is available for all three boosters.

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<sup>3</sup> United Nations Department of Economic and Social Affairs Population Division 2022 Revision of World Population Prospects, <https://population.un.org/wpp/>

<sup>4</sup> The latest aggregate vaccine volume forecast ("Base Demand Forecast" v21) is publicly available at: [https://www.gavi.org/sites/default/files/2024-01/BDF\\_v21\\_public-version.pdf/](https://www.gavi.org/sites/default/files/2024-01/BDF_v21_public-version.pdf/)

For HPV vaccine, note that the number of girls reached in Gavi 6.0 will depend on the launch timing of the HPV vaccine programme in India, including the extent to which multi-age cohort vaccinations (MACs) occur in late Gavi 5.0/5.1 versus early 6.0. The cumulative number of girls reached by 2030 since Gavi support for HPV vaccine began in 2014 will remain similar regardless of this timing. Forecasts suggest the cumulative number of girls reached with Gavi support by 2030 will exceed 200 million.

### Children immunised with Gavi support: 500 million in 2026–2030

‘Unique children immunised’, as defined in the Gavi 5.0/5.1 Measurement Framework<sup>5</sup> with a target of over 300 million children in Gavi 5.0/5.1, looks across all Gavi-supported routine vaccines within a country and counts the number of individuals immunised with the vaccine that reached the most individuals in that country in a given year. It therefore tends to pick up on infant vaccines, which usually have the highest coverage. As the Gavi portfolio is increasingly expanding to reach older children and adolescents, this indicator is now less suitable to measure the number of children reached each year through routine immunisation with Gavi supported vaccines.

To address this limitation, Gavi has developed a new indicator, which is referred to simply as ‘children immunised’. The definition of this indicator is similar to ‘unique children immunised’, with the important difference that it counts the number of children immunised separately for each age group. Based on Gavi’s current portfolio, it counts the number of immunised infants, children in their second year of life and adolescents; this could be expanded if other age groups are targeted by new vaccines in the future. Computationally, it involves conducting the ‘unique children immunised’ calculation for each age group separately (i.e. counting the Gavi supported vaccine that reaches the most individuals through routine immunisation in a given year, per age group, and then adding them together). For the commitment in the Investment Opportunity 2026–2030, this includes the following vaccines, accounting for different age groups separately, and only counting routine immunisations:

- infant: hepB3, Hib3, PCV3, IPV1, IPV2, rotaC, RCV1, YFV
- second year of life: MCV2, malaria4, first DTP-containing booster (including as part of hexavalent fourth dose)
- adolescent: HPV C

Gavi vaccine forecasts indicate that countries will immunise more than 500 million children through routine immunisation with Gavi support from 2026–2030. Based on historical data, under this definition of children immunised, countries immunised 1 billion children with Gavi support from 2000–2020 (Gavi 1.0–4.0). Forecasts indicate another 1 billion immunised from 2021–2030 (Gavi 5.0/5.1–6.0) – i.e. another billion in half the time for a total of 2 billion by 2030.

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<sup>5</sup> Gavi 5.0 Measurement Framework 2021-2025 Indicator Definitions, <https://www.gavi.org/sites/default/files/programmes-impact/Measuring%20our%20performance/Gavi-50-Measurement-Framework.pdf>

### Health systems touchpoints catalysed: 1.4 billion in 2026–2030

This indicator represents a count of the distinct health system contacts that a child has when vaccinated with Gavi-supported vaccines through routine systems, aggregated across all children immunised each year. To compute this number, we first specify groups of vaccines that would be on the same schedule, for example, a number of vaccines require three doses at ages 6, 10 and 14 weeks, while some other vaccines have their first dose at 9 months.

The groups are as follows: (1) pentavalent; hexavalent; PCV; rotavirus vaccine; inactivated polio vaccine (IPV); and malaria vaccine, which requires three health system visits in the first year of life; (2) malaria vaccine, which requires one additional visit beyond those three visits; (3) hexavalent vaccine, which requires one additional visit beyond those three visits; (4) measles and measles-rubella, which require two visits; (5) HPV vaccine, which requires one visit, assuming switch to one-dose schedule; (6) hepatitis B birth dose, which requires one visit; (7) DTP-containing boosters, which require one visit per booster dose; and where relevant, (8) yellow fever, which requires one visit. We then count the number of contact points with the health system required to complete the vaccination series for children immunised with the Gavi-supported vaccine achieving the highest projected coverage in each vaccine group in a country each year and sum up the results across countries. Because we are interested in touchpoints with the routine health system, campaigns and other supplementary immunisation activities are excluded.

### Health impact: 8-9 million future deaths averted in 2026–2030

Gavi relies on academic disease modelling groups to estimate health impact. Since 2017, the coordination of these modelling groups and the aggregation of impact estimates has been conducted through the Vaccine Impact Modelling Consortium (VIMC), which is led by a secretariat based at Imperial College London. One of VIMC's main aims is to coordinate vaccine impact modelling efforts, and deliver a more efficient and transparent approach to generating disease burden and vaccine impact estimates. In addition, VIMC works on aggregating the estimates across a portfolio of 13 vaccine-preventable diseases and advancing the research agenda in the field of vaccine impact modelling. VIMC is funded by Gavi, the Bill & Melinda Gates Foundation and Wellcome, and it is advised by a stakeholder group consisting of representatives from the funders as well as key partners, including UNICEF, WHO and regional modelling hubs.

### Background on VIMC models

The VIMC Secretariat coordinates the work of over 20 academic research groups, with each group estimating the impact of a specific vaccine based on a counterfactual in which no vaccines are administered.<sup>6</sup> Inputs and outputs are standardised by the VIMC Secretariat to ensure comparability across the disease models.

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<sup>6</sup> For vaccines with multiple delivery strategies (e.g. measles), the counterfactual is calculated as the incremental impact of each delivery strategy.

To generate Gavi’s impact estimates, individual models are run for each antigen, and then aggregated across the entire Gavi portfolio. At least two models for the same antigen are used to account for uncertainty in estimated impact due to model differences, and to understand plausible ranges around antigen-specific impact estimates. Full model runs are conducted every two to three years to incorporate the most recent versions of the models, which undergo methodological improvements and incorporate new data. Interim updates, using the impact extrapolation method (see below), are conducted bi-annually, coinciding with the updates to the WUENIC coverage estimates and the Gavi operational forecast. The VIMC models are listed in the following table, with more information available on the VIMC website<sup>7</sup> and the supplementary material in Toor et al., 2021. The VIMC methods are described in detail in Li et al., 2021 and Toor et al., 2021.<sup>8</sup>

Table 1: VIMC modelling groups and model types

Pathogen/vaccine	Lead institution for model	Model type
Cholera (OCV)*	International Vaccine Institute (IVI)	static
	Johns Hopkins University	static
Hepatitis B (hepB and hepB birth dose)	Burnet Institute	static
	Center for Disease Analysis	dynamic
	Imperial College London	dynamic
	Centrally run by the VIMC Secretariat (model developed by Goldstein et al. 2005)**	static
Human papillomavirus (HPV)	Boston University (previously the Harvard School of Public Health)	static
	London School of Hygiene & Tropical Medicine (LSHTM)	static
<i>Haemophilus influenzae</i> type B (Hib)	Johns Hopkins University	static
	LSHTM	static
Japanese encephalitis (JE)	National University of Singapore (previously Oxford University)	dynamic
	University of Notre Dame	dynamic
Malaria*	Imperial College London	dynamic
	Telethon Kids Institute (previously Swiss TPH)	dynamic
	Université d'Abomey-Calavi (UAC)/Mountain Top University	dynamic
Measles	LSHTM	dynamic
	Pennsylvania State University	dynamic
<i>Neisseria meningitidis</i> serogroup A (menA)	University of Cambridge	dynamic
	Kaiser Permanente Washington	dynamic

<sup>7</sup> <https://www.vaccineimpact.org/>
<sup>8</sup>Li X et al. Estimating the health impact of vaccination against ten pathogens in 98 low-income and middle-income countries from 2000 to 2030: a modelling study. *Lancet*. 2021 30;397(10272):398-408.

Toor J et al. Lives saved with vaccination for 10 pathogens across 112 countries in a pre-COVID-19 world. *Elife*. 2021

Pathogen/vaccine	Lead institution for model	Model type
<i>Neisseria meningitidis</i> serogroups A, C, W, X, Y (MMCV)*	University of Cambridge	dynamic
<i>Streptococcus pneumoniae</i> (PCV)	Johns Hopkins University	static
	LSHTM	static
Rotavirus (rota)	Emory University	dynamic
	Johns Hopkins University	static
	LSHTM	static
Rubella	University of Georgia (previously Johns Hopkins University)	dynamic
	Public Health England	dynamic
Typhoid (TCV)	IVI	static
	Yale University	dynamic
Yellow fever (YF)	University of Notre Dame	static
	Imperial College London	static

\*The cholera, typhoid, malaria and MMCV models were not included in Toor et al (2021). The first two were excluded as the modelling was still in progress at the time of the manuscript development. Malaria and MMCV were added to VIMC in 2022. Additional information on each of the models is available on the VIMC website. \*\*Goldstein., Susan T., et al. "A mathematical model to estimate global hepatitis B disease burden and vaccination impact." *International journal of epidemiology* 34.6 (2005): 1329-1339.

### Health impact projections in the Investment Opportunity

The future deaths averted as presented in the Investment Opportunity are calculated relative to the timing of the intervention and reflect the long-term impact of vaccination.<sup>9</sup> This is done by assigning model-based estimates of future deaths averted back to the year in which vaccines were administered. This approach links financing and vaccine delivery to impact irrespective of the timing of benefits and helps to put all vaccines on a comparable level even though effects vary by age (e.g. the benefits of measles-containing vaccine occur soon after vaccination, whereas the benefits of hepatitis B and HPV vaccines are realised decades later). More details on this approach to calculating impact, and comparison to alternative approaches considering cross-sectional impact and impact over the lifetime of a vaccinated cohort, are presented in Echeverria-Londono et al., 2021.<sup>10</sup>

The impact extrapolation (IE) method, developed by VIMC and described in Echeverria-Londono et. al., 2021,<sup>11</sup> was used to arrive at the projection of 8–9 million future deaths averted with Gavi support in 2026–2030. The IE method consists of applying country, pathogen and vaccine delivery-specific impact ratios (deaths

<sup>9</sup> The VIMC Secretariat aggregates the results generated by modeling groups using three different approaches. The first provides the cross-sectional view of impact in a particular calendar year, the second provides the long-term impact of vaccines by looking at the total number of future deaths averted over the lifetime of annual vaccinated birth cohorts, and the third provides an intervention view, by summing the future impact across all vaccinated cohorts attributed to the year vaccination occurred. The lifetime cohort and intervention views produce fairly similar results as both capture the impacts of vaccines with delayed impact, namely hepatitis B and HPV vaccines.

<sup>10</sup> Echeverria-Londono S, et al. How can the public health impact of vaccination be estimated? *BMC Public Health*. 2021

<sup>11</sup> Ibid.



averted per person immunised) generated by VIMC models to the total number immunised implied by the Gavi operational forecast. Rubella (as part of the measles-rubella vaccine) is excluded from the analysis as VIMC does not produce impact ratios for rubella.<sup>12</sup>

To ensure consistency and comparability with Gavi 5.0/5.1 impact estimates, impact ratios based on the '201910' full runs were used for the Investment Opportunity 2026–2030, with some exceptions:

- Malaria vaccine: since VIMC only recently added malaria models, estimates of impact were not available through VIMC. The estimates in the IO are based on modelling conducted for the Gavi malaria vaccine programme investment case<sup>13</sup> by the malaria modelling groups at Imperial College London (Hogan et al., 2020)<sup>14</sup> and the Swiss TPH (Penny et al. 2015, now at Telethon Kids Institute).<sup>15</sup> To arrive at an indicative estimate of impact from malaria in Gavi 6.0, the portfolio level average impact ratio of 344 deaths averted per 100,000 fully vaccinated children<sup>16</sup> was applied to the forecasted number of fully vaccinated children in Gavi 6.0. To note, as the Gavi malaria vaccine programme investment case was developed prior to the approval of the R21 vaccine, the impact ratio only reflects the impact of the RTS,S vaccine but was applied to the number of children projected to be reached with both vaccines. VIMC models that incorporate emerging data on the effectiveness of the R21 vaccine are expected later in 2024.
- MMCV: WHO recommended routine use of MMCV in September 2023 based on studies of the disease epidemiology in African meningitis belt countries and strategies for the introduction and routine use of the vaccine. As a result, VIMC estimates based on the WHO recommendation were not available for the IO, so indicative estimates of impact were used for this purpose. The estimates are based on a proxy approach developed by Cambridge University, one of the VIMC meningitis modelling groups, whereby MMCV impact is modelled to generate the impact of a booster dose of menA, and a proxy measure of the impact against menCWYX.
- Diphtheria, tetanus and pertussis (DTP)-containing boosters: impact estimates are currently unavailable through VIMC, so the estimates in the IO are based on modelling conducted for the Vaccine Investment Strategy

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<sup>12</sup> To avoid a shift in rubella disease burden to older age groups, the WHO recommends a catch-up campaign targeting children between the ages of 9 months and 15 years immediately prior to routine introduction of a rubella-containing vaccine. As such, the VIMC combines routine and campaign vaccinations in their modelling of the impact, as modelling them separately would artificially yield negative impacts (i.e. increased burden).

<sup>13</sup> Gavi, the Vaccine Alliance. Malaria vaccine programme investment case, Report to the Board, 30 November – 2 December 2021, accessed online at <https://www.gavi.org/sites/default/files/board/minutes/2021/30-nov/08%20-%20Malaria%20Vaccine%20Programme%20Investment%20Case.pdf>

<sup>14</sup> Hogan, AB et al. Estimated impact of RTS,S/AS01 malaria vaccine allocation strategies in sub-Saharan Africa: A modelling study. *PLOS Medicine* 2020. 17(11)

<sup>15</sup> Penny MA, et al. The public health impact of malaria vaccine RTS, S in malaria endemic Africa: country-specific predictions using 18-month follow-up Phase III data and simulation models. *BMC Medicine*. 2015

<sup>16</sup> Fully vaccinated is defined as children who received 4 doses of the RTS,S vaccine. The impact ratio represents the average between the impact ratios generated by Imperial College London and Swiss TPH teams for vaccinations in perennial settings.

2018<sup>17</sup> by the Gates Foundation’s Integrated Portfolio Management (IPM) team. A similar approach to the one taken for malaria was applied, i.e. the portfolio level impact ratio of 19 deaths averted per 100,000 was applied to the projected number of children vaccinated with the three booster doses with Gavi support.

VIMC is currently in the process of generating new estimates (the ‘202310’ full runs) based on the latest models and burden estimates for each of the disease areas, as well as the most recent WHO recommendations, including new runs for MMCV and malaria (considering both the RTS,S and R21 vaccines). These estimates will undergo peer review; and, once finalised, the underlying models will be ‘locked’ and used to report on Gavi 6.0 progress. The results of these updated models will be reviewed with the Gavi Board during the development of the Gavi 6.0 Measurement Framework.

Additional points to note on the future deaths averted projections in Figure 7 of Gavi’s Investment Opportunity 2026–2030:

- Pentavalent vaccine deaths averted represent the impact from Hib3 and HepB3. They do not include impact from diphtheria, tetanus and pertussis (DTP) infant vaccination, since countries had previously introduced infant DTP vaccine without Gavi support.
- Hexavalent vaccine deaths averted represent impact from third dose (Hib3+HepB3) and fourth dose (first DTP-containing booster). Thus, the per-person-vaccinated impact of the hexavalent vaccine is assumed to be equivalent to the pentavalent vaccine, with the exception of incremental impact from the first DTP-containing booster.
- The table includes the impact of Gavi’s current engagement in former- and never Gavi-eligible middle-income countries (the MICs Approach) in the Gavi 5.0/5.1 figures, but the potential impact of Gavi’s future MIC engagements are excluded, as coverage forecasts for these countries are highly uncertain. Preliminary analyses suggest Gavi’s maximum impact would be <100,000 deaths averted in Gavi 6.0.

### Economic benefits generated through Gavi support: over US\$ 100 billion in 2026–2030

Similarly to the health impacts, estimates of economic benefits generated by Gavi-supported immunisations are computed by an external academic institution, the Vaccine Economics Research for Sustainability and Equity (VERSE) team, previously the Decade of Vaccine Economics (DOVE) team, housed at the International Vaccine Access Center (IVAC) at Johns Hopkins University. VERSE aims to generate economic evidence on vaccine impact in low- and middle-income countries, focusing on building economic models to estimate the cost of illness, return on investment and the cost of financing vaccine programmes. It is funded by

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<sup>17</sup>Diphtheria, tetanus and pertussis (DTP)-containing boosters investment case, Vaccine Investment Strategy, October 2018. Accessed online: <https://www.gavi.org/sites/default/files/document/ppc-meeting-18-19-october-2018---vis-06a---annex-c--diphtheria-tetanus-and-pertussis-containing-boosters-investment-casepdf.pdf>

the Gates Foundation and is guided by an Advisory Group comprised of the Gates Foundation, Gavi Secretariat, WHO, UNICEF, World Bank, Institute for Health Metrics and Evaluation (IHME) and VIMC.

DOVE-cost of illness (DOVE-COI) models<sup>18</sup> serve as the primary method for estimating economic benefits. The models calculate the value of averting short- and long-term costs associated with the diseases that Gavi-supported vaccines protect against and use estimates of cases and deaths from VIMC-derived health impact estimates. The results reflect the incremental impact of Gavi-funded vaccinations based on the coverage estimates from the OPv21.1 forecast for 2026–2030.

The short- and long-term costs measured by the COI models include: (1) acute treatment costs associated with a specified illness; (2) transportation costs associated with a specified illness; (3) caretaker wages lost because of a child's illness; (4) productivity losses that occur due to premature death; and (5) productivity losses due to disability.

The human capital approach was used to determine the economic impact of lost productivity due to disability and death. This approach uses the discounted lifetime earnings of an individual in full health as an approximation of the economic value of their life. In the DOVE-COI models, GDP per capita is used as an analogue for the economic contribution of affected individuals in each year and assumes that individuals are economically productive between ages 15 and 64<sup>19</sup> and that labour participation is 100%. The analysis assumes constant value of productivity, using the 2022 value of GDP per capita.

To arrive at the projection of over US\$ 100 billion in economic benefits through Gavi-supported immunisation in 6.0, a method akin to the VIMC impact extrapolation method was used. Country, pathogen and vaccine-delivery specific ratios of COI averted per death averted were derived from previous estimates generated by the VERSE team, and these ratios were multiplied by the estimates of deaths averted in 2026–2030 associated with the forecasts.

## Other key data in the investment case

### Capacity to respond to at least 150 outbreaks from 2026–2030

In recent years, Gavi has supported an average of roughly 30 outbreak response campaigns per year according to data from the International Coordinating Group (ICG) on Vaccine Provision and the Measles & Rubella Partnership (MR&P). This includes programmes and vaccine stockpiles for outbreak-prone diseases including cholera, Ebola, measles, meningitis and yellow fever. To characterise the magnitude of outbreak response activity that Gavi will be prepared to support in Gavi 6.0 if needed, the number of 150 outbreaks was computed by multiplying the historical

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<sup>18</sup> Sim SY, et al. Return On Investment From Immunisation Against 10 Pathogens In 94 Low- And Middle-Income Countries, 2011-30. *Health Affairs*. 2020;39(8):1343-1353.

Watts E, et al. Economic Benefits of Immunisation for 10 Pathogens in 94 Low- and Middle-Income Countries From 2011 to 2030 Using Cost-of-Illness and Value-of-Statistical-Life Approaches. *Value Health*. 2021;24(1):78-85.

<sup>19</sup> OECD definition of the working age population

annual average of 30 outbreaks per year by five years. This is not a statement of ambition, as success in this regard would be zero outbreaks requiring response, but rather a statement of what Gavi will be prepared to respond to if necessary, in support of country needs.

### Number of immunisations supported by Gavi

This indicator provides a total count of routine immunisations supported by Gavi, to complement the measure of children immunised, which only counts each child once even if they receive multiple vaccines in the same year. It is defined as the total number of immunisations completed through routine immunisation with Gavi support, calculated as the sum of fully vaccinated persons (FVPs) across all antigens included in Gavi-supported vaccines, using WPP estimates for target population and WUENIC, JRF and Gavi's operational forecasts for coverage for routine vaccines, and applying Gavi support, as follows:

Counting Gavi-supported routine immunisations at antigen level:

- Count 1x: hepB monovalent, hepB birth dose, IPV, MCV2, menA, MMCV, JE, YFV, HPV, TCV, malaria, PCV, rota (count each antigen once)
- Count 2x: MR1 (count two antigens – M1 and R1)
- Count 2x: DTP second and third booster (count two antigens – D, T – given recommendation to use Td in these age groups)
- Count 3x: DTP first booster (count three antigens – D, T, P)
- Count 5x: pentavalent (count five antigens – Hib, HepB, D, T, P)
- Count 6x: hexavalent (count six antigens – Hib, HepB, D, T, P, IPV)

The number of supported immunisations will increase in Gavi 6.0 with the expansion of Gavi's vaccine portfolio.

### Return on investment of immunisation

The return on investment (ROI) to immunisation was computed by the International Vaccine Access Center (IVAC) at Johns Hopkins University.<sup>20</sup> The figure of 54:1 represents the estimated 2021–2030 ROI in 73 Gavi-supported countries of immunisation programmes against ten antigens, ignoring Gavi support, including measles, yellow fever, *Haemophilus influenzae* type b (Hib), Japanese encephalitis (JE), hepatitis B, *Neisseria meningitidis* serogroup A, rubella, *Streptococcus pneumoniae*, human papillomavirus and rotavirus; and includes the broader societal value of people living longer, healthier lives. When considering only the cost of illness averted from immunisation (i.e. savings of health care costs, lost wages and lost productivity due to illness and death), each dollar spent on immunisation is estimated to bring US\$ 21.

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<sup>20</sup> Sim SY, Watts E, Constenla D, Brenzel L, Patenaude BN. Return On Investment From Immunization Against 10 Pathogens In 94 Low- And Middle-Income Countries, 2011-30. Health Aff (Millwood). 2020 Aug;39(8):1343-1353. doi: 10.1377/hlthaff.2020.00103. PMID: 32744930.