

FAQs around impact estimates for the Gavi 2021-2025 Investment Opportunity

1. Why does Gavi present a range of 7– 8 million future deaths averted for 2021-2025 impact, instead of an exact figure?

As with the 2016–2020 investment case, Gavi presents a range of projected impact. The projection is based on a bottom-up approach, wherein the country-vaccine-year level forecasts of dose requirements created as part of Gavi's financial forecasts are translated into the number of people immunized and, through modeling, the expected impact of those immunizations on mortality. These numbers are then summed to provide a portfolio level projection of the number of future deaths that countries could avert with Gavi support from 2021-2025. As there are substantial uncertainties in the analysis, the final number is presented as a range.

The range provided is not a statistical uncertainty range. It reflects the use of multiple analyses to estimate the likely impact, including the use of alternative forecasts of routine coverage levels from the University of Washington Institute for Health Metrics and Evaluation (IHME) and the use of different disease impact models for each vaccine to account for model differences. For more information on the different analyses guiding the impact target, please see the technical appendix of the 2021-2025 investment opportunity.¹

2. How does Gavi estimate the impact of immunization on future deaths averted?

To generate Gavi's impact estimates, individual models are run for each vaccine, and then aggregated across the entire Gavi portfolio. At least two models for the same antigen are used to understand plausible ranges around antigen-specific impact estimates.

Model runs are conducted by academic modelling groups, with methods and results for overall impact published in peer-reviewed academic papers.² In 2017, the coordination of these modeling groups and the aggregation of impact estimates shifted from the Gavi Secretariat to the Vaccine Impact Modelling Consortium (VIMC), hosted by Imperial College London. For more information on the different analyses guiding the impact target, please see the technical appendix of the 2021-2025 investment opportunity.

¹ The technical appendix is available at <http://www.gavi.org/investment-case-technical-appendix/>

² See for example:

Lee, Lisa A., et al. "The estimated mortality impact of vaccinations forecast to be administered during 2011–2020 in 73 countries supported by the GAVI Alliance." *Vaccine* 31 (2013): B61-B72.

Ozawa, Sachiko, et al. "Return on investment from childhood immunization in low-and middle-income countries, 2011–20." *Health Affairs* 35.2 (2016): 199-207.

Ozawa, Sachiko, et al. "Estimated economic impact of vaccinations in 73 low- and middle-income countries, 2001–2020." *Bulletin of the World Health Organization* 95 (2017): 629-638

The VIMC now coordinates the work of 18 research groups modelling the impact of vaccination programmes worldwide.³ As its core objective, it aims to deliver a more efficient and transparent approach to generating disease burden and vaccine impact estimates. Furthermore, the Consortium works on aggregating the estimates across a portfolio of ten vaccine-preventable diseases and further advancing the research agenda in the field of vaccine impact modelling. It is co-funded by Gavi and the Bill and Melinda Gates Foundation, and guided by an independent Scientific Advisory Board which includes representatives from WHO, UNICEF, UNFPA, Wellcome Trust, Princeton University and Johns Hopkins School of Public Health.

3. Why does Gavi use the term “future” deaths averted?

Immunisation averts deaths over the lifetimes of vaccinated children by providing immunological protection from a young age. Gavi supports vaccines that prevent deaths from childhood diseases as well as deaths that would occur decades in the future (e.g., hepatitis B and liver cancer, HPV and cervical cancer). The mathematical models used for projecting the impact of vaccines on mortality allow us to track the benefits of vaccinations carried out today into the future, and then assign those benefits back to the year immunization occurred. This is important, as it places vaccines that impact mortality later in life, like hepatitis B and HPV vaccines, on the same playing field as vaccines that have more immediate impact, like measles or PCV vaccines.

Note that the Investment Opportunity uses “lives saved” and “deaths averted” interchangeably, and both refer to future deaths averted.

4. What vaccines and activities are included in the impact projections presented in the 2021-2025 investment opportunity?

The impact estimates include Gavi-supported immunisations through routine systems and supplementary immunisation activities against the following diseases: Hepatitis B, Haemophilis influenzae type B (Hib), Human Papillomavirus (HPV), Japanese Encephalitis, measles (2nd dose and supplementary immunisation activities), meningococcal A, rotavirus, rubella, typhoid, yellow fever, and pneumococcal disease. Estimates of the impact from the new Vaccine Investment Strategy (VIS) vaccines, as outlined in the Gavi Board decision in November 2018,⁴ are also included. The VIS vaccines are diphtheria, tetanus, pertussis-containing boosters, hepatitis B birth dose, preventive cholera, rabies post-exposure prophylaxis, meningitis multivalent conjugate, and respiratory syncytial virus.

The following Gavi-supported interventions are excluded from the impact estimates:

³ Information on each of the models is available on the VIMC website: <https://www.vaccineimpact.org/>

⁴ Additional information on VIS is available on Gavi’s website at: <https://www.gavi.org/about/strategy/vaccine-investment-strategy/>

- Vaccines included in national immunisation programmes before Gavi began funding them, such as diphtheria, tetanus and pertussis (DTP) or the first dose of measles vaccine.
- The global stockpiles of cholera, yellow fever and meningitis vaccines, which protect millions of people against these diseases every year.
- Gavi's support for the Ebola vaccine, which is currently being used in the DRC. The potential impact of a Gavi-supported stockpile once the vaccine is licensed and prequalified by the World Health Organization, is also excluded.
- Inactivated polio vaccine, which was initially funded by the Global Polio Eradication Initiative (GPEI) through Gavi's systems.
- Engagement with former and never Gavi Middle Income Countries (MICS), as those strategies are still under development.

Gavi does include time-limited impact (5 years) for vaccines that a country self-finances after direct support from Gavi ends, since the country would have benefited from Gavi's health system support and, as seen with other middle-income countries, may not have provided the vaccine without Gavi's support. Additionally, Gavi includes impact if a country self-finances a vaccine with access to Gavi prices.

5. Does Gavi rely on a counterfactual to calculate impact – i.e. a hypothetical in which all support for immunisation has been stripped away?

Gavi's figures for the number of future deaths averted that countries avert with Gavi support are computed based on a counterfactual in which no vaccines are administered. These figures only include the impacts of vaccines that Gavi is funding in each country, as opposed to total immunization activity. As seen in many middle-income countries which still do not provide new and underused vaccines like pneumococcal or rotavirus, countries may not have introduced these high impact vaccines without Gavi's support, suggesting the counterfactual is reasonable. Moreover, Gavi does not count the impacts of antigens that were introduced before Gavi support began (e.g., Diphtheria, Tetanus and Pertussis vaccine (DTP) and the first dose of measles vaccine).

6. How does Gavi's projected health impact compare to the target of 5-6 million in Gavi 4.0?

In Gavi 5.0 we expect a comparable impact to what we currently estimate to accomplish in Gavi 4.0. In the Gavi 4.0 investment case, Gavi estimated that countries could avert 5-6 million future deaths through its support from 2016-2020 and is on track to reaching that promise based on the activities that were included at the time. Since then, the Gavi Board approved additional programs from the use of strategic reserve funds - namely support for measles campaigns and the introduction

of PCV and rotavirus vaccines in India - which have resulted in a higher than expected impact than originally forecasted for 4.0 of around 7 million deaths averted.

7. How is Gavi able to maintain a similar level of impact in Gavi 5.0 compared to Gavi 4.0 with countries transitioning out of Gavi-support?

We expect to enter 2021 with 55 Gavi eligible countries, down from 68 countries in Gavi 4.0. It might therefore seem unintuitive that Gavi would maintain the same level of health impact in Gavi 5.0 as in Gavi 4.0 with fewer countries receiving support. There are a few reasons for this:

- While there are 13 countries transitioning out of Gavi support before the end of Gavi 4.0, they have relatively small population sizes. In Gavi 4.0, they only accounted for about 5% of total impact.
- India is expected to transition out of Gavi support early in Gavi 5.0, and total impact from Gavi support in India will be around 200K deaths averted in Gavi 5.0, as opposed to 1.3m in Gavi 4.0. This “loss” of impact will be offset by a forecasted increase of roughly 1m deaths averted in other countries we support in Gavi 5.0 through expanded breadth of protection with introductions and scale-up of HPV, PCV and Rotavirus vaccines.
- Modest increases in impact relative to 4.0 through new vaccines in the VIS are also expected, and potentially, engagement with never/former Gavi MICs.

8. Why are deaths averted increasing faster than the number of children reached?

By the end of 2018, Gavi-supported routine immunisations had reached over 760 million unique children. By 2025, we expect to reach 1.1 billion – an increase of 45 percent relative to 2018 levels. For future deaths averted, we expect a bigger increase of about 70 percent, going from 13 million by the end of 2018 to 22 million by 2025.

Children reached (or immunised) and future deaths averted with Gavi support are Gavi mission indicators,⁵ and each captures a different aspect of Gavi activities. Children reached refers to the number of unique children reached with the last recommended dose of a Gavi-supported vaccine delivered through routine systems. It is calculated as the count number of children immunized with the Gavi-supported vaccine achieving the highest projected coverage in a country each year (generally pentavalent) summed across all countries. In contrast, the deaths averted metric includes all immunisation activities, capturing the expanded breadth of protection through all Gavi supported routine vaccinations and campaigns. Therefore, relative increases will be larger for future deaths averted as compared to the number of unique children reached with immunization.

⁵ 2016-2020 Strategy Indicator Definitions, accessed: <https://www.gavi.org/results/measuring/2016-2020-indicators/>

9. How does the current HPV vaccine supply shortage affect Gavi's plans to scale HPV vaccinations?

Since Gavi accelerated its HPV ambitions to include multi-age cohort vaccinations (MACs) during the first year of introduction in 2016, HPV vaccine supply has turned out to be inadequate to fully realise this new ambition during Gavi 4.0. Even though 2019 and 2020 will see an increase in vaccine volumes over what was available in 2017-18, current supply is still not adequate to meet the demand of approved routine and MAC programmes. We are engaging with both current manufacturers to ensure an improved supply outlook as soon as possible. Pipeline HPV manufacturers are expected to enter the market in the 2021-25 period. In the meantime, routine introductions have been prioritized over MACs, with some routine introductions delayed. Current forecasts suggest built-up demand will be satisfied when global supply catches up early in Gavi 5.0. Based on this outlook, we will be able to help countries vaccinate approximately 50 million girls in 2021-2025 and get close to 1 million future deaths averted from HPV.

10. How is the return on investment (ROI) to immunisation of 54:1 derived?

The return on investment (ROI) to immunisation was computed by the International Vaccine Access Centre (IVAC) at Johns Hopkins University, as an update to the estimate published in 2016.⁶ The figure of 54:1 represents the estimated 2021-2030 ROI in 73 Gavi-supported countries of immunization programs against 10 antigens, including measles, yellow fever, haemophilus influenzae type b, Japanese encephalitis, Hepatitis B, Neisseria Meningitidis serogroup A, rubella, streptococcus pneumoniae, human papillomavirus and rotavirus, and includes the broader societal benefits of people living longer, healthier lives. When considering only the cost of illness averted from immunisation (i.e., savings of healthcare costs, lost wages and lost productivity due to illness), each dollar spent on immunisation is estimated to bring \$21.

These new estimates represent an upward revision from 2016 estimates, which were \$48 per \$1 spent when accounting for broader societal benefits, and \$18 in saved costs from illness averted for each dollar spent on vaccines. The new estimates are a result of methodological updates and revisions to the underlying forecast and costs for vaccines and vaccine delivery.

Pending the publication of the updated estimates in a peer-reviewed journal (estimated in late 2019), IVAC's methodology for calculating the ROI is posted here: <http://immunizationeconomics.org/dove-roi>

⁶ Ozawa, Sachiko, et al., 2016.