Methodology Report: Decade of Vaccines Economics (DOVE) Return on Investment Analysis

August 2019

Prepared by:

Johns Hopkins University
International Vaccine Access Center (IVAC)
Decade of Vaccine Economics-Phase IV (DOVE-IV) team

In collaboration with
Decade of Vaccine Economics (DOVE) Core Advisory Group

Funded by the Bill & Melinda Gates Foundation

Preferred citation:

Johns Hopkins University - International Vaccine Access Center (IVAC) (2019). Methodology Report: Decade of Vaccines Economics (DOVE) Return on Investment Analysis. Retrieved from http://immunizationeconomics.org/dove-roi

Decade of Vaccine Economics (DOVE) Core Advisory Group

The DOVE Return on Investment (ROI) analysis is a collaborative exercise between the IVAC-DOVE team and 18 DOVE-ROI Core Advisory Group ("Core Group") members who are experts in modeling, immunization economics and financing and who represent eight global health organizations. The Core Group is an advisory body that provides support to collect model inputs, offers technical guidance for methodology and reviews materials and documents produced from this analysis.

General meetings served as a platform for consensus building and project updates while topic-specific subgroups focused on discussions of methodology and validation of data sources and results. Subgroups focused on productivity loss, Value-of-Statistical-Life (VSL) and immunization delivery costs. The DOVE team also consulted with members of the Core Group on specific topics as needed on an *ad hoc* basis.

Members of the Core Group include:

Johns Hopkins University International Vaccine Access Center DOVE-IV team
- **Bryan N. Patenaude**, Project lead, Assistant Professor, International Health (2019)
- **Dagna Constenla**, Project lead, Director of Economics and Finance (2016 - 2019)
- **So Yoon (Yoonie) Sim**, Project Coordinator, Health Economist/Research Associate
- **Elizabeth (Libby) Watts**, Project Coordinator, Health Economist/Research Associate

Gavi, the Vaccine Alliance
- **Anais Colombini**, Senior Program Manager
- **Santiago Cornejo**, Director, Immunization Financing
- **Dan Hogan**, Head, Corporate Performance Monitoring & Measurement
- **Hope Johnson**, Director, Monitoring & Evaluation
- **Tewodaj Mengistu**, Senior Program Officer

Harvard T.H. Chan School of Public Health
- **Lisa Robinson**, Senior Research Scientist, Center for Health Decision Science
- **Stephane Verguet**, Assistant Professor of Global Health

Institute for Health Metrics and Evaluation (IHME)
- **Joe Dieleman**, Assistant Professor, IHME, University of Washington

World Health Organization
- **Xiao Xian Huang**, Health Economist
- **Raymond Hutubessy**, Health Economist
- **Jeremy Lauer**, Economist
- **Thomas O'Connell**, Health System Advisor, Health Governance and Financing
- **Claudio Politi**, Health Economist

UNICEF
- **Ulla Griffiths**, Senior Advisor, Immunization Financing and Health Systems Strengthening

The World Bank Group
- **Sarah Alkenbrack**, Senior Health Economist

Pan-American Health Organization
- **John Fitzsimmons**

Bill & Melinda Gates Foundation
- **Logan Brenzel**, Senior Program Officer
- **Emily Dansereau**, Program Officer

BACKGROUND AND OBJECTIVE

Increases in health investment are needed to achieve Universal Health Coverage and to make progress toward both national health objectives and Sustainable Development Goals. Return-on-investment (ROI) estimates and investment cases have been actively used by the global health community to describe the value of and articulate need for new investments. Leveraging newly available data and recently established methodological approaches, we aim to estimate the ROI for vaccines and immunization programs against 10 antigens for 73 low- and middle-income countries from 2021-2030.

This analysis differs from the previous 2016 DOVE ROI exercise[1] in several ways:

1) It incorporates updated methods and conforms to other global efforts on methodology development.[2]
2) Vaccine impact and cost results are derived from version 16 of Gavi's operational forecast, which has undergone major methodological updating.
3) The models utilize expanded and updated data sources from newly available publications and online databases.
4) The current analysis extends beyond the Decade of Vaccines (2011-2020) to inform a new vision and strategy for the next decade: 2021-2030. The results presented here reflect a re-estimated ROI projected for the future decade.

Due to these differences, a direct comparison between the current DOVE ROI estimates and the previous estimates published in 2016 should not be made.

This Working Paper details the core methodologies and main results of the updated DOVE ROI analysis for use by Gavi in the ramp-up to replenishment in mid-2020. Detailed results, sensitivity analysis, and scenario analyses are planned for publication in late 2019.

RETURN ON INVESTMENT: SCOPE & FRAMEWORK

The scope of the current DOVE model includes 94 low- and middle- income countries across six WHO regions. This report focuses on 73 Gavi supported countries although the results are also available for all 94 countries in Appendix I.

ROI estimates include 9 vaccines that contain 10 antigens (Measles, Yellow fever, *Haemophilus influenzae* type b, Japanese encephalitis, Hepatitis B, *Neisseria Meningitidis* serogroup A, Rubella, *Streptococcus pneumoniae,* Human papillomavirus and Rotavirus).

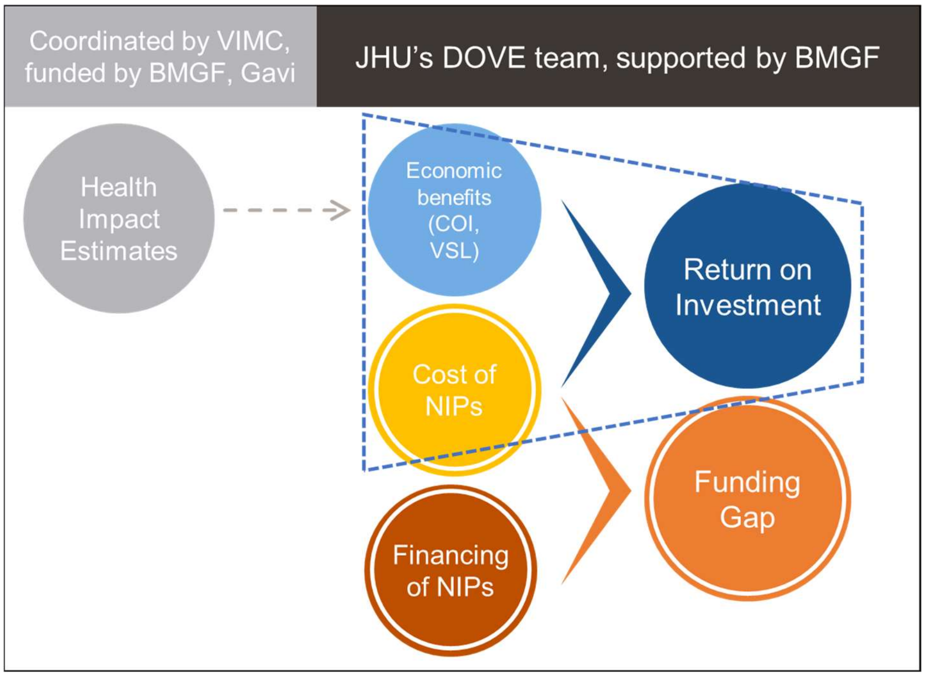
---

[1] The ROI of vaccination was estimated by the DOVE team as 16:1 for the Decade of Vaccines (2011-2020)and was critical in catalyzing resource mobilization for this decade (Ozawa et al., 2016). Suggest (1) qualifying that 16:1 applies to 94 -low and middle-income countries, (2) adding 18:1 for 73 Gavi supported countries, and (3) adding 48:1 for 73 Gavi-supported countries if we include broader benefits of immunisation

[2] The DOVE methods, data sources and models underwent a thorough vetting process by Gavi Alliance partners and modeling experts.

The DOVE Return on Investment analysis utilizes three models: two that estimate the economic benefits, and one that estimates the costs of national immunization programs (NIPs) (Figure 1). We estimated economic benefits using two standard approaches – Cost of illness (COI) and Value of Statistical Life (VSL) – to capture the observable impact of immunization programs on the economy (COI) as well as broader economic benefits (VSL). The total investment and impact of vaccines in terms of benefits and costs are compared to a counterfactual scenario of no vaccination.

Figure 1. DOVE-ROI Model Framework



Return on investment is calculated using the following formula:

$$ROI = \frac{Benefits - Costs}{Costs}$$

METHODS: ECONOMIC BENEFITS

The Economic Benefits models estimate the economic impact of vaccines using two approaches: Cost of Illness averted (COI) and value-of-statistical-life (VSL). The COI includes three short-term costs: treatment costs, transportation costs and lost caregiver wages; and two long-term costs: productivity loss due to disability and productivity loss due to death. Treatment costs reflect the avoidable burden on the health system, whereas transportation costs and caregiver wages reflect the burden on households that is external to the health system. Productivity loss shows the impact of vaccines on the labor force from preventing presenteeism and absenteeism caused by vaccine-preventable diseases. In contrast, the VSL approach reflects the value individuals place on their lives beyond their economic contribution to society and is a broader representation of the economic benefits.

The DOVE Economic Benefits models utilize estimates of cases and deaths averted by vaccination provided by modeling teams participating in the Vaccine Impact Modeling Consortium (VIMC), housed at Imperial College (Vaccine Impact Modelling Consortium [VIMC], 2019). The DOVE-ROI model used VIMC health impact estimates generated in Spring 2019.[3] The antigens, modeling teams, and delivery strategies included in the DOVE models are listed in Table 1.

Table 1. Vaccine-preventable antigens in the DOVE-COI Models

Antigen	Modeling Team*	Delivery Strategy	
		Routine	SIA†
Hepatitis B (Hep B) ‡	Li (Independent)	✓	
Haemophilus influenzae type b (Hib) ‡	Lives Saved Tool (LiST)	✓	
Human papillomavirus (HPV)	Harvard School of Public Health	✓	✓
Japanese Encephalitis (JE)	Oxford University Clinical Research Unit (OUCRU)	✓	✓
Measles	Penn State	✓	✓
Rubella §	Public Health England (PHE)	✓	✓
Meningococcal conjugate serotype A (Men A)	Kaiser Permanente Washington Health Research Institute (KPW)	✓	✓
Pneumococcal conjugate (PCV)	LiST (JHU)	✓	
Rotavirus (RV)	LiST (JHU)	✓	
Yellow fever (YF)	Imperial College	✓	✓

**DOVE-ROI based on estimates from VIMC focal models*
†SIA: Supplementary Immunization Activities
‡Hep B and Hib estimates based on coverage of pentavalent (DTP-HepB-Hib) vaccine; Hep B estimates exclude birth dose
§Rubella estimates based on coverage of Measles-Rubella vaccine

COI APPROACH

Acute Treatment Costs

To estimate treatment costs averted attributable to immunization, we calculated how many averted cases would have sought care from various levels of health facilities and their associated costs. First, care-seeking rates for fever, acute respiratory infection, and diarrhea were used to estimate the proportion of care-seeking cases for each syndrome (Demographic and Health Survey [DHS], various years; Multiple Indicator Cluster Survey [MICS], various years).

The number of inpatient cases was calculated using hospital admittance rates, which were determined based on disease severity and the proportion of outpatients who seek care from hospitals. Hospital admittance rates were multiplied by the number cases that sought care at hospitals. To reflect differences in treatment costs between rural and urban areas, the number of cases seeking care is further stratified by the percentage of the population living in rural versus urban settings.

[3] VIMC spring 2019 estimates were generated using impact estimates from the 2017 model run with coverage estimates from the 2018 Gavi operational forecast.

The DOVE team modeled country- and level-specific facility costs using the WHO-CHOICE regression framework (WHO-CHOICE, 2008). The facility costs were then multiplied by care-seeking cases at each location and facility level. For inpatient cases, the relevant per diem facility cost was multiplied by the average length of stay.

Due to wide variation and limited primary data on treatment costs for the ten diseases included in the DOVE models, additional costs of medications and diagnostics were estimated as a proportion of total facility fees. Based on the recent systematic review of cost of illness studies by the DOVE-IV team, this approach yields a conservative estimate of medication and diagnostic costs averted by vaccination (De Broucker, Sim, Gross, Brenzel & Constenla, 2018).

Total acute treatment costs are discounted from the age of disease onset back to the year of vaccination at a 3% discount rate. Facility and treatment costs are assumed to be constant over the model time horizon (2021-2030).

Transportation Costs

Transportation costs – the cost of roundtrip transportation to a health facility – are estimated by multiplying the country-specific cost per trip to a healthcare facility by the number of care-seeking cases and the number of trips to health facilities. Cases of long-term disability were assumed to require two round trips to a health facility in the first year of illness. For Hepatitis B and HPV, which occur later in life, transportation costs were discounted at a rate of 3% from the year of care-seeking to the year of vaccination. Estimates of transportation costs were extracted from a 2010 systematic review of the economic burden of rotavirus disease (Kim, Sweet, Slichter & Goldie, 2010).

Lost Caregiver Wages

Caregiver wages lost represent the opportunity cost of caring for a sick child in lieu of engaging in routine activities. Caregiver wages lost were only estimated for childhood diseases, for which the age of onset is under 15 years. Since caregivers in LMICs may be predominantly working either in the home or employed in a low-wage sector of the economy, minimum wage was used to approximate the value of a lost day of work. Minimum wage data was extracted from the International Labor Organization (ILO) and the U.S. Department of State Human Rights report for countries not included in the ILO database (International Labor Organization, n.d.; US State Department, n.d.).

Caregiver wages lost was calculated by multiplying the country-specific minimum wage by the number of days lost due to care seeking. For outpatient cases, we estimated that caregivers would lose 50% of one day's wages. For inpatient cases, caregiver wages lost is estimated by multiplying the daily minimum wage by the length of stay.

Long-term costs averted

Productivity loss due to disability and death averted reflects the economic value that vaccinated individuals contribute to society because of the absence of vaccine-preventable diseases. In order to focus on the impact of vaccines on the labor force, the DOVE models only included economic productivity between ages 15 and 64, the OECD definition of the working age population. Vaccine-preventable cases and deaths occurring before age 15 were multiplied by the probability of survival to age 15 to account for competing mortality risks.

We employed a human capital method to estimate productivity loss. Gross domestic product (GDP) per capita for 2018 was used as a proxy for an individual's annual economic contribution to society. The value of productivity was assumed to be constant over the time horizon.

Labor force participation rates only reflect the proportion of workers participating in the formal sector. In order to account for the value of labor in the informal sector, as well as unpaid and volunteer work, the DOVE models apply a labor force participation rate of 100% for all countries.

Productivity Loss due to Disability Averted

To estimate the productivity lost due to disability, cases of long-term disability were multiplied by remaining productive years at age of onset, or age 15 if the onset occurs prior to age 15, and discounted back to the year of vaccination. The discounted number of years was then multiplied by disability weights from the Global Burden of Disease study, representing the severity of each disease outcome. The number of disability-adjusted life-years (DALYs) lost between ages 15 and 64 was multiplied by GDP per capita.

For acute illness (short-term disability), productivity loss was estimated for illness occurring between ages 15 to 64. The discounted duration of illness was multiplied by the number of cases, the corresponding disability weight, and GDP per capita.

Productivity Loss due to Death Averted

The human capital approach used to estimate productivity loss due to disability was also used to estimate productivity loss averted due to death. The total number of deaths was multiplied by the number of remaining productive life years, discounted to year of vaccination, and 2018 GDP per capita.

The impact of baseline assumptions on the overall estimated productivity loss averted were explored in scenario analyses. The baseline assumptions yield a relatively conservative estimate of productivity loss averted by immunization (Watts, Sim, Brenzel & Constenla, 2019).

VSL Approach

The VSL approach includes economic benefits outside of what individuals contribute to society through participation in the labor force. VSL is typically derived from wage-risk studies and stated preference studies that elicit respondents' willingness-to-pay for a small reduction in mortality risk. The willingness-to-pay value is then multiplied across the study population to reflect the actuarial value society would place on saving a life.

Many studies have examined VSL in high-income settings, including the U.S. and Europe, but few to no studies have directly estimated VSL in low-income settings. Because of the limited available data for VSL in the DOVE target countries, the DOVE models apply the methods outlined in the *Reference Case Guidelines for Benefit-Cost Analysis in Global Health and Development* (Robinson et al, 2019).

To estimate VSL for each of the DOVE countries, the DOVE team adjusted the U.S. VSL to each country based on the ratio of GDP per capita in both countries and an income elasticity of 1.5, as shown in the formula below:

$$VSL_{LMIC} = \left(\frac{GDP\ per\ capita_{LMIC}}{GDP\ per\ capita_{HIC}}\right)^{1.5} * VSL_{HIC}$$

As recommended by Robinson et al (2019), the DOVE team set 20 times GDP per capita as a minimum value for VSL. Because VSL values reflect value of life beyond earnings, VSL is unlikely to fall below 20 times GDP per capita (the average value of future earnings for people of average age in a population). This method was used to impute the VSL for 30 of the 73 Gavi countries.

Deaths averted and the corresponding VSL benefits accrue years after the vaccination, thus the VSL was estimated based on projected GDP per capita in the year of impact and discounted back to the year of vaccination at a 3% discount rate. Data for projected GDP per capita from 2021-2050 was extracted from a recent study that projected trends in future health spending (Global Burden of Disease Health Financing Collaborator Network, 2018). The average GDP per capita growth rate from 2041-2050 was used to extrapolate GDP per capita values for the remaining time horizon.

METHODS: IMMUNIZATION PROGRAM COSTS

The analysis estimates immunization program costs for routine immunization and SIAs, which are largely divided into two components.

- **Vaccine cost:** costs to procure vaccines including injection supplies and freight.
- **Immunization delivery cost:** non-vaccine costs to deliver immunizations to target populations. It usually includes all or any of the following components:
    - *Labor function*: personnel costs (salaries, per diem and travel allowances)
    - *Storage function*: cold chain equipment, maintenance and overhead
    - *Transportation function*: vehicles, transport and fuel
    - *Other capital costs*: buildings, utilities and other overheads, building construction, capital equipment
    - *Other recurrent costs*: program management, training and capacity building, Information, Education and Communication (IEC)/social mobilization, disease surveillance, wastage management and other recurrent costs

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

VACCINE COSTS

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

Demand forecasts for routine and SIA vaccines were based on the coverage data projected in the version 16 of Gavi's operational forecast that was updated in 2018. Gavi provided the historical weighted average prices for vaccines, syringes and safety boxes as well as price forecast data (2018-2030) for all 73 countries (Gavi, 2018).

IMMUNIZATION DELIVERY COSTS: ROUTINE IMMUNIZATION

Similarly, the number of doses was multiplied by immunization delivery cost per dose for each vaccine, country and year to estimate the total immunization delivery costs.

To estimate immunization delivery cost per dose, we extracted the baseline year data from 89 comprehensive multi-year plan (cMYPs) costing tools from 65 countries and 135 cost estimates for routine immunization in 19 countries from the Immunization Delivery Cost Catalogue (IDCC) (ICAN, 2018). We matched the cost components from IDCC that are comparable with those from the cMYP costing tools and prepared a combined dataset that includes the detailed breakdown of immunization program costs as well as cost per dose estimates.

A multiple linear regression framework was used for predicting the cost per dose for each country based on country characteristics, which result in 19 independent variables. The cost per dose estimates, as the dependent variables, were log transformed given the right skewed cost data. For each dataset, Akaike's information criteria (AIC) and Bayesian information criteria (BIC) were examined to select the final model through stepwise variable selection. This process resulted in three final models obtained from 1) a combined dataset, 2) a dataset that contains cMYP costing tools only, and 3) a dataset that contains IDCC cost estimates only. We then conducted out-of-sample validation to determine which of the three models performs best for the combined dataset. K-fold cross-validation (k=10) was used to test each model for three different datasets mentioned above, and we chose the final model based on the average root mean square error. The final model was used to predict the routine immunization cost per dose for countries that do not have cMYP or IDCC data. For countries with data from either source, we used the average of all available cost per dose estimates for the specific country from the combined dataset.

To capture introduction and start-up costs for new vaccine introduction, we calculated mean incremental cost per dose estimates for HPV, PCV and Rotavirus vaccines and applied them to the introduction years only.

IMMUNIZATION DELIVERY COSTS: SUPPLEMENTAL IMMUNIZATION ACTIVITIES (SIA)

Immunization delivery cost for supplemental immunization activities (SIA), often referred to as operational costs, consists of non-vaccine costs to deliver vaccines to the target population and manage SIA efforts of a targeted and time-limited nature. Catch-up, follow-up or mass preventive campaigns were conducted for Measles, Measles-Rubella, MenA, JE and Yellow Fever vaccines. When introducing the HPV vaccine, some countries opted to vaccinate girls age 10-14, beyond the ages included in routine vaccination. Vaccinating multi-age cohorts (MACs) was classified as SIA in the DOVE models.

Since SIA are irregular in frequency, SIA years often do not match with cMYP baseline years. Due to missing data and inconsistency, we extracted data from other sources such as IDCC, a systematic review conducted by Gandhi et al 2013 and budget amount per dose estimates from country proposals submitted to Gavi (Gavi, 2016). We collected a total of 52 estimates from these three sources and calculated average cost per dose for each vaccine type. These average cost per dose estimates for each vaccine were then applied to all 73 countries. Table 2 below shows the summary statistics of the cost per dose estimates included in the analysis.

Table 2. Summary statistics for immunization delivery cost per dose

Category	Type	N	Average (SD)	Median	Range
Routine immunization	Total immunization delivery cost per dose	94	2.47 (1.96)	2.30	0.18-11.31
	Incremental cost per dose for introducing HPV	42	3.90 (3.30)	2.86	0.52-13.44
	Incremental cost per dose for introducing PCV	21	1.20 (1.00)	1.06	0.15-3.50
	Incremental cost per dose for introducing Rotavirus vaccine	12	1.04 (0.64)	0.85	0.10-2.31
SIA	Measles	17	0.95 (0.88)	0.70	0.04-3.63
	Measles-Rubella	13	0.88 (0.20)	0.84	0.69-1.46
	JE	2	0.69(0.01)	0.69	0.68-0.70
	MenA	15	0.51(0.39)	0.65	0.00-1.44
	Yellow Fever	4	0.65 (0.19)	0.69	0.42-0.81
	HPV SIA (Multi-age cohort)	1	0.53	0.53	0.53-0.53

**All costs are in USD 2018*

ALIGNMENT BETWEEN ECONOMIC BENEFITS AND COST MODELS

To align the economic benefits and cost models, the same demographic and coverage data used by the VIMC were used for both economic benefits and costs models. We cross-validated the data points for economic benefits and costs and found a small degree of misalignment between two models (less than 2%) due to missing data from either model. For data points with benefits only (no cost data), missing data were substituted with cost data based on the coverage rate extrapolated from previous years. Data points with costs only (no benefits data) were removed from this analysis as deriving health impact estimates is beyond the scope of the DOVE models. The costs of emergency vaccine stockpiles for meningitis and yellow fever were excluded from this analysis as they are not directly linked with health benefits.

RESULTS

ECONOMIC BENEFITS: COI

Using the COI approach, the total economic benefits of vaccines in 73 Gavi countries was projected to exceed $781 billion from 2021-2030 in 2021-2030. Short-term costs (treatment costs, transportation costs and caregiver wages lost) averted comprise just over one percent of economic benefits using the COI approach. Of the short-term costs, treatment costs are the primary source of costs averted by vaccines, making up approximately 75.81% of the short-term costs averted and 0.79% of total COI averted. Productivity loss due to disability and death are the largest drivers of the economic benefits, comprising 6.06%and 92.89% of the total, respectively (Table 3).

Table 3. Cost of Illness averted in 73 Gavi countries, 2021-2030

Cost of Illness averted	Total	Percent of Total
Treatment costs	$5,766,195,993	0.74%
Transportation costs	$972,244,329	0.12%
Caregiver wages lost	$842,753,517	0.11%
Productivity loss due to disability	$44,007,401,472	5.63%
Productivity loss due to death	$730,025,050,505	93.40%
Total	$781,613,645,815	100.00%

ECONOMIC BENEFITS: VSL

The VSL approach yields a higher estimate of the economic benefits of vaccines because it encompasses the value individuals place on life beyond their economic contributions through labor. From 2021-2030, the VSL benefits in Gavi countries was 1,977.8 billion dollars in 2018 USD.

IMMUNIZATION PROGRAM COSTS

Vaccine costs comprised 54.93% of the total immunization program costs in Gavi countries. The total costs in 73 Gavi countries from 2021-2030 were 35.89 billion dollars in 2018 USD (Table 4).

Table 4. Immunization program costs in 73 Gavi countries, 2021-2030

Immunization program cost	Total*	Percent of Total
Vaccine costs	$19,714,787,123	54.93%
Immunization delivery costs	$16,176,494,852	45.07%
Total costs	$35,891,281,975	100.00%

**Includes costs of Pentavalent vaccine (Hib, Hep B), HPV, Measles, Measles-Rubella, MenA, PCV, JE and Yellow Fever vaccines*

ROI

Using these results, we generated two ROI estimates. The first, using the COI approach to estimate the economic benefits, yields a more conservative estimate of the ROI. For every dollar invested in vaccine programs in Gavi countries from 2021-2030, the estimated ROI using COI was 20.77. The VSL approach encompasses the broader economic benefits of vaccines. Using VSL to estimate the economic benefits yields an ROI in Gavi countries of 54.11 from 2021-2030.

Table 5. ROI using the COI and VSL approach in 73 Gavi countries, 2021-2030

2021-2030	COI approach	VSL approach
Benefits	$781,613,541,378	$1,977,818,401,855
Costs	$35,891,281,975	$35,891,281,975
ROI[4]	21	54

LIMITATIONS

The DOVE-ROI analysis has several limitations, including that estimates for cases and deaths averted were not available for all countries, vaccines, and years. Of the more than 24,820 data points estimated for the benefits and costs, less than 2% of the data points for costs did not have corresponding estimates for the economic benefits. These data points were excluded from the analysis.

A second limitation is the inherent uncertainty of forecasted data and gaps in data for some countries. The DOVE-ROI models rely on modeled data to fill these gaps. Exogenous factors such as vaccine supply constraints, contract negotiation and implementation barriers may affect model parameters such as vaccine introduction years, number of doses and price, resulting in the difference between projected and actual trend of model parameters in the future decade.

Lastly, when interpreting these results, it is important to keep in mind that the impact and cost estimates compare projected vaccine coverage to no vaccine coverage; thus, these results cannot be used to infer the incremental return on investment of vaccines. These results reflect the expected return on investment for the nine vaccines included, if funding and coverage goals are achieved as outlined in the Gavi operational forecast.

[4] Unrounded ROI for the COI approach was 20.77; for the VSL approach, 54.11

REFERENCES

De Broucker, G., Sim, S.Y., Gross, M., Brenzel, L. &Constenla, D. (November 8, 2018). Systematic review of cost of illness evidence for 10 antigens in LMIC [Report]. 99 pages. http://immunizationeconomics.org/dove-sr

The Demographic and Health Survey Program (various years). Demographic and Health Surveys [Online]. Retrieved December 8, 2017 from https://dhsprogram.com/Data/.

Gandhi, G. & Lydon, P. (2014). Updating the evidence base on the operational costs of supplementary immunization activities for current and future accelerated disease control, elimination and eradication efforts. *BMC Public Health*, 14:67. https://doi.org/10.1186/1471-2458-14-67

Gavi, the Vaccine Alliance (September 2016). Operating cost for multi-age cohort: HPV programme 2.0.

Gavi, the Vaccine Alliance (November 2018). Gavi v16.B Public Price Forecast.

Global Burden of Disease Health Financing Collaborator Network (2018). Trends in future health financing and coverage: Future health spending and universal health coverage in 188 countries, 2016-40. The Lancet, 392(10132), https://doi.org/10.1016/S0140-6736(18)30697-4.

Kim, S. Y., Sweet, S., Slichter, D., & Goldie, S. J. (2010). Health and economic impact of rotavirus vaccination in GAVI-eligible countries. *BMC public health*, *10*, 253. doi:10.1186/1471-2458-10-253

Immunization Costing Action Network (ICAN) (2019). Immunization Delivery Cost Catalogue. Washington DC: ThinkWell. Retrieved from http://immunizationeconomics.org/ican-idcc

International Labor Organization (n.d.). ILOSTAT [Online]. Geneva: ILO. Retrieved July 9, 2018 from https://www.ilo.org/global/lang--en/index.htm

Ozawa S., Clark S., Portnoy A., Grewal S., Brenzel L. & Walker DG. (2016). Return on Investment from Childhood Immunization in Low- and Middle-income Countries, 2011-2020. *Health Affairs* 35, No.2 (2016):199-207.

Ozawa S., Grewal S., Portnoy A., Sinha A., Arilotta R., Stack ML. & Brenzel L. (2016). Funding gap for immunization across 94 low- and middle-income countries. *Vaccine* 34(2016) 6408-6416.

PAHO (n.d.). PAHO Revolving Fund. Retrieved from https://www.paho.org/hq/index.php?option=com_content&view=article&id=1864:paho-revolving-fund&Itemid=4135&lang=en

Portnoy A., Ozawa S., Grewal S., Norman BA.,Rajgopal J., Gorham KM., Haidari LA., Brown ST. & Lee BY. (2015) Costs of vaccine programs across 94 low- and middle-income countries. Vaccine 335: A99-A108.

Robinson, L. et al. (May 2019). Reference Case Guidelines for Benefit-Cost Analysis in Global Health and Development [PDF file]. Retrieved from https://cdn2.sph.harvard.edu/wp-content/uploads/sites/94/2019/05/BCA-Guidelines-May-2019.pdf

UNICEF (June 14, 2019). Vaccine Price Data. Retrieved from https://www.unicef.org/supply/index_57476.html

UNICEF Statistics and Monitoring (various years). Multiple Indicator Cluster Surveys [MICS]. Retrieved December 8, 2017 from https://www.unicef.org/statistics/index_24302.html

US State Department Country Reports on Human Rights Practices for 2016 [Online]. Retrieved December 15, 2017 from https://www.state.gov/j/drl/rls/hrrpt/

Vaccine Impact Modelling Consortium (VIMC) (2019). Estimating the health impact of vaccination against 10 pathogens in 98 low and middle income countries from 2000 to 2030. Manuscript in preparation.

Watts, E., Sim, S.Y., Brenzel, L. & Constenla, D. (2019). Methods for estimating productivity loss averted due to vaccination in 94 low- and middle-income countries [Poster]. International Health Economics Association 2019 Congress – Basel, Switzerland.

World Health Organization (2008). WHO-CHOICE country specific unit costs [Online]. Geneva: WHO; 2005. Retrieved April 5, 2019 from http://www.who.int/choice/en/

APPENDIX I

Table A1. Decade of Vaccine Economics: 94 Low- and Middle-income Countries

Index	Country	WHO Region	World Bank Income Group	Gavi Transition classification
			2018	2018
AFG	Afghanistan	EMRO	LIC	Initial self-financing
AGO	Angola	AFRO	LMIC	Fully self-financing
ARM	Armenia	EURO	UMIC	Fully self-financing
AZE	Azerbaijan	EURO	UMIC	Fully self-financing
BGD	Bangladesh	SEARO	LMIC	Preparatory transition phase
BLZ	Belize	AMRO	UMIC	Not eligible
BEN	Benin	AFRO	LIC	Initial self-financing
BTN	Bhutan	SEARO	LMIC	Fully self-financing
BOL	Bolivia	AMRO	LMIC	Fully self-financing
BFA	Burkina Faso	AFRO	LIC	Initial self-financing
BDI	Burundi	AFRO	LIC	Initial self-financing
KHM	Cambodia	WPRO	LMIC	Preparatory transition phase
CMR	Cameroon	AFRO	LMIC	Preparatory transition phase
CPV	Cape Verde	AFRO	LMIC	Not eligible
CAF	Central African Republic	AFRO	LIC	Initial self-financing
TCD	Chad	AFRO	LIC	Initial self-financing
COM	Comoros	AFRO	LIC	Initial self-financing
COD	Congo, Dem. Rep.	AFRO	LIC	Initial self-financing
COG	Congo	AFRO	LMIC	Fully self-financing
CIV	Cote d'Ivoire	AFRO	LMIC	Preparatory transition phase
CUB	Cuba	AMRO	UMIC	Fully self-financing
DJI	Djibouti	EMRO	LMIC	Preparatory transition phase
EGY	Egypt	EMRO	LMIC	Not eligible
SLV	El Salvador	AMRO	LMIC	Not eligible
ERI	Eritrea	AFRO	LIC	Initial self-financing
ETH	Ethiopia	AFRO	LIC	Initial self-financing
FJI	Fiji	WPRO	UMIC	Not eligible
GMB	Gambia	AFRO	LIC	Initial self-financing
GEO	Georgia	EURO	LMIC	Fully self-financing
GHA	Ghana	AFRO	LMIC	Preparatory transition phase
GTM	Guatemala	AMRO	UMIC	Not eligible
GIN	Guinea	AFRO	LIC	Initial self-financing
GNB	Guinea-Bissau	AFRO	LIC	Initial self-financing
GUY	Guyana	AMRO	UMIC	Fully self-financing
HTI	Haiti	AMRO	LIC	Initial self-financing
HND	Honduras	AMRO	LMIC	Fully self-financing
IND	India	SEARO	LMIC	Accelerated transition phase
IDN	Indonesia	SEARO	LMIC	Fully self-financing
IRQ	Iraq	EMRO	UMIC	Not eligible
KEN	Kenya	AFRO	LMIC	Preparatory transition phase
KIR	Kiribati	WPRO	LMIC	Fully self-financing
PRK	Korea, DPR	SEARO	LIC	Initial self-financing
XK	Kosovo	EURO	LMIC	Not eligible
KGZ	Kyrgyzstan	EURO	LMIC	Preparatory transition phase
LAO	Lao PDR	WPRO	LMIC	Accelerated transition phase
LSO	Lesotho	AFRO	LMIC	Preparatory transition phase
LBR	Liberia	AFRO	LIC	Initial self-financing
MDG	Madagascar	AFRO	LIC	Initial self-financing
MWI	Malawi	AFRO	LIC	Initial self-financing

MLI	Mali	AFRO	LIC	Initial self-financing
MHL	Marshall Islands	WPRO	UMIC	Not eligible
MRT	Mauritania	AFRO	LMIC	Preparatory transition phase
FSM	Micronesia	WPRO	LMIC	Not eligible
MDA	Moldova	EURO	LMIC	Fully self-financing
MNG	Mongolia	WPRO	LMIC	Fully self-financing
MAR	Morocco	EMRO	LMIC	Not eligible
MOZ	Mozambique	AFRO	LIC	Initial self-financing
MMR	Myanmar	SEARO	LMIC	Preparatory transition phase
NPL	Nepal	SEARO	LIC	Initial self-financing
NIC	Nicaragua	AMRO	LMIC	Accelerated transition phase
NER	Niger	AFRO	LIC	Initial self-financing
NGA	Nigeria	AFRO	LMIC	Accelerated transition phase
PAK	Pakistan	EMRO	LMIC	Preparatory transition phase
PNG	Papua New Guinea	WPRO	LMIC	Accelerated transition phase
PRY	Paraguay	AMRO	UMIC	Not eligible
PHL	Philippines	WPRO	LMIC	Not eligible
RWA	Rwanda	AFRO	LIC	Initial self-financing
WSM	Samoa	WPRO	UMIC	Not eligible
STP	Sao Tome and Principe	AFRO	LMIC	Accelerated transition phase
SEN	Senegal	AFRO	LIC	Initial self-financing
SLE	Sierra Leone	AFRO	LIC	Initial self-financing
SLB	Solomon Islands	WPRO	LMIC	Accelerated transition phase
SOM	Somalia	EMRO	LIC	Initial self-financing
LKA	Sri Lanka	SEARO	LMIC	Fully self-financing
SDN	Sudan: North	EMRO	LMIC	Preparatory transition phase
SSD	Sudan: South	AFRO	LIC	Preparatory transition phase
SWZ	Swaziland	AFRO	LMIC	Not eligible
SYR	Syria	EMRO	LIC	Not eligible
TJK	Tajikistan	EURO	LIC	Preparatory transition phase
TZA	Tanzania	AFRO	LIC	Initial self-financing
TLS	Timor-Leste	SEARO	LMIC	Fully self-financing
TGO	Togo	AFRO	LIC	Initial self-financing
TON	Tonga	WPRO	UMIC	Not eligible
TKM	Turkmenistan	EURO	UMIC	Not eligible
TUV	Tuvalu	WPRO	UMIC	Not eligible
UGA	Uganda	AFRO	LIC	Initial self-financing
UKR	Ukraine	EURO	LMIC	Fully self-financing
UZB	Uzbekistan	EURO	LMIC	Accelerated transition phase
VUT	Vanuatu	WPRO	LMIC	Not eligible
VNM	Viet Nam	WPRO	LMIC	Accelerated transition phase
PSE	West Bank and Gaza	EMRO	LMIC	Not eligible
YEM	Yemen	EMRO	LIC	Preparatory transition phase
ZMB	Zambia	AFRO	LMIC	Preparatory transition phase
ZWE	Zimbabwe	AFRO	LIC	Initial self-financing

Note: 94 countries were determined in 2010 as part of the Decade of Vaccines.

Table A2. Cost of Illness averted in 94 LMICs, 2021-2030

Cost of Illness averted	Total	% Total
Treatment costs	$6,574,457,947	0.79%
Transportation costs	$1,085,752,918	0.13%
Caregiver wages lost	$1,011,688,220	0.12%
Productivity loss due to disability	$50,228,078,301	6.06%
Productivity loss due to death	$769,621,268,682	92.89%
Total	$828,521,246,068	100.00%

Table A3. Immunization program costs in 94 LMICs, 2021-2030

Immunization program cost	Total	% Total
Vaccine costs	$21,097,485,500	53.21%
Immunization delivery costs	$18,555,107,875	46.79%
Total costs	$39,652,593,375	100.00%

Note: Historical vaccine prices from the PAHO Revolving fund price list were applied to 4 PAHO countries (PAHO, n.d.). For the other 17 non-Gavi, non-PAHO countries, we used historical price data from the UNICEF vaccine price list (UNICEF, 2019). We generated price forecasts (2021-2030) for PAHO and UNICEF assuming constant prices beyond forecast data based on the same principle of Gavi's price forecast. Gavi's immunization supply costs, for syringes and safety boxes, as well as freight cost were applied to all 94 countries.

Table A4. ROI in 94 LMICs, 2021-2030

2021-2030	COI approach	VSL approach
Benefits	$828,521,141,631	$2,125,064,171,582
Costs	$39,652,593,375	$39,652,593,375
ROI	19.89	52.59

APPENDIX II

A Rapid Approach to Estimating Government Financing for Immunization Delivery Costs

Methodology
The percentage estimates for government financing are based on data extracted from Comprehensive Multi-Year Plans (cMYPs) costing tools available for the Decade of Vaccines (2011-2020). The same data were previously used to estimate the funding gap for immunization programs in low- and middle-income countries from 2016-2020 (Portnoy et al. 2015; Ozawa et al. 2016). We applied these percentage estimates to Gavi's next strategic period (2021-2025) assuming that the financing shares from the previous decade will be kept constant. For immunization delivery costs, we have used baseline cost assumption where the cost per dose estimates remain constant across 2021-2025. We assumed that there will be no funding gap, and the total immunization delivery costs will be fully financed (total costs = total financing).

(Government financing for immunization delivery costs) =
(Total immunization delivery costs) x (Government financing share for immunization delivery cost from DOVE Costing, Financing and Funding Gap model)

- **Routine delivery costs**: the proportion of government financing for immunization delivery cost is on average 65% for Gavi countries in the CFF model. We applied country-specific constant percentage rates across 2021-2025.
- **SIA delivery costs ("operational costs"/ "campaign costs"):** the proportion of government financing for SIA delivery cost is on average 15% for Gavi supported countries. We applied country-specific percentage rates across 2021-2025.

Results

2021-2025	Government financing for Immunization delivery costs	% of total costs
Gavi-supported vaccines	$5,374,811,362	69.69%
Traditional vaccines	$897,675,414	76.49%
Total	$6,272,486,776	70.59%

*Traditional vaccines include BCG, DTP and HepB birth dose.

Limitations

- This exercise does *not* include some of the Gavi supported vaccines (IPV, Cholera and Typhoid) and thus presents conservative estimates for the total immunization delivery costs.
- The percentage estimates for government financing were extracted from baseline years from cMYP costing tools of 63 countries ranging from 2004-2011.
- DOVE team is currently updating the information on financing and funding gap for national immunization programs, and the percentage estimates of government financing will be updated in the future.