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ARTICLE

Sustainable Development Goal Halftime Project: Benefit-Cost Analysis Using Methods from the Decade of Vaccine Economics Model

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Abstract

In 2023, the world will be at "halftime" with respect to the sustainable development goals (SDGs). This midline acts as an important milestone to review the progress of the SDGs and develop policies based on the most effective interventions. To estimate the remaining resources needed to achieve SDG targets for vaccines from 2023 to 2030 as well the resulting economic benefits, in this analysis, the incremental economic benefit-cost ratio (BCR) for immunization programs in 80 low- and middle-income countries targeted by the Global Vaccine Action Plan from 2023 to 2030 is calculated. Of these 80 countries, 27 are classified as low-income countries and 53 are classified as lower-middle-income countries (LMICs). The economic evaluation covers 9 vaccines employed against 10 antigens and delivered through both routine immunization programs and supplemental immunization activities. The vaccines covered in the analysis include pentavalent vaccine, human papillomavirus vaccine, Japanese encephalitis vaccine, measles vaccine, measles-rubella vaccine, meningococcal conjugate A vaccine, pneumococcal conjugate vaccine, rotavirus vaccine, and yellow fever vaccine, and correspond to the vaccines covered in the return-on-investment estimates presented in Sim *et al.*, which covered 94 LMICs from 2011 to 2030. For these countries, we estimate program costs from the health system perspective, including vaccine costs such as costs to procure vaccines, which incorporate injection supplies and freight; and immunization delivery costs, which include nonvaccine commodity costs to deliver immunizations to target populations and incorporate labor, cold chain and storage, transportation, facilities, training, surveillance, and wastage. Economic benefits are calculated using a value of statistical life year (VSLY) approach applied to modeled cases, and deaths averted are converted into averted years of life lost using life expectancy data. BCRs are presented as the final output that compares incremental costs and benefits from the baseline of 2022 levels, assuming diminishing returns to scale. Overall, for this period, we estimate total costs of US$ 7,581,837,329.08 with VSLY benefits of US$ 762,172,371,553.54, resulting in a BCR of 100.53.

1. Introduction

In 2023, the world will be at "halftime" with respect to the sustainable development goals (SDGs). This midline acts as an important milestone to review the progress of the SDGs and develop policies based on the most effective interventions. As we advance toward 2030, both funders and governments will continue to face high demands for health and social investments in order to make progress toward the SDGs and the achievement of universal health coverage while dealing with new challenges such as emerging infectious diseases, humanitarian crises, and climate change. All of these concerns present a need for further political commitment and contributions to protect the hard-won gains achieved during the first half of the SDG timeline.

Building on the previous Decade of Vaccine Economics (DOVE) Return-on-Investment (ROI) study and the subsequent Vaccine Economics Research for Sustainability and Equity (VERSE) project (Sim *et al.,* 2020), this analysis aims to provide insights on the economic benefits and costs of immunization programs. Pediatric immunization is largely considered one of the most cost-effective interventions, with previous studies estimating the ROI for common pediatric vaccines to be between US$ 15 and US$ 52 per every US$ 1 invested (Ozawa *et al.,* 2016; Sim *et al.,* 2020). In addition, while immunization directly impacts health, and therefore the SDGs, it has also been found to play an indirect role in contributing toward advancements in 14 out of the 17 SDGs (Decouttere *et al.,* 2021). As such, it is important to understand the benefits and costs of immunization programs in a manner that allows comparison directly across both healthcare interventions as well as nonhealth interventions targeted at other SDGs.

2. Objective

The objective of this analysis is to provide estimates of the economic costs, benefits, and benefit-cost ratios (BCRs) for interventions to attain SDG targets within 80 low-income countries (LICs) and lower-middle-income countries (LMICs) in order to advocate for more funding to the most effective interventions and policies across all sectors over the next 7.5 years. This particular evaluation shines a light on pediatric immunization, estimating total and incremental BCRs for nine different vaccines in 80 LMICs (Sim *et al.,* 2020).

3. Scope

This analysis is focused on the economic benefits and costs of immunization programs in 80 low- and middle-income countries targeted by the Global Vaccine Action Plan (GVAP) from 2023 to 2030. Of these 80 countries, 27 are classified as LICs and 53 are classified as LMICs. The economic evaluation covers 9 vaccines employed against 10 antigens and delivered through both routine immunization programs and supplemental immunization activities (SIAs). The vaccines covered in the analysis include pentavalent vaccine, human papillomavirus (HPV) vaccine, Japanese encephalitis (JE) vaccine, measles (MCV) vaccine, measles-rubella (MR) vaccine, meningococcal conjugate A (Men A) vaccine, pneumococcal conjugate (PCV) vaccine, rotavirus vaccine, and yellow fever (YF) vaccine and correspond to the vaccines covered in the return-on-investment estimates presented in Sim *et al.* (2020), which covered 94 LMICs from 2011 to 2030. Table 1 contains the full list of countries and detailed categorization of the countries according to the World Health

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Table 1. *Full list of countries.*

ISO	Country	WHO region	World Bank Income Group 2021	Eligibility for GAVI support 2021
AFG	Afghanistan	EMRO	Low income	Eligible
AGO	Angola	AFRO	Lower-middle income	Eligible
BGD	Bangladesh	SEARO	Lower-middle income	Eligible
BLZ	Belize	AMRO[a]	Lower-middle income	Not eligible
BEN	Benin	AFRO	Lower-middle income	Eligible
BTN	Bhutan	SEARO	Lower-middle income	Eligible
BOL	Bolivia	AMRO[a]	Lower-middle income	Eligible
BFA	Burkina Faso	AFRO	Low income	Eligible
BDI	Burundi	AFRO	Low income	Eligible
KHM	Cambodia	WPRO	Lower-middle income	Eligible
CMR	Cameroon	AFRO	Lower-middle income	Eligible
CPV	Cape Verde	AFRO	Lower-middle income	Not eligible
CAF	Central African Republic	AFRO	Low income	Eligible
TCD	Chad	AFRO	Low income	Eligible
COM	Comoros	AFRO	Lower-middle income	Eligible
COD	Congo, Dem. Rep.	AFRO	Low income	Eligible
COG	Congo	AFRO	Lower-middle income	Eligible
CIV	Cote d'Ivoire	AFRO	Lower-middle income	Eligible
DJI	Djibouti	EMRO	Lower-middle income	Eligible
EGY	Egypt	EMRO	Lower-middle income	Not eligible
SLV	El Salvador	AMRO[a]	Lower-middle income	Not eligible
ERI	Eritrea	AFRO	Low income	Eligible
ETH	Ethiopia	AFRO	Low income	Eligible
GMB	Gambia	AFRO	Low income	Eligible
GHA	Ghana	AFRO	Lower-middle income	Eligible
GIN	Guinea	AFRO	Low income	Eligible
GNB	Guinea-Bissau	AFRO	Low income	Eligible
HTI	Haiti	AMRO[a]	Lower-middle income	Eligible
HND	Honduras	AMRO[a]	Lower-middle income	Eligible
IND	India	SEARO	Lower-middle income	Eligible
IDN	Indonesia	SEARO	Lower-middle income	Eligible
KEN	Kenya	AFRO	Lower-middle income	Eligible
KIR	Kiribati	WPRO	Lower-middle income	Eligible
PRK	Korea, DPR	SEARO	Low income	Eligible
XK	Kosovo	EURO	Lower-middle income	Not eligible
KGZ	Kyrgyzstan	EURO	Lower-middle income	Eligible
LAO	Lao PDR	WPRO	Lower-middle income	Eligible
LSO	Lesotho	AFRO	Lower-middle income	Eligible
LBR	Liberia	AFRO	Low income	Eligible
MDG	Madagascar	AFRO	Low income	Eligible
MWI	Malawi	AFRO	Low income	Eligible

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Table 1. *Continued*

ISO	Country	WHO region	World Bank Income Group 2021	Eligibility for GAVI support 2021
MLI	Mali	AFRO	Low income	Eligible
MRT	Mauritania	AFRO	Lower-middle income	Eligible
FSM	Micronesia	WPRO	Lower-middle income	Not eligible
MNG	Mongolia	WPRO	Lower-middle income	Eligible
MAR	Morocco	EMRO	Lower-middle income	Not eligible
MOZ	Mozambique	AFRO	Low income	Eligible
MMR	Myanmar	SEARO	Lower-middle income	Eligible
NPL	Nepal	SEARO	Lower-middle income	Eligible
NIC	Nicaragua	AMRO[a]	Lower-middle income	Eligible
NER	Niger	AFRO	Low income	Eligible
NGA	Nigeria	AFRO	Lower-middle income	Eligible
PAK	Pakistan	EMRO	Lower-middle income	Eligible
PNG	Papua New Guinea	WPRO	Lower-middle income	Eligible
PHL	Philippines	WPRO	Lower-middle income	Not eligible
RWA	Rwanda	AFRO	Low income	Eligible
WSM	Samoa	WPRO	Lower-middle income	Not eligible
STP	Sao Tome and Principe	AFRO	Lower-middle income	Eligible
SEN	Senegal	AFRO	Lower-middle income	Eligible
SLE	Sierra Leone	AFRO	Low income	Eligible
SLB	Solomon Islands	WPRO	Lower-middle income	Eligible
SOM	Somalia	EMRO	Low income	Eligible
LKA	Sri Lanka	SEARO	Lower-middle income	Eligible
SDN	Sudan: North	EMRO	Low income	Eligible
SSD	Sudan: South	AFRO	Low income	Eligible
SWZ	Swaziland	AFRO	Lower-middle income	Not eligible
SYR	Syria	EMRO	Low income	Eligible
TJK	Tajikistan	EURO	Lower-middle income	Eligible
TZA	Tanzania	AFRO	Lower-middle income	Eligible
TLS	Timor-Leste	SEARO	Lower-middle income	Eligible
TGO	Togo	AFRO	Low income	Eligible
UGA	Uganda	AFRO	Low income	Eligible
UKR	Ukraine	EURO	Lower-middle income	Not eligible
UZB	Uzbekistan	EURO	Lower-middle income	Eligible
VUT	Vanuatu	WPRO	Lower-middle income	Not eligible
VNM	Viet Nam	WPRO	Lower-middle income	Eligible
PSE	West Bank and Gaza	EMRO	Lower-middle income	Not eligible
YEM	Yemen	EMRO	Low income	Eligible
ZMB	Zambia	AFRO	Lower-middle income	Eligible
ZWE	Zimbabwe	AFRO	Lower-middle income	Eligible

[a]Eligible for PAHO's revolving fund.

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Table 2. *Pathogens, vaccines, and delivery strategies included in the analysis.*

Pathogen (short name)	Vaccines	Strategy	RI	SIA
Hepatitis B (HepB)	Pentavalent	Infants (3 doses)	Yes	No
Haemophilus influenzae type B (Hib)	Pentavalent	Infants (3 doses)	Yes	No
Human papillomavirus (HPV)	Human papillomavirus	Girls age 9; Multi-age cohort 10–14 (2 doses)	Yes	Yes
Japanese encephalitis (JE)	Japanese encephalitis	Infants (1 dose); Campaign (1 dose)	Yes	Yes
Measles (measles)	Measles, measles-rubella (MR)	Infants (1st and 2nd); Campaign (1 dose)	Yes	Yes
Rubella (rubella)	Measles-rubella (MR)	Infants (1st and 2nd); Campaign (1 dose)	Yes	Yes
Neisseria meningitidis serogroup A (MenA)	Meningococcal conjugate A	Infants (1 dose) Campaign (1 dose)	Yes	Yes
Streptococcus pneumoniae (PCV)	Pneumococcal conjugate	Infants (3 doses)	Yes	No
Rotavirus (RV)	Rotavirus	Infants (2 or 3 doses)	Yes	No
Yellow fever (YF)	Yellow fever	Infants (1 dose) Campaign (1 dose)	Yes	Yes

RI, routine immunization; SIA, supplemental immunization activities.

Organization (WHO) region, the World Bank income group, and GAVI-eligibility and country-transition classification. Table 2 contains the complete list of vaccines and assumptions about corresponding immunization strategies.

4. Method

4.1. Costs

4.1.1. Scope of costing analysis and components

The analysis estimates different components of immunization-program costs for routine immunization and SIAs, which are largely divided into two components: *vaccine costs*, which include costs to procure vaccines, including injection supplies and freight; and *immunization delivery costs*, which include nonvaccine commodity costs to deliver immunizations to target populations. Immunization delivery costs usually include all or any of the following components:

(i) Labor function: personnel costs (salaries, per diem, and travel allowances).
(ii) Storage function: cold chain equipment, maintenance, and overheads.
(iii) Transportation function: vehicles, transport, and fuel.
(iv) Other capital costs: buildings, utilities and other overheads, building construction, and capital equipment.

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(v) Other recurrent costs: program management, short-term training, information, education and communication (IEC)/social mobilization, disease surveillance, wastage management, and other recurrent costs.

The analysis was conducted from the health system perspective, and it does not factor in household costs such as transportation or lost productive time due to immunization sessions.

Vaccine cost. We generated demand forecasts for each type of routine and SIA vaccine. The number of doses procured is a function of the size of target population, vaccine coverage rate, the number of recommended doses for a fully immunized person, a wastage rate, and a buffer stock rate. The Vaccine Impact Modelling Consortium (VIMC) (n.d.) secretariat provided the demographic data based on the UN World Population Prospect 2019 as well as data for each antigen based on GAVI's operational forecast updated in 2018. For SIAs, we used separate data on target populations and the coverage rate provided by the VIMC. Vaccine-specific, time-invariant wastage rates are based on GAVI's Detailed Product Profile (World Health Organization, 2005). Based on consultations with the GAVI market-shaping team, uniform buffer stock rates (25% for routine immunization and 0% for SIAs) were applied to all vaccines (Public Price Forecast, 2021).

$$\text{Number of doses}_{ijk} = \begin{array}{l}\text{Target population}_{ijk} \times \text{Coverage rate}_{ijk} \\ \times \text{Number of recommended doses}_{ij} \times \left(1 + \text{Wastage rate}_{ij}\right) \\ \times \left(1 + \text{Buffer stock rate}_{i}\right),\end{array}$$

where i = vaccine, j = country, and k = year.

Vaccine prices are from three different sources. The GAVI provided the public price forecast information (2023–2030) for 73 GAVI countries (Pan American Health Organization (PAHO)/WHO, 2021). The other countries included both PAHO countries and non-GAVI/non-PAHO countries. Since PAHO and United Nations International Children's Emergency Fund (UNICEF) do not conduct price forecasts for future years, we generated price forecasts (2023–2030) based on the same principle applied to the GAVI price forecasts, which takes the estimates from the latest year where data are available and assumes a constant price throughout the remaining years. This assumption is made due to difficulties associated with long-term forecasts of the market landscape and corresponding vaccine prices. The historical vaccine prices for PAHO countries were obtained from the *PAHO Revolving Fund* price list (Pan American Health Organization (PAHO)/WHO, 2021). For the other non-GAVI and non-PAHO countries, the UNICEF vaccine price list was applied (UNICEF, 2018).

For PAHO, UNICEF, and GAVI's forecasted prices, we took an average price per dose for each vaccine across all listed products offered by multiple manufacturers, given the uncertainty in volume procured for each product type. GAVI's immunization supply costs (syringe, recon syringe, and safety box) and freight costs (as a percentage of the unloaded vaccine price) were applied to all 80 countries.

The number of doses was multiplied by price per dose for each vaccine, country, and year to estimate the total vaccine costs.

$$\text{Vaccine costs}_{ijk} = \sum_{k=2023}^{2030} \sum_{j=1}^{80} \sum_{i=1}^{9} \left(\text{number of doses}_{ijk} \times \text{price per dose}_{ijk}\right).$$

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Immunization delivery cost. Routine immunization. Estimates of routine delivery cost per dose were derived from the most recent empirical results estimated by Portnoy *et al.* (2020), which generated standardized delivery costs for 134 LMICs through a Bayesian meta-regression model. The study used the Immunization Delivery Cost Catalogue (IDCC) to help predict future delivery cost per dose. For Kosovo, West Bank, and Gaza – where estimates are not available through the Portnoy *et al.* (2020) model, we used the estimates from the immunization costing study conducted by Sim *et al.* (2021).

$$\text{Immunization delivery costs}_{ijk} = \sum_{k=2023}^{2030} \sum_{j=1}^{80} \sum_{i=1}^{9} \left(\text{number of doses}_{ijk} \times \text{delivery cost per dose}_{ij}\right).$$

Incremental cost for introducing new vaccines: The empirical studies from the IDCC provide unprecedented opportunities for estimating incremental cost for new vaccine introduction in addition to estimating total costs (Immunization Delivery Costs in Low- and Middle-Income Countries, 2020). Due to a lack of data for other vaccines, we estimated only the average incremental cost per dose for HPV, PCV, and rotavirus vaccines. We also assumed that, in the future, pentavalent and MR vaccines will slowly replace traditional vaccines against the same antigens (i.e., DTP and measles). Incremental costs include both introduction and startup costs for newly introduced vaccines, as well as recurrent costs. No distinction was made between HPV cost estimates from routine delivery via health facility and school delivery given a large degree of heterogeneity in costs of each method as well as decisions regarding HPV vaccine delivery strategies, even within countries.

Incremental delivery cost per percentage increase in coverage: Earlier modeling analyses took different perspectives on how routine immunization delivery cost per dose will change beyond baseline years. Gandhi *et al.* (2013) assumed a constant delivery cost per dose that is not linked to the coverage rate or additional doses. Portnoy *et al.* (2015) applied a marginal delivery cost for additional doses derived from a regression analysis of cMYP costing tools separately for countries with DTP3 coverage rates above and below 80%. Because it is increasingly important to understand the additional costs required to increase immunization coverage rates, we have used results from several recent studies (Batt *et al.,* 2004; Pegurri *et al.,* 2005; Ozawa *et al.,* 2016).

Ozawa *et al.* (2018) is an update to two systematic reviews (Batt *et al.,* 2004; Pegurri *et al.,* 2005) that aimed to summarize evidence in peer-reviewed or grey literature that examined the cost and effect of increasing the immunization coverage. Interventions used to increase coverage differs across studies, ranging from text message reminders to education, publicity, and incentives for healthcare personnel. Unlike these two reviews that focused on low- and middle-income countries, the new study by Ozawa *et al.* (2018) also included evidence from high-income countries and quantitatively examined the relationship between intervention cost per dose and coverage changes, which shows increasing intervention cost per dose for higher levels of coverage. We used the cost function derived from Ozawa *et al.* (2018) to estimate the incremental cost per dose for each annual coverage rate increase for each country.

We present side-by-side the results from a constant delivery cost per dose assumption ("baseline assumption") and from an increasing delivery cost per dose assumption ("diminishing returns to scale assumption"). However, the results under the diminishing returns to scale assumption should be interpreted with caution. Underlying data from the systematic review have inherent limitations due to lack of standardized reporting, recall bias, and heterogeneity of study settings and designs. In addition, the cost function presented is based on data from both LMICs and high-income countries, presenting the possibility of

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Table 3. *Summary table for immunization delivery cost per dose estimates.*

Category	Type	N^a	Average (*SD*)	Median	Range
Routine immunization	Total immunization delivery cost per dose	80	2.73 (1.96)	2.21	0.49–9.48
	Incremental cost per dose for introducing HPV	42	4.02 (3.30)	2.95	0.54–13.85
	Incremental cost per dose for introducing PCV	21	1.24(1.03)	1.09	0.15–3.61
	Incremental cost per dose for introducing Rotavirus vaccine	12	1.07(0.66)	0.88	0.1–2.38
SIA	Measles	17	0.98(0.91)	0.72	0.04–3.74
	Measles-rubella	13	0.91(0.21)	0.87	0.71–1.5
	JE	2	0.71(0.01)	0.71	0.7–0.72
	MenA	15	0.53(0.4)	0.67	0–1.48
	Yellow fever	4	0.67(0.2)	0.71	0.43–0.83
	HPV SIA (Multi-age cohort)	1	0.55(0.55)	0.55	0.55–0.55

[a]Number of estimates in the model; all costs in US$ 2020; no distinction was made with respect to HPV cost estimates from routine delivery via health facility and school delivery given the uncertainties about country decisions regarding delivery strategies.

overestimation. When excluding high-income settings from the analysis, a linear relationship between coverage increases and cost per dose cannot be rejected, and as a result, the assumption of increasing delivery cost per dose across all countries and baseline coverage rates remains a subject of debate.

SIAs. Immunization delivery costs for SIAs, often referred to as "operational costs" (Gandhi *et al.,* 2013), consist of nonvaccine costs to deliver vaccines to the target population and manage SIA efforts that are targeted and time-limited. SIAs were conducted for six of the nine vaccines included in this analysis. Catch-up, follow-up, or past preventive campaigns were conducted for measles, measles-rubella, MenA, JE, and yellow fever vaccines. Multi-age cohort (girls of age 10–14) for HPV is optional for countries that choose to immunize additional girls beyond the routine cohort and such efforts are also categorized as SIA.

To quantify the delivery cost per dose for SIAs, we used information from the IDCC, a systematic review by Gandhi *et al.* (2013), and budgeted amount per dose estimates from country proposals submitted to GAVI. We collected 52 estimates from these sources and calculated the average cost per dose for each vaccine type (see Table 3). These estimates were then applied to 80 countries.

Sensitivity analysis. We conducted probabilistic sensitivity analysis (PSA) using Monte Carlo simulations to determine uncertainty ranges for each scenario. We varied five parameters simultaneously and performed 10,000 model runs to construct a 95% uncertainty range for total immunization program costs. We used a Gamma distribution for the cost per dose estimates from the compiled data mentioned above for three parameters –

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country-specific routine immunization delivery cost per dose, vaccine-specific SIA delivery cost per dose, and incremental delivery cost per dose for PCV, HPV, and RV vaccines. A uniform distribution was used for the percent change in vaccine price per year (between ±15%) (Briggs *et al.,* 2006).

Scenario analysis. Under the base-case scenario, we produced estimates with constant returns to scale for delivery costs at an 8% discounted rate per guidance from the Copenhagen Consensus Center. This scenario is presented as the primary result. We conducted additional scenario analyses by adopting a diminishing returns to scale assumption, using discount rates of 0 and 3% and adopting a wastage rate of 0% instead of the wastage rate based on GAVI's detailed product profile (GAVI, 2018) to demonstrate the impact of diseconomies of scale, vaccine wastage, and discounting on immunization program costs.

In addition, we estimated the incremental cost of achieving 2030 targets by comparing the total costs of achieving the 2030 coverage targets to the cost of immunization programs if the coverage level in 2022 was held constant over time.

$$\text{Incremental to achieve 2030 target at halftime} = \text{Total costs}_{2030\ \text{target coverage}} - \text{Total costs}_{2022\ \text{coverage}}.$$

In summary, the scenarios evaluated included the following:

(i) The total cost of immunization programs (discounted at 8%, constant returns to scale, and GAVI DPP wastage rates).
(ii) The total cost of immunization program (discounted at 8%, 0% wastage rate, and constant returns to scale).
(iii) The total cost of immunization program (discounted at 8%, GAVI DPP wastage rates, with diminishing returns to scale).
(iv) The total cost of immunization program (discounted at 3%, constant returns to scale, and GAVI DPP wastage rates).
(v) The total cost of immunization program (undiscounted, constant returns to scale, and GAVI DPP wastage rates).
(vi) Incremental costs of achieving 2030 target at halftime compared to 2022 coverage level (discounted at 8%, constant returns to scale for routine immunizations, and GAVI DPP wastage rates).
(vii) Incremental costs of achieving 2030 target at halftime compared to 2022 coverage level (discounted at 3%, constant returns to scale for routine immunizations, and GAVI DPP wastage rates).
(viii) Incremental costs of achieving 2030 target at halftime compared to 2022 coverage level (discounted at 0%, constant returns to scale for routine immunizations, and GAVI DPP wastage rates).
(ix) Incremental costs of achieving 2030 target at halftime compared to 2022 coverage level (discounted at 8%, diminishing returns to scale for routine immunizations, and GAVI DPP wastage rates).

Furthermore, due to limited data availability and no standardized vaccine impact models, we were unable to estimate comparable economic benefits for BCG and TCV vaccines. Therefore, these two vaccines were not included in the total immunization program costs or

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BCRs presented in the results. Instead, we generated cost estimates for both BCG and TCV vaccines and present these estimates separately in Section 5.

4.1.2. Economic benefits

Due to the scarcity of country-specific costs and epidemiologic data and the complexity of estimating the economic burden associated with the antigens modeled, the DOVE-COI models draw upon a variety of data sources. Health impact data are drawn from the focal models of the Goldstein *et al.* (2005, 2008), Chen *et al.* (2012), Tartof *et al.* (2013), Walker *et al.* (2013), Garske *et al.* (2014), Vynnycky *et al.* (2019), Quan *et al.* (2020), and VIMC (n.d.). The modeler and modeling teams that produced these outcomes are listed in Table 4. Key input values that are uniform across the DOVE-COI models are described in Table 5. In addition to these uniform parameters, literature reviews were conducted to identify sources of information for all model inputs that vary by antigen (see Table 6). The use of these parameters in the DOVE-COI models is illustrated in Figure 1 and described in more detail in Section 4.1.4.

Additional input data not represented in the tables were drawn from validated, multilateral agency sources and include real gross domestic product (GDP) per capita, consumer price indices (CPI), US$ to local currency unit (LCU) exchange rates, and percentage of population living in urban areas (IMF, 2010; World Bank, 2013). Wherever possible, disease burden inputs (including the age of vaccination, age of infection, and age of death) were based on epidemiological data and assumptions provided by health impact modeling teams to ensure continuity by aligning the two sets of models as much as possible (VIMC, n.d.).

4.1.3. Antigen-specific model inputs

The parameters listed in Table 6 varied by antigen-specific model and were primarily derived from country-level surveys (DHS, SOWC) and estimates in the published literature (The DHS Program, n.d.; UNICEF, n.d.; Okanurak *et al.,* 1997; Campagne *et al.,* 1999; Ehrenkranz *et al.,* 2001; Monath, 2001; Hui *et al.,* 2002; Parashar *et al.,* 2003; Lanzieri *et al.,* 2004; Fischer *et al.,* 2005; Nielsen *et al.,* 2005; Podewils *et al.,* 2005; Chu & Liaw, 2006; Akumu *et al.,* 2007; Broughton, 2007; Isakbaeva *et al.,* 2007; Kim *et al.,* 2007, 2010; Rheingans *et al.,* 2007; Gessner *et al.,* 2008; Hussain *et al.,* 2008; Mendelsohn *et al.,* 2008; Nokes *et al.,* 2008; Sinha *et al.,* 2008; Clark *et al.,* 2009; Flem *et al.,* 2009; Tate *et al.,* 2009; Wilopo *et al.,* 2009; Berry *et al.,* 2010; Giglio *et al.,* 2010; Bishai *et al.,* 2011; Lee *et al.,* 2011; Atherly *et al.,* 2012; Yin *et al.,* 2012; Tam *et al.,* 2012; Center for Disease Control [CDC], 2021). If reliable estimates could not be found, assumptions were made based on a review of the available data. In certain cases, given the similarity in disease outcome (i.e., Hib and PCV) and a lack of antigen-specific data, it was also necessary to incorporate the same antigen-specific inputs/assumptions across different models. Where multiple disease outcomes are associated with a single antigen, separate estimates for each outcome are listed below the applicable antigen.

4.1.4. Methodology

All model costs are presented in 2020 US$ and represent the net present value at year of vaccination, calculated using the discount rates applied in the costing scenarios. Costs

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Table 4. *Overview of health impact models used in the economic benefits analysis (continued next page).*

Pathogen	HepB	Hib[a]	HPV[b]	JE	Measles	MenA[c]	PCV[a]	Rota[d]	Rubella	YF[c]
Institution (modelers/ modeling team)	Independent (Xi Li)	Johns Hopkins University (Lives Saved Tool [LiST])	Harvard School of Public Health	Oxford University Clinical Research Unit (OUCRU) – Vietnam	Pennsylvania State University	Kaiser Permanente Washington Health Research Institute/ Centers for Disease Control and Prevention	Johns Hopkins University (LiST)	Johns Hopkins University (LiST)	Public Health England	Imperial College London
Model characteristics	Static (no herd effects), deterministic	Static (no herd effects), deterministic, linear mathematical model	Static (no herd effects), cohort simulation	Dynamic (no herd effects), deterministic force of infection model	Dynamic, semi-mechanistic, discrete time-step annual SIR	Dynamic, stochastic, age-structured, compartmental transmission model	Static (no herd effects), deterministic, linear mathematical model	Static (no herd effects), deterministic, linear mathematical model	Dynamic, age and sex-structured, deterministic, compartmental model of transmission dynamics	Static force of infection model (no herd effects)
Syndromes included	Acute early hepatitis, acute late (>5 years) hepatitis, cirrhosis, hepatocellular carcinoma (HCC)	Pneumonia, meningitis	HPV-related cervical cancer	Symptomatic JE	Acute measles, encephalitis	Meningitis and sequelae	Pneumonia, meningitis	Severe diarrhea	Congenital rubella syndrome	Mild cases and severe hemorrhagic disease
Vaccine efficacy	95% for 3 doses; protection from partial immunization not modeled	93% for 3 doses; protection from partial immunization not modeled	100% with full dose schedule; lifelong immunity; protection from partial immunization not modeled	100% (single dose), lifelong immunity	First dose: 85% at age 9 months or 93% at age 12 months; second dose: 99%; campaign: 99%	First stage: 75% against colonization; 100% against invasive disease; second stage: 25% against colonization; 90% against disease	3 doses of PCV provides 58% efficacy against all serotypes of invasive pneumococcal disease	Asia: 87.9%; North Africa: 87.9%; Southern Africa, West Africa, and East Africa: 49.7%; Eastern Europe: 82%, Latin America: 81%	95% efficacy with lifelong protection	97.5% efficacy with lifelong protection
Age at vaccination	3 doses prior to age 1 year (economic benefits not modeled for birth dose)	3 doses prior to age 1 year	Age 9 years	Routine: age 9 months; campaign: age 9 months–15 years	First dose: age 0; second dose: age 1; campaign dose age 9 months–15 years	Routine: 1 dose age 9 months; campaign: ages 1–29 years	3 doses prior to age 1 year	2 or 3 doses prior to age 1 year, depending on formulation	First dose: age 0 years; second dose: age 1 year; campaign dose age 9 months−15 years	Routine: 1 dose at 9 months; campaign dose age 9 months−15 years

Table 4. *Continued*

Pathogen	HepB	Hib[a]	HPV[b]	JE	Measles	MenA[c]	PCV[a]	Rota[d]	Rubella	YF[e]
Average age of infection	Early childhood: age 2.5 years; late: age 17.5 years; chronic disease asymptomatic until late adulthood	Prior to age 5 years (only childhood cases and deaths included in the model)	Disease onset at ages 50–56 years (varies by country)	Age 15–33 years (varies by country)	Susceptible at ages 2–25 years if not previously infected and never vaccinated (varies by country)	Routine: age 10–12 years (varies by country); campaign age 30–31 years (varies by country)	Prior to age 5 years (only childhood cases and deaths included in the model)	Prior to age 5 years (only childhood cases and deaths included in the model)	Congenital rubella syndrome diagnosed in the perinatal period	Age 9–38 years (varies by country)
Case fatality ratio	70% for fulminant hepatitis, 100% for HCC	Applied using overall <5 mortality envelope	80%	20–30%	Varies by age and country	Varies by age (ranges from 8.6%–12.2%)	Applied using overall <5 mortality envelope	Applied using overall <5 mortality envelope	30%	10% of cases are severe and 20% of severe cases are fatal
Source	Goldstein *et al.* (2005)	Walker *et al.* (2013)	Goldie *et al.* (2008)	Quan *et al.* (2020)	Chen *et al.* (2012)	Tartof *et al.* (2013)	(see Hib)	(see Hib)	Vynnycky *et al.* (2019)	Garske *et al.* (2014)

[a]Hib/PCV: Only includes impact on children under 5 years. Model estimates deaths averted using residual deaths after accounting for existing interventions, thus reducing the risk of double counting deaths averted from other (nonvaccine interventions); coverage of other interventions (sanitation, antibiotic treatment) held constant.

[b]HPV: Vaccine provides protection against vaccine-type (HPV 16 and 18), no cross-protection.

[c]MenA: Vaccination is assumed to be superior to natural immunity.

[d]Rotavirus: Model accounts for regional variation in the proportion of severe diarrhea caused by rotavirus; only includes protection from complete vaccination (either 2-dose or 3-dose rotavirus vaccine).

[e]YF: Proportion of cases leading to severe disease and the case fatality ratio has been updated to 12 and 47%, respectively for model runs following 2015. This analysis applies the lower estimates for consistency with previous analyses, therefore generating a conservative estimate of the economic impact.

Table 5. *Sources of key input values used across DOVE-COI models.*

Model input	Description	Sources
Input: Cases and deaths averted by vaccine antigen	Estimates of economic benefits used results from the "focal" models in the VIMC (n.d.). Modelers and modeling teams that provided inputs for the analysis are listed in the table below. In mid-2019, VIMC began producing health impact estimates using averages of the "focal" and "nonfocal" models, which will be available in a forthcoming publication. All models use data from the United Nations (2017) to estimate the target population and demographic data. Coverage data are provided by the VIMC Secretariat, with historical coverage data based on WHO/UNICEF Estimates of National Immunization Coverage (WUENIC) and forecasted coverage estimated by GAVI (Watts *et al.,* 2021)	(Goldstein *et al.,* 2005, 2008; Chen *et al.,* 2012; Tartof *et al.,* 2013; Walker *et al.,* 2013; Garske *et al.,* 2014; Vynnycky *et al.,* 2019; Quan *et al.,* 2020)
Inpatient and outpatient costs at the primary, secondary, and tertiary levels	The cost-effectiveness and strategic planning division of the WHO's *Choosing Interventions that are Cost-Effective* (WHO-CHOICE) project built a cost database that allows users to estimate the unit cost of health services at difference facility levels (primary, secondary, and tertiary) in 191 countries for the base years 2007 and 2008. Costs are provided for hospital bed days and outpatient visits and the assumptions underlying these costs can be altered to reflect differences in health facilities including: location (urban/rural), status (private/public/NGO), occupancy rate (0–100%), and average length of stay. These estimates represent only the "hotel" component of hospital costs, that is, excluding the cost of drugs and diagnostic tests but including costs such as personnel, capital, and food	WHO-CHOICE country-specific unit costs (WHO n.d.-a)
Household level average cost per trip of transportation to a health facility	Kim *et al.* (2010) estimated the price of transportation (one-time, roundtrip) to health facilities by extracting cost information from 14 studies, identified and narrowed down from a total of 1300 articles	Kim *et al.* (2010)

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Table 5. *Continued*

Model input	Description	Sources
	identified as pertaining to transportation or travel costs in GAVI countries via a literature search. The search was not disease-specific, as transportation costs will not vary by disease. For countries with no available estimates, costs were extrapolated out from the available data by identifying a proximal country within the same World Bank income group and applying that transportation cost	
Daily minimum wage	The U.S. Department of State Human Rights Report is a congressionally mandated, yearly report chronicling human rights conditions in 200 states and territories. Reports are compiled using information from U.S. embassies and consulates abroad, foreign government officials, nongovernmental and international organizations, and published reports. U.S. diplomatic missions abroad prepare the initial drafts of the individual country reports using information they gathered throughout the year from a variety of sources, including government officials, jurists, the armed forces, journalists, human rights monitors, academics, and labor activists. These initial reports are then analyzed and edited using information from reports provided by U.S. and other human rights groups, foreign government officials, representatives from the United Nations and other international and regional organizations and institutions, experts from academia, and the media	U.S. Department of State Human Rights Report (2021)
Life expectancy at a given age	Per the standards of the Copenhagen Consensus Center, adult individuals are defined as being age 15 or older	United Nations (2017)
Disability weights used to estimate the decrease in productivity/ quality of life due	Disability weights were estimated based on responses from household surveys of adults (Bangladesh, Indonesia, Peru, Tanzania, and the USA) and open-access, web-based surveys conducted between Oct. 28, 2009, and May 16, 2011. The surveys used paired	Salomon *et al.* (2012)

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Table 5. *Continued*

Model input	Description	Sources
to long-term illness	comparison questions in which respondents considered two hypothetical individuals with different, randomly selected health states and indicated which person they regarded as healthier. The web survey added questions about population health equivalence, which compared the overall health benefits of different life-saving or disease-prevention programs A probit regression was run on the paired comparison responses for all 200 unique health states in the study. Population health equivalence responses were used to anchor the results from the paired comparisons on the disability weight scale from 0 (implying no loss of health) to 1 (implying a health loss equivalent to death).	
GDP/capita used to estimate productivity lost per year due to death and disability	The IMF (2010) *World Economic Outlook* (WEO) database contains selected macroeconomic data series from the statistical appendix, which presents the IMF staff's analysis and projections of economic developments at the global level, in major country groups and in 189 individual countries. The WEO is released in April and September/October each year Historical data and projections in the report are based on the information gathered by the IMF country desk officers in the context of their missions to IMF member countries and through their ongoing analysis of the evolving situation in each country. Historical data are updated on a continual basis as more information becomes available The IMF's *World Economic Outlook report* uses a "bottom-up" approach in producing its forecasts; that is, country teams within the IMF generate projections for individual countries. These are then aggregated, and through a series of iterations where the aggregates fed back into individual countries' forecasts, forecasts converge to	International Monetary Fund (IMF, 2010)

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Table 5. *Continued*

Model input	Description	Sources
	the projections reported in the WEO Because forecasts are made by the individual country teams, the methodology can vary from country to country and series to series depending on many factors	
Medication and diagnostic costs	WHO CHOICE estimates, which account for personnel and facility costs, were inflated 25% to account for medications and diagnostics	Assumption based on a review of six studies (Platonov *et al.,* 2006; Akumu *et al.,* 2007; Broughton, 2007; Gessner *et al.,* 2008; Hussain *et al.,* 2008; Kim *et al.,* 2010)
Value of statistical life year (VSLY)	This is calculated as being 160 times the GDP per capita of a country adjusted to involve levels of the United States assuming an income elasticity of 1.5	Copenhagen Consensus Center internal communication

were adjusted to US$ 2020 through an initial conversion of all nonlocal currency unit (LCU) data to LCU, followed by an application of Consumer Price Index (CPI) growth in LCU, and then a conversion between 2020 LCU and US$ 2020 using IMF (2010) exchange rates. Costs for antigens where disease onset occurred at or before age one were not discounted and antigens with disease onset occurring past 1 year were discounted accordingly. If information was not available for a country-specific model input, a WHO region and World Bank country group-specific[1] average for the relevant parameter was calculated and applied. For parameters where cost estimates were abstracted from country-specific studies, these costs were extrapolated out to all model countries using WHO-CHOICE inpatient bed-day costs at a secondary facility as a weighting factor, as illustrated below:

$$\text{Cost}_{\text{country X}} = \text{Cost}_{\text{Study country}} \times \left(\text{WHO-CHOICE}_{\text{country X}} / \text{WHO-CHOICE}_{\text{Study country}}\right).$$

[1] World Bank country group classifications are based on a country's GNI per capita. Countries included in the analysis fell into one of three country categories: LICs, with a GNI per capita of $1045 or less; LMICs, with a GNI per capita between $1045 and $4125; and upper-middle-income countries (UMICs), with a GNI per capita between $4125 and $12,746.

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Table 6. *DOVE-COI model/antigen-specific sources of key input values.*

Model input	Antigen	Source
Care-seeking behavior	Hepatitis B	Assumption
	Haemophilus influenzae type b (Hib)	(The DHS Program, n.d.; UNICEF, n.d.)
	Human papillomavirus (HPV)	N/A
	Japanese encephalitis (JE)	
	Acute – Caveat: Dengue is used as a proxy	Lee *et al.* (2011)
	Sequelae	Assumption
	Measles	The DHS Program (n.d.)
	Meningococcal conjugate A (MenA)	(The DHS Program, n.d.; UNICEF, n.d.)
	Pneumococcal conjugate (PCV)	(The DHS Program, n.d.; UNICEF, n.d.)
	Rotavirus	The DHS Program n.d.
	Rubella	
	Acute	UNICEF, n.d.
	Hearing impairment	Assumption
	Vision impairment (cataracts)	Assumption
	Cardiac	Assumption
	Yellow Fever	
	Severe (hemorrhagic fever)	Lee *et al* (2011)
	Nonsevere (fever)	The DHS Program (n.d.)
Hospitalization rate	Hepatitis B	Kim *et al.* (2007)
	H. influenzae type b (Hib)	Estimate based on two studies (Sinha *et al.,* 2008; Kim *et al.,* 2010)
	Human papillomavirus (HPV)	N/A
	Japanese encephalitis (JE)	Yin *et al.* (2012)
	Measles	Bishai *et al.* (2011)
	Meningococcal conjugate A (MenA)	Assumption
	Pneumococcal conjugate (PCV)	Estimate based on two studies (Sinha *et al.,* 2008; Kim *et al.,* 2010)
	Rotavirus	Parashar *et al.* (2003)
	Rubella	Assumption
	Yellow fever (YF) (severe and nonsevere)	Lee *et al.* (2011)
Duration of illness	Hepatitis B	
	Acute	Assumption
	Chronic	Chu and Liaw (2006)
	Compensated cirrhosis	Chu and Liaw (2006)
	Decompensated cirrhosis	Hui *et al.* (2002)
	Hepatocellular carcinoma (HCC)	(39)

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Table 6. *Continued*

Model input	Antigen	Source
	H. influenzae type b (Hib)	Estimate based on a review of seven studies (Akumu *et al.,* 2007; Broughton, 2007; Gessner *et al.,* 2008; Hussain *et al.,* 2008; Sinha *et al.,* 2008; Giglio *et al.,* 2010; Kim *et al.,* 2010)
	Human papillomavirus (HPV)	N/A
	Japanese encephalitis (JE)	Yin *et al.* (2012)
	Measles	Center for Disease Control (2021)
	Meningococcal conjugate A (MenA)	Campagne *et al.* (1999)
	Pneumococcal conjugate (PCV)	Estimate based on a review of seven studies (Akumu *et al.,* 2007; Broughton, 2007; Gessner *et al.,* 2008; Hussain *et al.,* 2008; Sinha *et al.,* 2008; Giglio *et al.,* 2010; Kim *et al.,* 2010)
	Rotavirus	Rheingans *et al.* (2009)
	Rubella	Assumption
	Yellow fever (YF) (severe and nonsevere)	Monath (2001)
Inpatient bed days/ Outpatient visits	Hepatitis B	Kim *et al.* (2007)
	H. influenzae type b (Hib)	Estimate based on a review of seven studies (Akumu *et al.,* 2007; Broughton, 2007; Gessner *et al.,* 2008; Hussain *et al.,* 2008; Sinha *et al.,* 2008; Giglio *et al.,* 2010)
	Human papillomavirus (HPV)	N/A
	Japanese encephalitis (JE)	Yin *et al.* (2012)
	Measles	Bishai *et al.* (2011)
	Meningococcal conjugate A (MenA)	Estimate based on a review of seven studies (Akumu *et al.,* 2007; Broughton, 2007; Gessner *et al.,* 2008; Hussain *et al.,* 2008; Sinha *et al.,* 2008; Giglio *et al.,* 2010)
	Pneumococcal conjugate (PCV)	Estimate based on a review of seven studies (Akumu *et al.,* 2007; Broughton, 2007; Gessner *et al.,* 2008; Hussain *et al.,* 2008; Sinha *et al.,* 2008; Giglio *et al.,* 2010)
	Rotavirus	Estimate based on 14 studies (Ehrenkranz *et al.,* 2001; Fischer *et al.,* 2005; Nielsen *et al.,* 2005;

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Table 6. *Continued*

Model input	Antigen	Source
		Podewils *et al.,* 2005; Isakbaeva *et al.,* 2007; Rheingans *et al.,* 2007; Mendelsohn *et al.,* 2008; Nokes *et al.,* 2008; Clark *et al.,* 2009; Flem *et al.,* 2009; Tate *et al.,* 2009; Wilopo *et al.,* 2009; Berry *et al.,* 2010; Atherly *et al.,* 2012)
	Rubella	(Lanzieri *et al.,* 2004)
	Yellow fever (YF)	
	Severe (hemorrhagic fever) – Caveat: dengue is used as a proxy	Estimate based on two studies (Okanurak *et al.,* 1997; Tam *et al.,* 2012)
	Nonsevere (fever)	Monath (2001)
Incidence of long-term disability	Please contact the corresponding author for an example of how this is calculated	Available upon request

Additional disease burden/epidemiological assumptions. To properly account for long-term disability and convalescence resulting from acute disease, some additional epidemiological assumptions and parameters were incorporated into the DOVE-COI models. These assumptions are listed in Table 7.

Short-term costs. *Treatment costs:* To measure treatment costs averted that are attributable to immunization, it was necessary to determine how many vaccine-averted cases would have sought care, from where, and how much it would have cost. The number of cases that would have sought care during an illness episode was calculated by applying country- and symptom-specific care-seeking rates to total cases averted estimates provided by the health impact modeling teams (UNICEF n.d.; World Bank, 2013). Parameters for the rate of hospital admittance based on disease severity and the percentage of outpatients seeking care from hospitals were then applied to the overall number of care-seeking cases to determine the facility level at which these cases would have received care. In order to reflect the differential costs of treatment at facilities located in different areas (rural vs. urban), the number of cases seeking outpatient, health center, or hospital care was further stratified by the percentage of the population living in rural versus urban areas (World Bank, 2013). Each estimate of care-seeking cases by location and facility level was then multiplied by WHO country-specific costs of care at each facility level to estimate treatment costs (World Health Organization, n.d.-a). A diagrammatic depiction of treatment cost calculation is provided in Figure 2.

Due to wide-ranging uncertainty and a lack of available data on long-term treatment costs for the antigens modeled, only short-term acute and first-year disability treatment costs are estimated in the models. Care-seeking for children suffering from acute disease managed at

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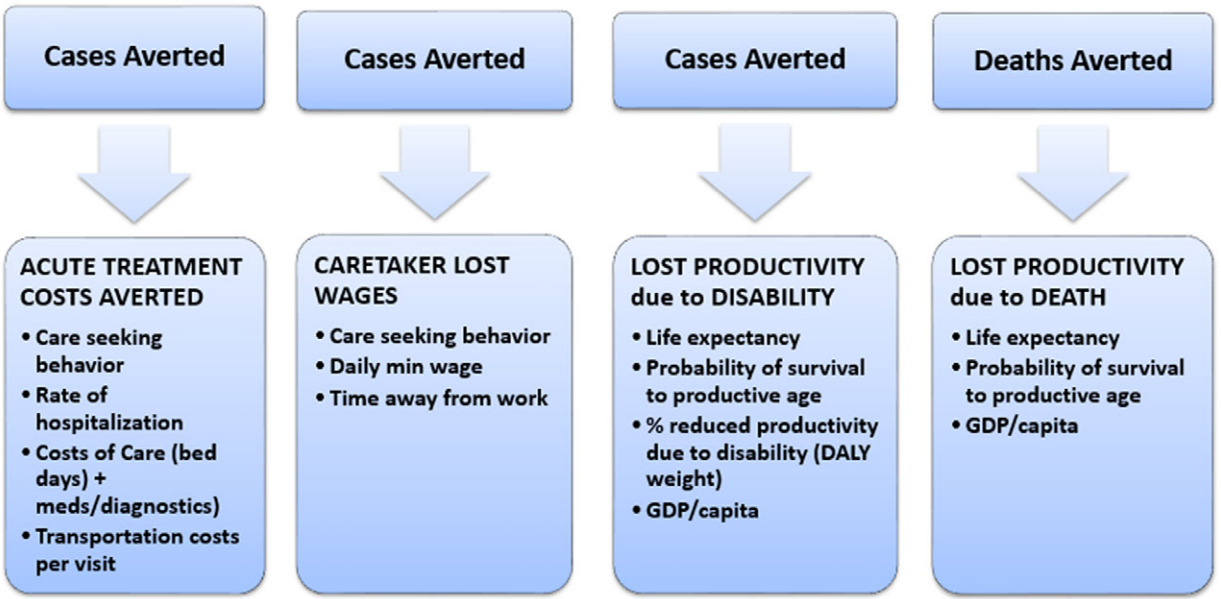

Figure 1. *Key parameters used in COI models by model component.*

Table 7. *Additional disease burden/epidemiological parameters.*

Antigen	Assumptions/Model notes
Hepatitis B	For late in life diseases incurred due to hepatitis B infection (cirrhosis compensated and decompensated as well as hepatocellular carcinoma (HCC)), which were not modeled by health impact modeling teams, the average age of disease onset and death was derived from the published literature (el-Serag, 2001)
	Patients can experience cirrhosis or HCC but not both. In reality, patients with cirrhosis are at increased risk of HCC
	Patients experiencing cirrhosis experience either compensated or decompensated cirrhosis but not both. In reality, patients may experience compensated and progress to decompensated cirrhosis. For simplicity, we have broken these apart and applied separate durations of illness for compensated and decompensated
	The disability weight for compensated and decompensated cirrhosis is the same based on weighted average calculations and is consistent with previous studies (Stouthard *et al.,* 1997)
	20% of cirrhosis cases are symptomatic. The remainder are asymptomatic and do not accrue treatment costs (Wiersma, 2010)
	No effects of coinfections with HIV are included
	Chronic hepatitis B infection results in no disability until symptomatic cirrhosis or HCC develops
	No perinatal infections are prevented by vaccination and thus no costs from perinatal outcomes are included
	Averted infections result from "early childhood" or "late" stage infection. The former is defined as under 5 years old and the latter is greater than 5 years old
	Cirrhosis age of death is calculated based on WHO region and is the same for compensated and decompensated cirrhosis
	HCC age of death is calculated based on the incidence of the countries, classified as either low, intermediate, or high (el-Serag, 2001)
Hib/PCV	Cases/deaths averted arise only from Hib/PCV pneumonia and meningitis. Acute otitis media, other upper respiratory infections, and other invasive syndromes were not considered
	Average age of onset is 1 year (no discounting)
	DALY weights for Hib and PCV disease outcomes were assumed to be the same
HPV	Only cervical cancer resulting from HPV is modeled
Measles	Measles infection is assumed to be independent of HIV status
	Mother-to-child (MTC) HIV transmission rate is assumed at a constant 25%
	The proportion of measles inclusion body encephalitis (MIBE) is assumed to be 50% of measles cases with HIV
Men A	Only long-term disability associated with deafness, vision impairment, motor impairment, and seizure disorder was modeled. Other vaccine preventable

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Table 7. *Continued*

Antigen	Assumptions/Model notes
	disabilities were not included in this analysis because of lower prevalence and lack of country-level data on their incidence
Rotavirus	Only deaths from severe rotavirus are modeled
Rubella	All congenital rubella syndrome (CRS) cases are symptomatic
	Deaths from CRS occur in early infancy
	No first-year treatment costs for CNS (only acute hospitalization and diagnostics)
	Only estimated treatment costs for the first year of life were included
	For cases with multiple syndromes, the lowest estimate of care-seeking for the syndromes present was used
	CRS cases of cardiac abnormality will not go on to develop diabetes since age of death is 1
Yellow Fever	Only cases and deaths due to the most severe form of yellow fever, involving hepatitis, oliguric renal insufficiency, and thrombocytopenia are included
	Only epidemic disease is modeled
	All severe disease survivors enter a convalescent-phase following acute infection (LaBeaud *et al.,* 2011)
	The transmission dynamics of the yellow fever vector, *Aedes aegypti*, is not captured in the modeling approach used

the outpatient level alone was allocated one outpatient visit, regardless of the antigen (Table 8).

Transportation costs: Acute illness transportation costs were estimated by applying a country-specific cost per trip to a healthcare facility (described in Table 5) to each acute outpatient visit and hospital stay (Kim *et al.,* 2010). Long-term disability transportation costs in the first year of life were estimated using the same method, but it was assumed that these cases would require two round trips to a health facility. For antigens like hepatitis B, where disease outcomes occur later in life, transportation costs were discounted from discount rates varying from 0 to 8%, dependent on the scenario, from the year of care-seeking to the year of vaccination.

Caregiver wages: Caretaker productivity loss was calculated by multiplying an estimate of a caretaker's daily productivity by the number of days lost due to care-seeking (hospital bed days). Given that individuals responsible for caretaking in GVAP countries may be predominantly working either in the home or employed in an informal or low-wage sector of the economy, U.S. State Department estimates of the legal minimum or lowest wage in these countries were used to approximate the value of a lost day of work (Country Reports on Human Rights Practices, 2015).

The loss of caregiver wages was only calculated for individuals seeking treatment under the age of 15, as this was the maximum age at which care-seeking would require supervision/the presence of a guardian in GVAP countries. After this age, it was assumed that care would be sought independently with no associated caretaker wage loss. For each bout of illness, we estimated that caretakers would lose 50% of one day's wages for seeking outpatient care and 100% of their daily wage multiplied by the number of hospital bed-days per illness for hospitalized cases.

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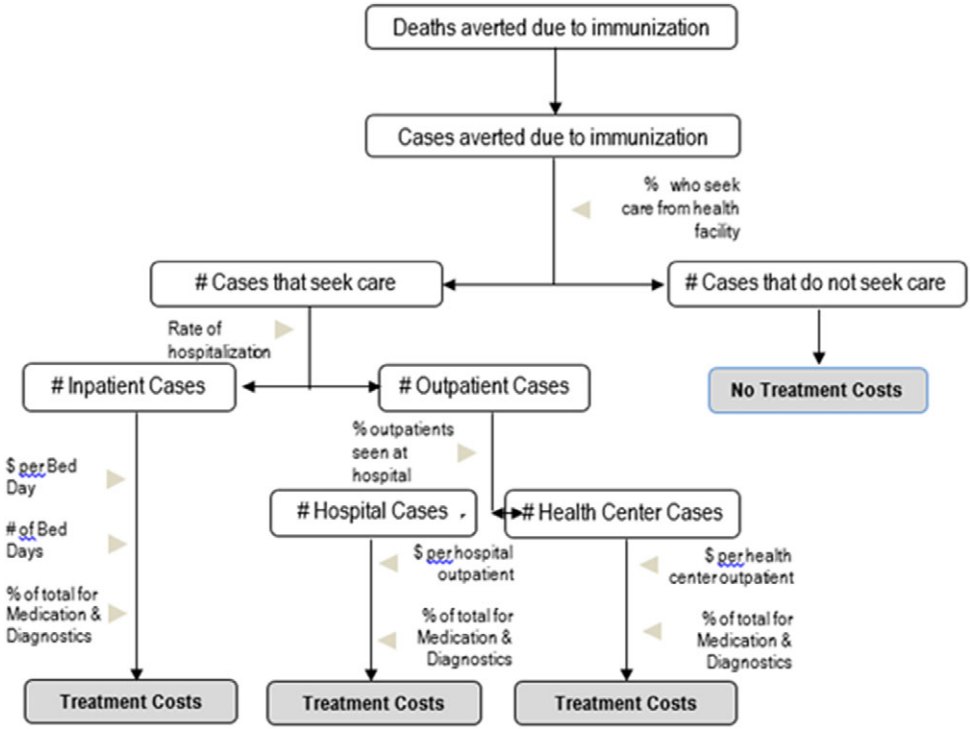

Figure 2. *Decision tree model for treatment costs.*

Long-term costs. A human capital approach was used to determine the economic impact of lost productivity due to disability and death under the COI scenario. For this value, we take the discounted lifetime earnings of an individual, assuming that the individual is in full health (Johannesson, 1996). In the DOVE-COI models, GDP per capita was used as an analogue for the economic contribution of affected individuals in each year (Watts *et al.,* 2021). We assumed that work/economic productivity began at age 15 and that labor participation was 100%.

Productivity loss due to disability: To estimate the number of productive life years lost due to disability, total cases of disability were multiplied by life expectancy at age 16 and discounted back to the year of vaccination. This discounted life expectancy was then multiplied by projected GDP per capita, calculated using the IMF's estimated GDP per capita for the years 2011–2018 and extrapolating these estimates out for the years 2019–2020 using projected GDP per capita growth based on data from the years 2011–2018. Disability weights representing the severity (estimated on a 0–1 scale, with 1 being equivalent to death and 0 being equivalent to perfect health) of each disease outcome were then applied to adjust for the impact of illness on productivity over the duration of an individual's life.

In cases of acute illness, the discounted duration of illness was used in place of discounted life expectancy and multiplied by the number of acute cases. Age-specific survival rates were incorporated in the calculation of productivity loss for antigens where disease onset occurred

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Table 8. *Antigen-specific treatment cost assumptions.*

Antigen	Assumptions/Model notes
Hep B	Every acute symptomatic case and chronic case had one outpatient visit, either at the time of infection (year 5 or 30) or at year of death (varied if cirrhosis or HCC). If the same person was symptomatic at the acute stage and later developed a chronic condition that would count as two outpatient visits (Kim *et al.,* 2007)
	100% of acute symptomatic and chronic hepatitis B cases sought care at a health facility
Hib/PCV	Of those cases that sought care, 50% of pneumonia and 100% of meningitis cases were hospitalized
	Estimates of access to care were derived from Demographic and Health Survey (DHS) data regarding proportions seeking care for acute respiratory infections
HPV	Treatment costs estimates were not modeled by the JHU DOVE team
JE	First-year long-term disability costs were extracted from four studies (Ding *et al.,* 2003; Liu *et al.,* 2008; Touch *et al.,* 2010; Yin *et al.,* 2012) for three countries. These countries (China, Indonesia, and Cambodia) were used to represent treatment costs in each of the three World Bank income groups represented in the models: upper-middle-income (UMIC), lower-middle-income (LMIC), and low-income countries (LIC), respectively
	The WHO-CHOICE cost from each country in the model was multiplied by the ratio of treatment costs to WHO-CHOICE cost per bed-day for China, Indonesia, or Cambodia depending on World Bank income group
	Care was sought for 10% of JE cases suffering from long-term disabilities
Measles	Estimates of access to care were derived from Demographic and Health Survey (DHS) data regarding proportions seeking care for fever
	All cases taken to outpatient health facilities incurred the cost of a vitamin A supplement in addition to medication and diagnostic costs
Men A	All cases taken to a health facility were subsequently hospitalized
	Chronic-care costs could not be quantified and were not included
Rotavirus	Estimates of access were derived from Demographic and Health Survey (DHS) data regarding proportions seeking care for diarrhea
Rubella	Estimates of access to care were derived from UNICEF (n.d.) data regarding percent of children born in an institutional health facility
	For cases suffering from multiple CRS syndromes, the lowest estimate of care-seeking for the syndromes present was used to remain conservative.
	All care-seeking acute and long-term CRS cases are hospitalized
	Medication and diagnostic costs are equivalent to 50% of the WHO-CHOICE cost of a bed-day at a secondary hospital (Lanzieri *et al.,* 2004)
	CRS long-term disability
	To determine the cost of treating CRS disability in the first year of life in each country, we multiplied each country's WHO CHOICE cost per bed-day estimate by the ratio of treatment costs gathered in Brazil (Lanzieri *et al.,* 2004) over the WHO CHOICE cost per-bed day in Brazil

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Table 8. *Continued*

Antigen	Assumptions/Model notes
	As treatment options and access to care may be low in GVAP countries, we assumed that only 10% of children suffering CRS-caused cardiac difficulty and 20% of all other long-term disability cases would seek care in the first year of life
	No first-year treatment costs for CNS were modeled (only acute hospitalization and diagnostics)
	Diabetes treatment costs were not included in the analysis
	No long-term treatment costs for diabetes were included
Yellow fever	Estimates of access to care were derived from Demographic and Health Survey (DHS) data regarding proportions seeking care for fever

before age 15. Due to a lack of data for 15–16 year old children in many countries, we use age 15 data as a proxy for age 16 in order to calculate the number of children that would have reached productive age due to competing risks (WHO, n.d.-b).

Productivity loss due to death: The same human capital approach used to estimate productivity loss due to disability was used in the estimation of productivity loss due to premature death. Total deaths for each country were initially multiplied by the probability of survival to age 15 because we do not have this probability of survival for age 16, and then this number was multiplied by the disease-specific life expectancy at death (discounted to year of vaccination) and finally by GDP per capita.

Value of statistical life and VSLY: As an alternative to COI, a value of statistical life (VSL) approach was also adopted to estimate the economic benefits of cases and deaths averted. For these calculations, we rely upon VSL averages for LICs and LMICs, as provided by the Copenhagen Consensus Center. The VSL, derived from the marginal rate of substitution between willingness-to-pay and mortality risk reduction, represents the average value to society of reducing mortality, without respect to wage or productivity (Klose, 1999; Viscusi, 2004). In the United States, VSL is derived from both willingness-to-pay surveys and wage-risk studies. In previous applications of the Decade of Vaccines Economics (DoVE) model, VSL was allowed to vary between country and was estimated using a value-transfer, or benefits-transfer, approach as given by the following equation (Robinson *et al.,* 2019):

$$\mathrm{VSL}_{\mathrm{LMIC}} = \left(\frac{\text{GDP per capita}_{\mathrm{LMIC}}}{\text{GDP per capita}_{\mathrm{U.S.}}}\right)^{1.5} \times \mathrm{VSL}_{\mathrm{U.S.}}.$$

This approach assumes an income elasticity of 1.5 and uses GDP per capita values for the USA and LMICs calculated using long-term growth forecasts modeled by the Institute of Health Metrics and Evaluation (IHME, 2022).

However, this report presents a VSL calculated using the standardized Copenhagen Consensus Center VSL for low- and lower-income settings ($\mathrm{VSL}_{\mathrm{LIC/LMIC(CCC)}}$) and applies it directly to all LMICs using the following formula:

$$\text{Benefits} = \mathrm{VSL}_{\mathrm{LIC.LMIC(CCC)}} \times \text{Deaths averted}_{\mathrm{LMIC}}.$$

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In addition to the VSL approach, we also adopt a value of statistical life-year (VSLY) approach. VSLY is defined based on the marginal rate of substitution between willingness-to-pay and changes in life expectancy and therefore places a larger weight on the value of children's lives, who have a greater life expectancy as compared to older adults (Kniesner & Viscusi, 2019). In previous iterations of the DoVE model VSLY was calculated as:

$$\text{VSLY} = \frac{\text{VSL}}{\text{Discounted life years remaining}}.$$

For the purposes of this report, the model was adjusted to compute VSLY based on the Copenhagen Consensus Center's standardized halftime estimates and so the $\text{VSLY}_{\text{LMIC(CCC)}}$ takes on the formula:

$$\text{VSLY}_{\text{LIC/LMIC(CCC)}} = \frac{\text{VSL}_{\text{LIC/LMIC(CCC)}}}{0.5 \times \text{Life expectancy at birth}_{\text{LIC/LMIC}}}.$$

Similarly to the total VSL impact, that of VSLY is calculated by multiplying the VSLY for LMICs by the total number of life years averted:

$$\text{Benefits} = \text{VSLY}_{\text{LIC/LMIC(CCC)}} \times \text{Life years averted}_{\frac{\text{LIC}}{\text{LMIC}}}.$$

Scenario analysis: Under the base-case scenario, we produced estimates for economic benefits using an 8% discount rate. This scenario is presented as the primary results. We also conducted additional analyses for discount rates of 0 and 3%.

In addition, we estimated the incremental benefits of achieving 2030 target by taking the difference between the total economic benefits of achieving 2030 targets and the benefits of immunization programs assuming the level of cases and deaths averted in 2022 were held constant over time.

In total, 12 benefit estimation scenarios were conducted:

(i) The total COI of immunization programs (discounted at 8%).
(ii) The total COI of immunization programs (discounted at 3%).
(iii) The total COI of immunization programs (undiscounted).
(iv) The total VSL of immunization programs (discounted at 8%).
(v) The total VSL of immunization programs (discounted at 3%).
(vi) The total VSL of immunization programs (undiscounted).
(vii) The total VSLY of immunization programs (discounted at 8%).
(viii) The total VSLY of immunization programs (discounted at 3%).
(ix) The total VSLY of immunization programs (undiscounted).
(x) Incremental benefit of achieving 2030 target at halftime compared to 2022 level through the COI approach.
(xi) Incremental benefit of achieving 2030 target at halftime compared to 2022 level through the VSL approach.
(xii) Incremental benefit of achieving 2030 target at halftime compared to 2022 level through the VSLY approach.

4.1.5. BCR

The BCR compares the present value of all benefits with that of the costs and investments in the immunization program. This is shown in the following equation:

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$$\text{BCR} = \frac{\text{PV benefits}}{\text{PV costs}},$$

where PV benefits, present value of benefits and PV costs, present value of cost.

Please note that while the DOVE programmatic costing model accommodates BCG and TCV vaccines, these vaccine antigens are absent from the benefits model as their health impacts have yet to be estimated. Therefore, the costs of BCG and TCV vaccination programs are presented separately in Section 5.

5. Results

5.1. Economic benefits: COI

Through the COI approach, the total economic benefits of vaccines in 80 LICs and LMICs were projected to exceed US$ 254 billion from 2023 to 2030, assuming a discount rate of 8%. The largest share of economic benefits from vaccination is owed to productivity loss due to deaths averted, accounting for 93.7% of the total benefits. Productivity loss due to disability averted comprises the second most influential component, responsible for 4.5% of the estimated economic benefits (Tables 9 and 10).

5.2. Economic benefits: VSL/VSLY

Using a discount rate of 8%, total economic benefits of vaccination for all pathogens for 2023–2030 via the VSL approach for all 80 countries totals over US$ 2.8 trillion. When applying the same parameters for the VSLY method, the benefits of vaccination are nearly US$ 5.7 trillion (Tables 11 and 12).

5.3. Immunization program costs

Under the base assumption of an 8% discount rate, the total programmatic costs of vaccination in 80 LICs and LMICs from 2023 to 2030 were estimated to be US$ 20.9 billion (see Table 13). Immunization delivery costs accounted for the greatest proportion of future total immunization program costs at 56.6%, with vaccine costs comprising the remaining costs 43.4% of costs.

We estimated that under a diminishing returns to scale scenario, delivery costs increased by US$ 24.9 billion (19.2%) over the period of 2023–2030. Under the 0% wastage rate scenario, the total vaccine costs decreased by US$ 1.1 billion (9.5%). The results for the different discount rate scenarios are presented annually in Table 13.

Incremental cost calculations show that the costing gap of achieving 2030 target coverage rates for routine immunization compared to the 2022 coverage level is significant. Under constant returns to scale with an 8% discount rate, the incremental costs were estimated at US$ 2.3 billion for vaccines and US$ 1.3 billion for immunization delivery (see Table 14). In other words, it would cost a total of US$ 3.6 billion to reach the 2030 target.

For the diminishing returns to scale scenario with 8% discounted rate, an additional US$ 7.6 billion is needed to reach the 2030 target (US$ 2.3 billion for vaccines and US$ 5.3

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Table 9. *Total COI averted (2020 US$) from vaccination programs for 2023–2030, using VIMC health impact estimates.*

	Economic Benefits	2023	2024	2025	2026	2027	2028	2029	2030	Total
Discounted at 8%	Treatment costs	$374,218,973	$391,678,171	$390,193,117	$393,300,054	$391,881,438	$404,597,005	$406,370,739	$396,375,277	$3,148,614,773
	Transportation costs	$79,344,645	$81,175,166	$80,110,990	$79,677,650	$84,569,439	$81,720,151	$83,117,029	$84,995,286	$654,710,355
	Lost caretaker wages	$96,835,456	$98,371,352	$99,606,918	$101,113,348	$102,210,802	$102,837,644	$103,458,336	$104,382,894	$808,816,751
	Productivity loss by disability	$1,413,445,251	$1,431,907,739	$1,406,392,919	$1,405,631,741	$1,428,741,098	$1,449,697,419	$1,463,105,099	$1,481,183,410	$11,480,104,677
	Productivity loss by death	$27,564,573,854	$29,268,806,104	$29,451,045,459	$29,223,618,934	$29,521,965,406	$31,326,094,889	$31,395,736,334	$30,552,729,189	$238,304,570,169
	Total cost of illness	$29,536,272,995	$31,279,122,482	$31,434,279,564	$31,207,609,869	$31,535,817,143	$33,372,568,967	$33,459,665,171	$32,624,859,418	$254,450,195,608
Discounted at 3%	Treatment costs	$554,953,120	$590,411,021	$578,680,702	$600,821,609	$586,092,196	$610,628,900	$604,735,510	$594,968,571	$4,721,291,632
	Transportation costs	$103,364,038	$105,874,982	$104,594,012	$104,657,647	$110,081,865	$106,830,365	$108,065,293	$110,605,399	$854,073,601
	Lost caretaker wages	$119,560,099	$121,356,205	$122,823,673	$124,915,333	$125,878,023	$126,452,614	$127,146,503	$128,938,503	$997,070,954
	Productivity loss by disability	$6,348,367,012	$6,425,708,101	$6,373,732,180	$6,477,414,454	$6,546,642,150	$6,605,752,169	$6,662,386,726	$6,909,145,112	$52,349,147,903
	Productivity loss by death	$119,773,212,273	$128,150,092,315	$128,232,983,928	$129,591,491,093	$129,442,100,333	$137,058,300,609	$136,600,452,539	$133,697,919,080	$1,042,546,552,171
	Total cost of illness	$126,908,856,308	$135,402,133,500	$135,421,214,675	$136,904,622,968	$136,818,524,371	$144,517,200,809	$144,112,251,842	$141,447,981,098	$1,101,532,785,570
Undiscounted (0%)	Treatment costs	$953,806,265	$1,015,704,104	$991,527,661	$1,045,666,207	$1,015,809,633	$1,059,048,209	$1,045,083,292	$1,039,049,810	$8,165,695,180
	Transportation costs	$130,360,349	$133,735,674	$132,340,435	$133,444,395	$139,076,527	$135,733,110	$136,799,795	$140,039,487	$1,081,529,774
	Caretaker wages	$137,756,020	$139,774,621	$141,413,038	$144,316,303	$144,838,153	$145,260,665	$146,020,248	$149,123,815	$1,148,502,863
	Productivity loss, disability	$17,630,027,553	$17,856,754,256	$17,718,020,740	$17,929,065,133	$18,207,909,530	$18,575,587,186	$18,901,751,549	$18,990,363,475	$145,809,479,421
	Productivity loss, death	$365,577,002,045	$392,603,663,670	$391,823,003,547	$399,710,669,167	$397,009,985,032	$420,232,032,656	$417,756,555,090	$409,186,315,146	$3,193,899,226,353
	Total cost of illness	$384,439,500,435	$411,759,449,247	$410,815,797,571	$418,969,299,697	$416,526,311,394	$440,158,101,761	$437,996,851,792	$429,512,215,083	$3,350,177,526,979

Note: These are total impacts for vaccines administered in the indicated year in US$.

Table 10. *Incremental COI (2020 US$) averted from vaccination programs for 2023–2030, comparing estimates from Table 8 to base case COI assuming constant VIMC health impact estimates from 2022 for all years.*

	Economic benefits	2023	2024	2025	2026	2027	2028	2029	2030	Total
Discounted at 8%	Treatment costs	$100,012	$22,502,341	$16,983,693	$26,093,982	$19,223,068	$35,104,139	$33,364,997	$23,523,231	$176,895,465
	Transportation costs	$1,958,068	$3,787,774	$2,722,878	$2,288,772	$7,179,903	$4,330,126	$5,726,597	$7,604,464	$35,598,581
	Lost caretaker wages	$1,628,034	$3,152,100	$4,378,351	$5,874,580	$6,962,412	$7,582,954	$8,199,234	$9,119,441	$46,897,107
	Productivity loss by disability	$81,924,668	$100,236,345	$73,625,242	$72,746,976	$95,752,161	$116,651,409	$130,027,520	$148,071,149	$819,035,470
	Productivity loss by death	$1,517,385,204	$2,661,189,742	$3,129,502,478	$2,252,937,553	$3,018,360,471	$4,510,268,483	$4,918,056,787	$4,037,528,556	$26,045,229,275
	Total cost of illness	$1,605,693,011	$2,792,894,458	$3,228,985,011	$2,359,052,214	$3,148,769,185	$4,676,401,179	$5,098,094,978	$4,225,882,412	$27,135,772,447
Discounted at 3%	Treatment costs	($16,813,616)	$32,475,555	$10,137,344	$48,933,830	$19,884,723	$53,189,314	$38,085,840	$28,830,470	$214,723,460
	Transportation costs	$1,959,721	$4,469,614	$3,187,717	$3,250,361	$8,673,727	$5,421,594	$6,655,994	$9,195,598	$42,814,327
	Lost caretaker wages	$1,600,775	$3,383,562	$4,840,544	$6,920,718	$7,872,577	$8,440,075	$9,128,996	$10,916,099	$53,103,343
	Productivity loss by disability	$278,009,268	$353,896,427	$295,992,494	$398,509,088	$466,695,845	$525,234,183	$581,559,754	$827,990,611	$3,727,887,669
	Productivity loss by death	$5,627,449,708	$10,371,283,681	$12,424,879,601	$9,512,296,413	$12,480,217,517	$18,062,235,068	$19,875,952,441	$16,750,113,826	$105,104,428,253
	Total cost of illness	$5,895,212,463	$10,767,806,558	$12,741,044,721	$9,968,840,086	$12,984,681,035	$18,657,363,227	$20,514,455,139	$17,627,057,879	$109,156,461,107
Undiscounted (0%)	Treatment costs	($33,724,667)	$54,580,004	$11,146,603	$96,850,754	$40,997,979	$100,882,101	$70,225,830	$65,319,649	$406,278,253
	Transportation costs	$1,949,971	$5,324,012	$3,927,636	$5,030,376	$10,661,459	$7,317,263	$8,383,300	$11,622,376	$54,216,393
	Caretaker wages	$1,295,105	$3,299,365	$4,926,493	$7,817,391	$8,327,578	$8,742,452	$9,496,688	$12,594,982	$56,500,054
	Productivity loss, disability	$987,390,610	$1,208,201,680	$1,047,289,741	$1,253,465,912	$1,527,950,406	$1,893,229,110	$2,218,120,515	$2,305,423,044	$12,441,071,016
	Productivity loss, death	$15,978,780,538	$29,878,327,484	$36,064,701,711	$28,427,290,639	$36,995,244,610	$52,840,158,341	$58,626,612,094	$49,247,721,096	$308,058,836,513
	Total cost of illness	$16,938,909,448	$31,152,219,153	$37,134,154,021	$29,789,263,251	$38,584,544,237	$54,853,438,888	$60,936,149,930	$51,642,674,183	$321,031,353,113

Note: These are total impacts for vaccines administered in the indicated year in US$.

billion for immunization delivery, an increase of US$ 4.0 billion[2] compared to constant returns to scale).

5.3.1. BCG and TCV vaccine costs

Per Copenhagen Consensus Center request, we also estimated the vaccine-specific commodities and delivery costs for Bacille Calmette-Guérin vaccine (BCG) and typhoid conjugated vaccine (TCV). Note that the costs associated with BCG and TCV are omitted from the BCR calculation as benefits models for these two vaccines are still under production. Under the base-case scenario with an 8% discount rate, the cost of BCG and TCV programs would add an additional US$ 3.85 billion to the total vaccination costs between 2023 and 2030 (Tables 15 and 16).

5.3.2. BCR

Using the economic benefits and costing scenarios generated above, we calculated 3 BCR estimates through the COI, VSL, and VSLY approaches. At baseline, with an 8% discount rate, the BCR for attaining 2030 target coverage was estimated at 13.12 (8.20–16.40) through the COI approach, 143.27 (89.60–179.12) through the VSL approach, and 286.12(178.95–357.72) through the VSLY approach. The incremental BCR of attaining 2030 targets was under an assumption of diminishing returns was 3.58, 48.91, and 100.53 for the COI, VSL, and VSLY approaches, respectively (Tables 17–19).

5.3.3. Additional scenarios

6. Conclusions

A general upward trend in total immunization program costs between 2023 and 2030 is observed in undiscounted scenarios and can be explained by changes over time in the number of doses, vaccine prices, and additional delivery costs for new vaccines. However, this increasing total cost is offset when an 8% discount rate is applied. The projection method adopted from GAVI's operational forecast also leads to an increasing number of routine doses administered for all vaccines over the time horizon as a result of population growth and increasing overall coverage. In addition, it is also projected that more countries will introduce newer vaccines (e.g., for HPV, PCV, and rotavirus) between 2023 and 2030. These newer vaccines are more expensive than other existing vaccines and require additional introduction costs. Similarly, our models predict that total economic benefits from vaccination will remain relatively constant over time under an 8% discounting scenario, but generally increase over the time horizon as lower discount rates are applied. This is primarily a result of increases in coverage as well as new vaccine introduction.

[2] These increased costs can be interpreted to include the time costs of mothers for additional immunization visits. A conservative estimate shows that this would at most take 19% of the US$4 billion incremental cost. The incremental scenario sees an additional 2.37 billion doses given in 2023–2030. Assuming a generous 5 hr time cost per maximum of four additional visits, valued at 50% of the estimated average hourly wage (GDP per capita adjusted for labor participation and labor share of GDP), and equal probability of each incremental dose to result in a new additional visit, totals USD$ 747 million discounted (19% of US$ 4 billion).

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Table 11. *Total economic benefits (2020 US$) using VSL and VSLY from vaccination programs for 2023–2030, using VIMC health impact estimates.*

	Economic benefits	2023	2024	2025	2026	2027	2028	2029	2030	Total
Discounted at 8%	VSL	$253,882,292,986	$282,972,703,546	$300,538,908,604	$331,457,863,950	$369,761,317,541	$420,838,077,001	$441,383,727,199	$452,568,368,239	$2,853,403,259,065
	VSLY	$510,549,157,732	$568,974,028,033	$604,211,431,436	$662,265,950,753	$739,496,448,155	$843,044,213,691	$885,235,351,490	$906,382,383,608	$5,720,158,964,898
Discounted at 3%	VSL	$346,923,056,590	$387,442,124,522	$412,563,394,369	$458,425,358,897	$508,291,496,670	$572,441,034,744	$598,876,878,489	$621,402,650,138	$3,906,365,994,419
	VSLY	$655,878,610,398	$731,800,391,509	$779,640,865,739	$858,299,475,948	$954,354,464,117	$1,079,014,741,938	$1,129,075,833,629	$1,166,472,940,212	$7,354,537,323,491
Undiscounted (0%)	VSL	$517,112,042,390	$578,396,375,800	$614,966,187,399	$691,138,864,692	$759,966,384,772	$847,472,911,107	$889,398,354,430	$936,284,858,762	$5,834,735,979,352
	VSLY	$845,363,534,229	$945,128,343,640	$1,007,989,471,307	$1,117,550,571,288	$1,235,594,041,304	$1,385,760,466,673	$1,446,498,349,098	$1,509,228,139,451	$9,493,112,916,991

Note: These are total impacts for vaccines administered in the indicated year in US$.

Table 12. *Incremental economic benefits (2020 USD) from VSL and VSLY from vaccination programs for 2023–2030, comparing estimates from Table 9 to base case COI assuming constant VIMC death impact estimates from 2022 for all years.*

	Economic benefits	2023	2024	2025	2026	2027	2028	2029	2030	Total
Discounted at 8%	VSL	$20,235,670,525	$29,326,276,722	$25,787,868,750	$33,266,163,807	$47,089,325,324	$75,191,526,647	$75,962,604,175	$64,002,315,900	$370,861,751,850
	VSLY	$41,795,448,359	$60,350,660,496	$53,607,968,981	$68,226,497,544	$96,843,603,644	$154,257,927,260	$156,002,748,093	$131,087,517,178	$762,172,371,554
Discounted at 3%	VSL	$22,757,562,067	$34,144,388,476	$28,820,323,261	$40,048,720,961	$55,316,023,819	$88,101,041,946	$90,986,909,272	$80,766,740,039	$440,941,709,841
	VSLY	$47,743,821,626	$69,466,814,744	$61,717,562,045	$80,665,110,708	$113,281,753,782	$178,543,448,441	$182,092,859,583	$158,909,002,596	$892,420,373,524
Undiscounted (0%)	VSL	$26,108,434,761	$41,638,264,369	$29,801,599,850	$50,718,587,370	$65,486,194,321	$105,707,858,501	$115,912,124,392	$111,891,435,862	$547,264,499,426
	VSLY	$53,382,309,208	$79,338,951,797	$67,413,476,913	$94,330,895,663	$128,606,443,236	$201,993,616,910	$210,437,631,001	$192,768,371,860	$1,028,271,696,588

Note: These are total impacts for vaccines administered in the indicated year in US$.

Table 13. *Total immunization program costing (2020 US$) for 2023–2030 (95% CI).*

Scenarios	Costs	2023	2024	2025	2026	2027	2028	2029	2030	Total
Scenario 1. The total cost of immunization programs (discounted at 8%, constant returns to scale, and GAVI DPP wastage ratess)	Vaccine costs	$1,852,431,753 ($1,790,201,428–$2,084,208,778)	$1,695,896,699 ($1,622,835,691–$1,892,562,696)	$1,557,505,506 ($1,464,377,289–$1,715,427,300)	$1,525,666,030 ($1,447,137,070–$1,690,297,182)	$1,429,846,833 ($1,361,142,507–$1,589,815,098)	$1,346,454,228 ($1,294,652,287–$1,510,318,175)	$1,241,548,592 ($1,175,962,251–$1,377,874,660)	$1,166,074,981 ($1,104,941,761–$1,294,449,465)	$11,815,424,621 ($11,263,084,096–$13,153,971,797)
	Vaccine delivery costs	$1,473,316,345 ($836,946,451–$3,197,660,592)	$1,333,732,253 ($753,816,467–$2,939,071,996)	$1,197,938,026 ($667,772,430–$2,690,063,128)	$1,164,424,145 ($656,093,171–$2,550,633,472)	$1,084,993,061 ($607,338,794–$2,381,037,226)	$1,031,959,903 ($575,390,394–$2,248,298,444)	$926,970,637 ($505,789,086–$2,068,263,143)	$863,964,918 ($473,159,769–$1,928,064,108)	$9,077,299,288 ($5,076,147,265–$20,033,852,165)
	Total costs	$3,t325,748,098 ($2,738,324,814–$5,135,482,248)	$3,029,628,952 ($2,479,471,098–$4,671,062,101)	$2,755,443,532 ($2,226,842,401–$4,267,492,193)	$2,690,090,175 ($2,196,296,846–$4,127,695,676)	$2,514,839,894 ($2,054,815,248–$3,861,796,592)	$2,378,414,131 ($1,950,763,297–$3,657,862,368)	$2,168,519,228 ($1,758,860,544–$3,360,614,885)	$2,030,039,900 ($1,649,108,274–$3,144,976,162)	$20,892,723,909 ($17,047,468,661–$32,178,101,881)
Scenario 2. The total cost of immunization program (discounted at 8%, 0% wastage rate, and constant returns to scale))	Vaccine costs	$1,676,828,212 ($1,602,218,382–$1,877,510,005)	$1,534,039,757 ($1,452,175,608–$1,700,883,989)	$1,408,703,445 ($1,308,947,979–$1,537,817,461)	$1,381,170,428 ($1,296,427,602–$1,520,452,868)	$1,294,199,666 ($1,217,985,539–$1,428,295,501)	$1,218,961,156 ($1,158,493,936–$1,358,696,665)	$1,124,190,076 ($1,053,018,525–$1,239,494,926)	$1,055,900,811 ($989,050,134–$1,164,755,634)	$10,693,993,550 ($10,077,120,544–$11,835,490,515)
	Vaccine delivery costs	$1,473,316,345 ($836,946,451–$3,197,660,592)	$1,333,732,253 ($753,816,467–$2,939,071,996)	$1,197,938,026 ($667,772,430–$2,690,063,128)	$1,164,424,145 ($656,093,171–$2,550,633,472)	$1,084,993,061 ($607,338,794–$2,381,037,226)	$1,031,959,903 ($575,390,394–$2,248,298,444)	$926,970,637 ($505,789,086–$2,068,263,143)	$863,964,918 ($473,159,769–$1,928,064,108)	$9,077,299,288 ($5,076,147,265–$20,033,852,165)
	Total costs	$3,150,144,557 ($2,447,068,209–$4,369,303,571)	$2,867,772,010 ($2,206,023,979–$3,975,397,292)	$2,606,641,471 ($1,977,525,397–$3,632,574,156)	$2,545,594,573 ($1,952,814,891–$3,513,744,124)	$2,379,192,727 ($1,831,817,978–$3,284,552,267)	$2,250,921,058 ($1,740,700,683–$3,122,496,101)	$2,051,160,712 ($1,570,476,194–$2,836,798,687)	$1,919,865,729 ($1,471,055,702–$2,648,297,897)	$19,771,292,838 ($15,227,152,665–$27,452,006,856)
Scenario 3. The total cost of immunization program (discounted at 8%, GAVI DPP wastage rates, with diminishing returns to scale)	Vaccine costs	$1,852,431,753 ($1,790,201,428–$2,084,208,778)	$1,695,896,699 ($1,622,835,691–$1,892,562,696)	$1,557,505,506 ($1,464,377,289–$1,715,427,300)	$1,525,666,030 ($1,447,137,070–$1,690,297,182)	$1,429,846,833 ($1,361,142,507–$1,589,815,098)	$1,346,454,228 ($1,294,652,287–$1,510,318,175)	$1,241,548,592 ($1,175,962,251–$1,377,874,660)	$1,166,074,981 ($1,104,941,761–$1,294,449,465)	$11,815,424,621 ($11,263,084,096–$13,153,971,797)
	Vaccine delivery costs	$2,052,417,644 ($1,416,047,750–$3,776,761,891)	$1,890,567,149 ($1,310,651,363–$3,495,906,892)	$1,732,575,795 ($1,202,410,198–$3,224,700,896)	$1,680,472,232 ($1,172,141,257–$3,066,681,559)	$1,577,895,029 ($1,100,240,762–$2,873,939,194)	$1,501,257,405 ($1,044,687,897–$2,717,595,946)	$1,373,565,850 ($952,384,300–$2,514,858,356)	$1,285,962,052 ($895,156,903–$2,350,061,242)	$13,094,713,155 ($9,093,561,132–$24,051,266,032)
	Total costs	$3,904,849,397 ($2,738,324,814–$5,135,482,248)	$3,586,463,848 ($2,479,471,098–$4,671,062,101)	$3,290,081,300 ($2,226,842,401–$4,267,492,193)	$3,206,138,262 ($2,196,296,846–$4,127,695,676)	$3,007,741,862 ($2,054,815,248–$3,861,796,592)	$2,847,711,633 ($1,950,763,297–$3,657,862,368)	$2,615,114,442 ($1,758,860,544–$3,360,614,885)	$2,452,037,033 ($1,649,108,274–$3,144,976,162)	$24,910,137,776 ($17,047,468,661–$32,178,101,881)
Scenario 4. The total cost of immunization program (discounted at 3%, constant returns to scale, and	Vaccine costs	$2,036,644,732 ($1,968,225,984–$2,291,470,561)	$1,955,055,035 ($1,870,829,213–$2,181,774,531)	$1,882,676,552 ($1,770,105,322–$2,073,568,756)	$1,933,713,505 ($1,834,181,558–$2,142,376,132)	$1,900,241,079 ($1,808,934,249–$2,112,836,066)	$1,876,278,534 ($1,804,092,738–$2,104,622,282)	$1,814,078,048 ($1,718,247,130–$2,013,269,710)	$1,786,509,189 ($1,692,848,781–$1,983,187,961)	$15,185,196,674 ($14,468,788,053–$16,904,078,205)
		$1,619,828,622	$1,537,546,454	$1,448,039,717	$1,475,855,562	$1,441,936,533	$1,438,031,960	$1,354,435,174	$1,323,655,246	$11,639,329,268

Table 13. *Continued*

Scenarios	Costs	2023	2024	2025	2026	2027	2028	2029	2030	Total
GAVI DPP wastage ratess)	Vaccine delivery costs	($920,175,644–$3,515,648,331)	($869,010,877–$3,388,206,077)	($807,187,834–$3,251,685,952)	($831,568,770–$3,232,813,929)	($807,142,484–$3,164,356,241)	($801,804,193–$3,132,994,809)	($739,029,374–$3,022,024,904)	($724,914,169–$2,953,930,324)	($6,503,586,727–$25,712,563,853)
	Total costs	$3,656,473,354 ($3,010,634,426–$5,646,174,469)	$3,492,601,488 ($2,858,371,301–$5,384,870,129)	$3,330,716,269 ($2,691,755,475–$5,158,445,642)	$3,409,569,067 ($2,783,708,092–$5,231,669,786)	$3,342,177,612 ($2,730,813,018–$5,132,259,174)	$3,314,310,494 ($2,718,380,783–$5,097,216,450)	$3,168,513,222 ($2,569,943,958–$4,910,333,539)	$3,110,164,435 ($2,526,550,293–$4,818,325,497)	$26,824,525,942 ($21,875,668,330–$41,311,949,652)
Scenario 5. The total cost of immunization program (undiscounted, constant returns to scale, and GAVI DPP wastage ratess)	Vaccine costs	$2,160,676,396 ($2,088,090,946–$2,431,021,118)	$2,136,341,423 ($2,044,305,594–$2,384,083,938)	$2,118,969,046 ($1,992,269,135–$2,333,819,903)	$2,241,703,933 ($2,126,319,128–$2,483,601,108)	$2,268,987,225 ($2,159,962,095–$2,522,836,757)	$2,307,585,933 ($2,218,806,509–$2,588,419,941)	$2,298,019,796 ($2,176,624,057–$2,550,349,834)	$2,330,989,283 ($2,208,783,694–$2,587,610,470)	$17,863,273,035 ($17,017,672,466–$19,881,813,860)
	Vaccine delivery costs	$1,718,476,185 ($976,214,341–$3,729,751,315)	$1,680,118,524 ($949,591,649–$3,702,384,262)	$1,629,781,459 ($908,497,018–$3,659,801,187)	$1,710,921,090 ($964,016,116–$3,747,717,375)	$1,721,747,629 ($963,770,337–$3,778,406,836)	$1,768,597,925 ($986,118,022–$3,853,188,436)	$1,715,757,956 ($936,180,300–$3,828,210,734)	$1,727,069,869 ($945,848,568–$3,854,209,074)	$13,672,470,638 ($7,629,785,115–$30,205,517,463)
	Total costs	$3,879,152,582 ($3,193,982,062–$5,990,026,494)	$3,816,459,946 ($3,123,419,496–$5,884,192,981)	$3,748,750,505 ($3,029,594,502–$5,805,876,016)	$3,952,625,023 ($3,227,080,621–$6,064,939,149)	$3,990,734,854 ($3,260,733,555–$6,128,185,853)	$4,076,183,858 ($3,343,265,482–$6,268,933,298)	$4,013,777,752 ($3,255,528,117–$6,220,263,617)	$4,058,059,152 ($3,296,575,070–$6,286,821,899)	$31,535,743,672 ($25,717,210,758–$48,565,861,810)

Table 14. *Incremental cost (2020 US$) of immunization programs for 2023–2030 to achieve 2030 target coverage under constant and diminishing returns to scale scenario.*

Scenarios	Costs	2023	2024	2025	2026	2027	2028	2029	2030	Total
Scenario 6. Incremental costs of achieving 2030 target at halftime compared to 2022 coverage level (discounted at 8%, constant returns to scale for routine immunizations, and GAVI DPP wastage rates)	Vaccine costs	$329,298,702	$270,095,074	$267,013,312	$273,135,063	$305,451,646	$300,924,496	$276,686,045	$256,143,278	$2,278,747,617
	Vaccine delivery costs	$209,071,222	$188,139,892	$148,218,584	$140,470,489	$163,269,602	$184,921,852	$140,700,124	$110,884,080	$1,285,675,845
	Total costs	$538,369,924	$458,234,966	$415,231,896	$413,605,552	$468,721,248	$485,846,348	$417,386,169	$367,027,359	$3,564,423,462
Scenario 7. Incremental costs of achieving 2030 target at halftime compared to 2022 coverage level (discounted at 3%, constant returns to scale for routine immunizations, and GAVI DPP wastage rates)	Vaccine costs	$362,045,439	$311,369,634	$322,759,503	$346,186,485	$405,939,820	$419,337,071	$404,277,435	$392,429,585	$2,964,344,971
	Vaccine delivery costs	$229,862,073	$216,890,476	$179,163,189	$178,040,067	$216,982,404	$257,687,855	$205,582,776	$169,882,239	$1,654,091,079
	Total costs	$591,907,512	$528,260,111	$501,922,691	$524,226,552	$622,922,224	$677,024,925	$609,860,212	$562,311,824	$4,618,436,050
Scenario 8. Incremental costs of achieving 2030 target at halftime compared to 2022 coverage level (discounted at 0%, constant returns to scale for routine immunizations, and GAVI DPP wastage rates)	Vaccine costs	$384,094,006	$340,242,006	$363,268,664	$401,325,017	$484,713,374	$515,731,704	$512,126,560	$512,031,599	$3,513,532,929
	Vaccine delivery costs	$243,860,674	$237,002,079	$201,649,747	$206,397,234	$259,088,338	$316,923,558	$260,426,110	$221,657,790	$1,947,005,530
	Total costs	$627,954,679	$577,244,086	$564,918,411	$607,722,251	$743,801,712	$832,655,262	$772,552,670	$733,689,388	$5,460,538,459
Scenario 9. Incremental costs of achieving 2030 target at halftime compared to 2022 coverage level (discounted at 8%, diminishing returns to scale for routine immunizations, and GAVI DPP wastage rates)	Vaccine costs	$329,298,702	$270,095,074	$267,013,312	$273,135,063	$305,451,646	$300,924,496	$276,686,045	$256,143,278	$2,278,747,617
	Vaccine delivery costs	$788,172,521	$744,974,788	$682,856,353	$656,518,576	$656,171,569	$654,219,354	$587,295,337	$532,881,214	$5,303,089,712
	Total costs	$1,117,471,223	$1,015,069,862	$949,869,665	$929,653,639	$961,623,216	$955,143,850	$863,981,382	$789,024,492	$7,581,837,329

Table 15. *Total BCG vaccine costing (2020 US$, routine only) for 2023–2030.*

Scenarios	Costs	2023	2024	2025	2026	2027	2028	2029	2030	Total
Discounted at 8%, constant returns to scale, and GAVI DPP wastage rates	Vaccine costs	$23,825,190	$22,244,622	$20,766,631	$19,355,794	$18,035,532	$16,801,385	$15,650,854	$14,576,669	$151,256,676
	Vaccine delivery costs	$206,443,012	$192,538,755	$179,555,562	$167,279,593	$155,792,157	$145,073,644	$135,103,731	$125,818,254	$1,307,604,708
	Total costs	$230,268,202	$214,783,378	$200,322,193	$186,635,387	$173,827,689	$161,875,029	$150,754,585	$140,394,923	$1,458,861,384
Discounted at 3%, constant returns to scale, and GAVI DPP wastage rates	Vaccine costs	$26,194,459	$25,643,933	$25,102,222	$24,532,603	$23,968,902	$23,412,662	$22,868,110	$22,332,486	$194,055,376
	Vaccine delivery costs	$226,972,504	$221,961,552	$217,042,601	$212,019,408	$207,045,013	$202,159,538	$197,405,655	$192,762,447	$1,677,368,717
	Total costs	$253,166,963	$247,605,484	$242,144,823	$236,552,011	$231,013,915	$225,572,200	$220,273,765	$215,094,933	$1,871,424,093
Discounted at 0%, constant returns to scale, and GAVI DPP wastage rates	Vaccine costs	$27,789,702	$28,021,818	$28,252,772	$28,440,011	$28,620,122	$28,794,621	$28,968,638	$29,138,829	$228,026,512
	Vaccine delivery costs	$240,795,129	$242,543,380	$244,283,360	$245,788,603	$247,222,573	$248,630,732	$250,067,577	$251,511,272	$1,970,842,627
	Total costs	$268,584,831	$270,565,198	$272,536,132	$274,228,614	$275,842,696	$277,425,353	$279,036,215	$280,650,101	$2,198,869,138

Table 16. *Total TCV vaccine costing (2020 US$, routine and SIA) for 2023–2030.*

Scenarios	Costs	2023	2024	2025	2026	2027	2028	2029	2030	Total
Discounted at 8%, constant returns to scale, and GAVI DPP wastage rates	Vaccine costs	$209,506,498	$237,966,319	$296,525,095	$189,447,079	$219,311,147	$81,467,157	$113,004,121	$106,955,532	$1,454,182,948
	Vaccine delivery costs	$118,498,234	$134,665,495	$165,229,444	$116,033,236	$129,764,543	$62,646,360	$75,791,472	$71,245,569	$873,874,353
	Total costs	$328,004,731	$372,631,814	$461,754,539	$305,480,315	$349,075,690	$144,113,517	$188,795,593	$178,201,101	$2,328,057,301
Discounted at 3%, constant returns to scale, and GAVI DPP wastage rates	Vaccine costs	$230,340,634	$274,331,125	$358,432,661	$240,115,705	$291,460,625	$113,524,154	$165,115,000	$163,863,425	$1,837,183,330
	Vaccine delivery costs	$130,282,156	$155,244,394	$199,725,521	$147,066,941	$172,454,776	$87,297,450	$110,742,057	$109,153,242	$1,111,966,537
	Total costs	$360,622,791	$429,575,519	$558,158,183	$387,182,646	$463,915,401	$200,821,605	$275,857,057	$273,016,667	$2,949,149,868
Discounted at 0%, constant returns to scale, and GAVI DPP wastage rates	Vaccine costs	$244,368,379	$299,769,027	$403,419,118	$278,359,912	$348,019,228	$139,620,391	$209,162,742	$213,804,603	$2,136,523,400
	Vaccine delivery costs	$138,216,340	$169,639,740	$224,792,834	$170,490,892	$205,920,021	$107,364,853	$140,284,724	$142,420,223	$1,299,129,627
	Total costs	$382,584,719	$469,408,768	$628,211,952	$448,850,804	$553,939,249	$246,985,243	$349,447,466	$356,224,825	$3,435,653,027

Table 17. *BCR using the COI, VSL, and VSLY approach at 8% discounted rate using 2020 US$, 2023–2030 (95% CI only available for the primary results).*

Discounted at 8%		Baseline 2022 coverage	2030 target coverage	2030 target coverage (diminishing returns)	Incremental costs/benefits to achieve 2030 target coverage (constant returns)	Incremental costs/benefits to achieve 2030 target coverage (diminishing returns)
COI	COI	$227,314,423,160.15	$254,450,195,607.51	$254,450,195,607.51	$27,135,772,447.36	$27,135,772,447.36
	Cost (95% CI)	$ 17,328,300,447.20 ($13,860,016,080–$27,706,256,357)	$20,892,723,909.46 ($17,047,468,661–$32,178,101,881)	$24,910,137,776.28	$3,564,423,462.26	$7,581,837,329.08
	BCR (95% CI)	13.12 ($8.20–$16.40)	12.18 ($7.91–$14.93)	$10.21	7.61	3.58
VSL	VSL	$2,482,541,507,215.55	$2,853,403,259,065.31	$2,853,403,259,065.31	$ 370,861,751,849.76	$ 370,861,751,849.76
	Cost (95% CI)	$ 17,328,300,447.20 ($13,860,016,080–$27,706,256,357)	$20,892,723,909.46 ($17,047,468,661–$32,178,101,881)	$24,910,137,776.28	$3,564,423,462.26	$7,581,837,329.08
	BCR (95% CI)	143.27 (89.60–179.12)	136.57(88.68–167.38)	$114.55	104.05	48.91
VSLY	VSLY	$4,957,986,593,344.45	$5,720,158,964,897.98	$5,720,158,964,898.98	$ 762,172,371,553.54	$ 762,172,371,553.54
	Cost (95% CI)	$ 17,328,300,447.20 ($13,860,016,080–$27,706,256,357)	$20,892,723,909.46 ($17,047,468,661–$32,178,101,881)	$24,910,137,776.28	$3,564,423,462.26	$7,581,837,329.08
	BCR (95% CI)	286.12(178.95–357.72)	273.79(177.77–335.54)	$229.63	213.83	100.53

Table 18. *BCR using the COI, VSL and VSLY approach at 3% discounted rate using 2020 US$, 2023–2030.*

Discounted at 3%		Baseline 2022 coverage	2030 target coverage	Incremental costs/ benefits to achieve 2030 target coverage
COI	COI	$992,376,324,463	$1,101,532,785,570	$109,156,461,107
	Cost	$22,206,089,892	$26,824,525,942	$4,618,436,050
	BCR	$44.69	$41.06	$23.63
VSL	VSL	$3,465,424,284,578	$3,906,365,994,419	$440,941,709,841
	Cost	$22,206,089,892	$26,824,525,942	$4,618,436,050
	BCR	$156.06	$145.63	$95.47
VSLY	VSLY	$6,462,116,949,966	$7,354,537,323,491	$892,420,373,524
	Cost	$22,206,089,892	$26,824,525,942	$4,618,436,050
	BCR	$291.01	$274.17	$193.23

Table 19. *BCR using the COI, VSL and VSLY approach at 0% discounted rate using 2020 US$, 2023–2030.*

Discounted at 0%		Baseline 2022 coverage	2030 target coverage	Incremental costs/ benefits to achieve 2030 target coverage
COI	COI	$3,029,146,173,866	$3,350,177,526,979	$321,031,353,113
	Cost	$26,075,205,213	$31,535,743,672	$5,460,538,459
	BCR	$116.17	$106.23	$58.79
VSL	VSL	$5,287,471,479,926	$5,834,735,979,352	$547,264,499,426
	Cost	$26,075,205,213	$31,535,743,672	$5,460,538,459
	BCR	$202.78	$185.02	$100.22
VSLY	VSLY	$8,464,841,220,403	$9,493,112,916,991	$1,028,271,696,588
	Cost	$26,075,205,213	$31,535,743,672	$5,460,538,459
	BCR	$324.63	$301.03	$188.31

Overall, benefits and costs are comparable to previous studies estimating the economic benefits and costs of immunization programs over time using the COI and VSL approaches, once discount rates are used (Stack *et al.,* 2011; Portnoy *et al.,* 2015; Ozawa *et al.,* 2016; Sim *et al.,* 2020). The VSLY approach, however, generates benefit estimates exceeding other studies after correcting for discount rate differences. Overall, the 8% discount rate employed in the base case is significantly higher than the maximum rates employed by all other immunization studies, making the benefits and costs assessed under this scenario significantly lower in magnitude than those estimated in other studies. There are significant benefits to examining the impact under all three benefits estimation approaches because while adopting a VSL approach treats all lives equally, VSLY

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accounts for differences in the age of mortality impact thereby making the assumption that all life years are treated equally.

The global BCR estimates from this study are large ranging from 12.18 to 273.79 and can inform decision-makers of funding agencies as they prioritize investments across the SDGs as well as contribute to resource mobilization efforts for immunization programs in order to reach the goals set by the global community as part of SDGs.

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