Costs of vaccine programs across 94 low- and middle-income countries

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25 Abstract:

26

27 While new mechanisms such as advance market commitments and co-financing policies of the GAVI
28 Alliance are allowing low- and middle-income countries to gain access to vaccines faster than ever,
29 understanding the full scope of vaccine program costs is essential to ensure adequate resource
30 mobilization. This costing analysis examines the vaccine costs, supply chain costs, and service delivery
31 costs of immunization programs for routine immunization and for supplemental immunization activities
32 (SIAs) for vaccines related to 18 antigens in 94 countries across the decade, 2011-2020.

33

34 Vaccine costs were calculated using GAVI price forecasts for GAVI-eligible countries, and assumptions
35 from the PAHO Revolving Fund and UNICEF for middle-income countries not supported by the GAVI
36 Alliance. Vaccine introductions and coverage levels were projected primarily based on GAVI's
37 Adjusted Demand Forecast. Supply chain costs including costs of transportation, storage, and labor were
38 estimated by developing a mechanistic model using data generated by the HERMES discrete event
39 simulation models. Service delivery costs were abstracted from comprehensive multi-year plans for the
40 majority of GAVI-eligible countries and regression analysis was conducted to extrapolate costs to
41 additional countries.

42

43 Results indicate that the delivery of the full vaccination program across 94 countries would cost a total
44 of \$62 billion (95% uncertainty range: \$43–\$87 billion) over the decade, including \$51 billion (\$34–\$73
45 billion) for routine immunization and \$11 billion (\$7–\$17 billion) for SIAs. More than half of these
46 costs stem from service delivery at \$34 billion (\$21–\$51 billion) – with an additional \$24 billion (\$13–
47 \$41 billion) in vaccine costs and \$4 billion (\$3–\$5 billion) in supply chain costs.

48

49 The findings present the global costs to attain the goals envisioned during the Decade of Vaccines to
50 prevent millions of deaths by 2020 through more equitable access to existing vaccines for people in all
51 communities. By projecting the full costs of immunization programs, our findings may aid to garner
52 greater country and donor commitments toward adequate resource mobilization and efficient allocation.
53 As service delivery costs have increasingly become the main driver of vaccination program costs, it is
54 essential to pay additional consideration to health systems strengthening.

55

56 Keywords: costs; vaccine; routine immunization; supplemental immunization activities; supply chain

1. Introduction:

This decade (2011-2020) has been labeled “the Decade of Vaccines” after various country governments and international donors committed to help discover, develop, and deliver vaccines to people in the world’s poorest countries. Understanding the full scope of vaccination program costs is vital to ensuring adequate resource mobilization to attain the goals envisioned by the Decade of Vaccines Collaboration. This costing analysis responds to the requests of the World Health Organization (WHO) Strategic Advisory Group of Experts (SAGE) as part of the Decade of Vaccines Economics (DOVE) project to strengthen methods for estimating and projecting immunization program resource requirements [1]. While the study builds on lessons learned from previous costing exercises, it extends beyond prior efforts by transparently modeling more detailed cost components (vaccine, supply chain, service delivery), exploring enhanced model methods, and providing sensitivity and scenario analyses. By taking a bottom-up approach to cost each component, this analysis identifies specific cost drivers of immunization programs. The aim of this paper is to detail the model structure, input sources, modeling methods, and baseline results of vaccination program costs.

2. Methodology:

2.1. Analysis scope:

The costing analysis focused on 94 low- and middle-income countries identified by the Global Vaccine Action Plan (GVAP) and country eligibility policy of the GAVI Alliance across the Decade of Vaccines, 2011-2020. The GVAP, endorsed by 194 Member States at the World Health Assembly in 2012, centered around low- and middle-income countries that currently or have previously received support

81 from the GAVI Alliance [2]. Based on current GAVI classifications, the 94 countries include 36 low-
82 income countries, 17 intermediate countries, 20 graduating countries, and 21 countries not eligible for
83 GAVI support [3].¹ A full list of countries is included in the online supplement.

84
85 The vaccines included in this analysis are relevant to 18 antigens and encompass immunizations
86 delivered through routine immunization programs and supplemental immunization activities (SIAs). The
87 complete list of vaccines is provided in Table 1.

88
89 Introduction years for routine vaccines, the timing of SIAs and the number of vaccine doses annually
90 delivered to each country rely on GAVI's Adjusted Demand Forecast version 9.0 (ADF v9) [4]. The
91 ADF also includes forecasts for introductions of future vaccines, both licensed and unlicensed, in
92 countries' national immunization programs. For the frequency and timing of SIAs for measles, measles-
93 rubella (MR), and measles-mumps-rubella (MMR) vaccinations, forecasts additionally used information
94 from the World Health Organization (WHO) [5]. For SIAs for oral polio vaccine (OPV), forecasts relied
95 on information from the Global Polio Eradication Initiative [6].

96
97 As for the model structure, separate methodologies were developed for vaccine, supply chain, and
98 service delivery cost components associated with routine immunization and SIAs. The methodologies
99 and assumptions relied on the most recent information and price data from the GAVI Alliance [3,4,7-
100 11], the PAHO Revolving Fund [12-15], UNICEF Supplies and Logistics [16], as well as country-
101 specific models developed by the HERMES (Highly Extensible Resource for Modeling Event-Driven
102 Supply Chains) Logistics Modeling Team [17,18]. For additional data underlying the model such as
103 population data, immunization coverage rates and economic growth, we relied on datasets validated by

¹ The GAVI Alliance's co-financing support policy: Low-Income = GNI per capita < \$1,035. Intermediate = GNI per capita between \$1,035 and \$1,570. Graduating = GNI per capita > \$1,570.

104 third-party multilateral agencies [19-22]. Service delivery cost projections relied primarily on data
105 obtained from country-specific comprehensive multi-year plans (cMYPs) overseen by the World Health
106 Organization [23].

107

108 2.2. Costing scope and components:

109

110 This costing analysis assesses the vaccine costs, supply chain costs, and service delivery costs of
111 immunization programs for routine immunization and for SIAs, consisting of the following components:

112

113 Routine immunization:

- 114 1. Vaccine costs: Costs to procure vaccines, related injection equipment and safety boxes
- 115 2. Supply chain costs: Costs for transportation, both immunization-specific and shared², including
116 amortization for vehicles, fuel costs, and per diems; costs for storage including amortization for
117 equipment, maintenance, and energy cost; and costs of labor
- 118 3. Service delivery costs: Costs of personnel, both immunization-specific and shared³; and non-
119 personnel costs including program management, training, social mobilization, surveillance, and
120 other recurrent costs related to vaccination

121

122 Supplemental immunization activities:

- 123 1. Vaccine costs: Costs to procure vaccines, related injection equipment and safety boxes
- 124 2. Operational costs: Cost to deliver vaccines and manage vaccination campaign efforts

125

² Shared transportation costs are defined as the costs of transportation when vehicles are utilized across multiple programs or activities in the health sector including immunization.

³ Shared personnel costs are defined as the value of human resources providing immunization services as well as other curative and preventive services where a health workers' time may be shared across different programs or activities.

126 The categorization of costs reflects cMYP classifications and definitions utilized in previous vaccine
127 program analyses [24-26]. All costs are presented in constant 2010 US dollars (US\$2010).

128

129 2.3. Baseline cost estimations and projections:

130 2.3.1. Routine and supplemental vaccine costs:

131

132 The costs of vaccines for both routine and SIA delivery strategies encompass: (1) vaccine-specific price
133 per dose (including freight); (2) vaccine-specific injection equipment and safety box price per dose; and
134 (3) the number of required vaccine doses (including wastage and buffer doses), relying on data from the
135 GAVI Secretariat for GAVI-supported vaccines⁴ and GAVI Strategic Demand Forecast (SDF)-based
136 demand forecasts for traditional vaccines⁵ [27].

137

138 The analysis incorporates the prices of vaccines relevant to 18 individual antigens of three different
139 types: (1) GAVI country prices; (2) PAHO country prices; (3) and non-GAVI, non-PAHO prices.

140

141 Input prices for injection equipment and safety boxes including freight were obtained from GAVI price
142 forecasts and consistently applied across countries. Prices of freight were not included for India and
143 Indonesia, which locally produce vaccines for their national immunization programs [8,16].

144

145 For the 73 GAVI countries, we relied on ADF v9 2011-2020 vaccine price per dose projections provided
146 by the GAVI Secretariat for GAVI-supported vaccines [8]. UNICEF price projections were utilized for
147 traditional vaccines for GAVI countries and non-GAVI, non-PAHO countries [16]. For PAHO

⁴ GAVI-supported vaccines include Pentavalent, Rotavirus, Pneumococcal, HPV, Measles, Measles-Rubella, Yellow Fever, and Meningococcal A, as well as vaccines that are under consideration to receive GAVI support within the decade—Japanese Encephalitis, Typhoid, IPV (inactivated polio vaccine), and Cholera (stockpiles only).

⁵ Traditional vaccines are defined as BCG, DTP, HepB birth dose, Measles-Mumps-Rubella, and OPV (oral polio vaccine).

148 countries, we relied on price listings from the PAHO Revolving Fund for relevant PAHO-supported
149 vaccines for available years [12-15]. For projections in additional years, we assumed that vaccine prices
150 were 30% higher than GAVI prices based on the historical difference between PAHO and GAVI prices.
151 For non-GAVI, non-PAHO countries, we relied on the higher price between the PAHO Revolving Fund
152 price listings and 2011-2015 price projections from UNICEF Supplies and Logistics. Where prices were
153 not available for non-GAVI, non-PAHO countries, vaccine prices were assumed to be 32% higher than
154 GAVI prices based on the historical difference between UNICEF and GAVI prices [16].

155

156 While price inputs were available for the majority of the vaccines in the analysis, the one unlicensed
157 vaccine – malaria – required separate price assumptions. The malaria vaccine price was assumed to be
158 \$5.00 based on expert discussions and review of the available literature [28-31]. Table 1 presents
159 vaccine costs used in this analysis.

160

161 2.3.2. Routine supply chain costs:

162

163 In order to address the complex interactions of transportation, storage, and labor costs in the vaccine
164 supply chain, cost estimation for this component proceeded in three phases (see Figure 1).

165

166 **Phase 1.** First, we relied on the HERMES simulation models of four reference countries [Benin, Niger,
167 Mozambique (Gaza province), and India (Bihar state)] to estimate supply chain costs with current
168 vaccine regimens and scenarios in which additional vaccines were introduced. HERMES is a software
169 decision-support tool that can generate discrete event simulation models of any supply chain,
170 representing all of the components and processes of the supply chain and the movement of vaccines
171 from the central store to vaccine administration locations. HERMES-generated simulation models

172 include virtual representations of each vaccine vial (including the antigen type, presentation, and
173 packaged volume) that enters the system, vaccine storage device (e.g., refrigerators and freezers),
174 building, transport vehicle, and personnel. As a simulation run proceeds, millions of these virtual
175 vaccine vials flow down through the system from the central storage location through a series of storage
176 locations to where the vaccines are finally administered. At each location, the vaccines remain in
177 storage devices until they are transported via vehicles to the next location in the chain, based on shipping
178 frequencies and policies. Previous publications have described HERMES-generated models and data
179 inputs in detail [17,18,32-40].

180

181 As a simulation run proceeds, three general categories of costs accrue: transport, storage and labor.
182 Transportation costs accrue with each kilometer traveled by each transport vehicle. The cost per
183 kilometer includes an amortization of the original purchase price of the vehicle over its anticipated
184 lifetime mileage and the cost per kilometer of fuel and maintenance. A storage device's cost accrues by
185 the day, which includes an amortization of the original purchase price of the device over its anticipated
186 lifetime (10 years) and the daily cost of energy and maintenance. Labor costs accrue on a daily basis per
187 a person's salary multiplied by the percentage of time dedicated to the immunization program. By
188 running the simulation models, Phase 1 estimated supply chain costs for current vaccine regimens for
189 four reference countries and a limited number of new regimens including new vaccines.

190

191 **Phase 2.** Phase 2 examined how costs from Phase 1 would vary with a whole range of per capita vaccine
192 regimen volumes. Phase 2 entailed developing a simplified spreadsheet version of each HERMES
193 model in order to extrapolate the Phase 1 HERMES-generated costs to other countries that have
194 different vaccine regimens, and thus volumes of vaccines, flowing through their systems. This
195 spreadsheet model established a linear relationship (i.e., the slope and intercept) between per capita

196 vaccine regimen volume and costs of transportation and storage. The resulting slopes and intercepts
197 from this analysis are listed in Table 2.

198

199 **Phase 3.** The last phase extrapolated results from the four reference countries to the remaining 90
200 countries in the analysis. The analysis also projected costs from 2011 to the remaining years of the
201 decade using specific anticipated per capita vaccine regimen volumes for each year according to the
202 ADF [4]. Each target country was matched with one of the four reference countries with the most similar
203 supply chain structure, based on the number of tiers in the supply chain (3, 4, or 5) and by the relative
204 distribution of storage locations (top heavy, middle heavy, or bottom heavy clusters, among countries
205 with 4-tier supply chains), as detailed in the online supplement. Our team separated the 4-level supply
206 chains into three clusters based on the morphology of the supply chain and the average “branching
207 ratios” for each level. Each location on a level has an average branching ratio that equals the number of
208 locations in the next lower level that a location on that level serves on average (e.g., a district level on
209 average has a branching ratio of ten if a district store on average serves ten locations below it). “Top-
210 heavy” supply chains tend to have higher branching ratios for the upper levels compared to “middle
211 heavy” and “bottom-heavy” ones. “Middle-heavy” supply chains tend to have higher branching ratios
212 for the middle levels compared to top heavy and bottom heavy ones. Next, we extrapolated the costs for
213 the assigned reference country to each target country separately for transportation, storage, and labor:

- 214 1. Transportation Costs: Extrapolated by the ratio of the square root of the target country’s
215 geographic area over the square root of the reference country’s area (since transportation costs
216 increase with increasing distance traveled), which were adjusted by the ratio of the target
217 country’s fuel costs over the reference country’s fuel costs;
- 218 2. Storage Costs: Extrapolated by the ratio of the population of the target country over the
219 population of the reference country (because population is proportional to the number of

vaccines delivered, which in turn is proportional to the number of storage devices required), which were adjusted by the ratio of the target country's energy costs over the reference country's energy costs (because storage facility expenses depend on energy costs – in this case electricity prices served as a proxy scalar); and

3. Labor Costs: Extrapolated by the ratio of the target country's population to the reference country's population (because total personnel required varies with population served) and the ratio of wages (because personnel costs vary based on per capita wages) — see online supplement for country-specific scalar values.

The estimated supply chain costs for transportation, storage, and labor were subsequently disaggregated by vaccine, relying on the proportion of the volume contributed by each vaccine as a function of the packed volume per dose and the number of doses delivered relative to the total volume of vaccines delivered.

2.3.3. Routine service delivery costs:

Service delivery costs consist of the following components and respective data sources:

1. Immunization-specific personnel costs: cMYP-specified line item for routine recurrent personnel costs, minus supply chain relevant personnel costs
2. Shared personnel costs: cMYP-specified line item for costs of personnel who provide immunization services as well as other curative and preventive services
3. Non-personnel costs: aggregate of cMYP-specified line items for training, social mobilization, disease surveillance, program management, and other recurrent costs

244 All component costs associated with service delivery were obtained directly from respective line items
245 from baseline years of country cMYPs. It was assumed that cMYP line-item costs are mutually
246 exclusive and therefore no overlap exists between costing categories. This analysis abstracted country-
247 specific service delivery cost data from 63 cMYP costing tools, with baseline years ranging from 2004-
248 2011. The majority (80%) of cMYP data was extracted from baseline years 2009 and later.

249

250 For the remaining 31 countries, service delivery cost data was modeled based on a regression analysis of
251 the cMYP data. Since the cMYP-derived cost data were not normally distributed, a natural log
252 transformation was performed. The three service delivery cost components were examined against
253 variables that were considered potential drivers of routine immunization program costs. Analyzed
254 variables included economic indicators, demographic/population data, child health indicators, health
255 financing data, health systems capacity indicators, healthcare seeking variables, geography, and routine
256 immunization schedule/coverage. The initial list of 42 variables was narrowed down based on the
257 number of observations available across countries, correlations among variables, principle of parsimony
258 and statistical significance in univariate and multivariate regression analyses. Accounting for
259 collinearity, significance of variable effect size, and overall model fit, the following variables were
260 selected to estimate total baseline costs for countries without cMYP data (see online supplement for
261 details):

- 262 • Immunization-specific personnel costs were scaled by birth cohort size and land area
- 263 • Shared personnel costs were related to birth cohort and DTP3 coverage
- 264 • Non-personnel costs were modeled based on birth cohort, land area and the proportion of the
265 population living in rural areas

266

267 For validation, the above regressions were applied against the 63 countries with cMYP data and resulted
268 in a regression-derived service delivery costs that only differed by 2.45%.

269

270 For the baseline year, the average service delivery costs per dose were multiplied by GAVI's ADF v9
271 total doses to obtain baseline service delivery costs for each country. Beyond the baseline year,
272 additional service delivery costs were modeled by applying a marginal cost per dose value for all
273 additional doses. Marginal service delivery costs were obtained from a regression of cMYP-extracted
274 service delivery cost components against total routine vaccine doses from respective baseline cMYP
275 years. Thus, marginal costs in the model reflect the service delivery requirements necessary to deliver
276 one additional dose beyond baseline year levels. Marginal cost per dose was considered to be modified
277 by the national immunization schedule, represented by coverage of three doses of DTP. Separate
278 marginal costs were obtained for two bins of DTP3 coverage under or above 80%, which was the
279 median coverage level among countries in the analysis. The average and marginal service delivery costs
280 per dose estimated across 94 countries are provided in Table 3.

281

282 2.3.4. Supplemental operational costs:

283

284 Operational costs of supplemental immunization activities (SIAs) consist of non-vaccine costs necessary
285 to deliver vaccines and manage campaign efforts. All costs associated with SIA operational costs were
286 obtained directly from vaccine-specific line items from the baseline year of cMYPs. SIA operational
287 costs per dose were calculated separately for small and large countries (population less than or greater
288 than 10 million).

289

290 For the 63 countries with cMYP data, a population-weighted average operational cost per dose was
291 calculated specific to measles (\$0.65–\$0.87), OPV (\$0.65), and yellow fever vaccines (\$0.71–\$1.10).
292 For other SIA vaccines, average operational cost per dose (\$0.65–\$0.68) was estimated across all
293 injectable vaccines (measles, yellow fever, and tetanus). Higher costs per dose were estimated for larger
294 countries, likely reflecting the relatively greater operational support to reach target populations in these
295 countries. Variations in vaccine-specific operational costs reflect: (1) the relatively larger investment in
296 eradication and elimination campaigns (e.g., measles); and (2) lower costs of delivering oral vaccines
297 (e.g., OPV).

298

299 2.4. Sensitivity and scenario analysis:

300

301 Sensitivity analysis was carried out varying seven key inputs in model simulations to construct the 95%
302 uncertainty ranges around baseline estimates. Specifically, we performed a probabilistic sensitivity
303 analysis using the Monte Carlo method, building distributions around key model parameters including
304 total doses, vaccine prices, slopes and extrapolations of supply chain costs from reference countries,
305 average and marginal cost per dose for service delivery, and operational cost per dose for SIA. For each
306 parameter, random draws were taken from specified distributions 10,000 times. Non-cost values were
307 given a beta distribution, while cost values used gamma distributions in order to represent the skew of
308 observed costing data. Values were ranged between half and double the base estimate to examine the
309 effect of each variable. This analysis was implemented using the latest version of the @RISK software.

310

311 In addition to the baseline scenario for costing immunization programs, we also estimated the costs of
312 two different scenarios: (1) a scenario in which all 94 countries reach 90% routine vaccine coverage by
313 2020; and (2) a scenario in which the GAVI vaccine prices were applied to non-GAVI countries. The

314 first scenario examines the costs to reach the GVAP goal of 90% routine vaccine coverage, where a
315 linear scale-up was assumed from current coverage to 90% for vaccines introduced prior to 2017. The
316 second scenario projects costs if 21 non-GAVI countries in our analysis were to access GAVI vaccine
317 prices.

318

319 3. Results:

320

321 The total cost of the full vaccination program across 94 low- and middle-income countries is projected
322 to be US\$61.9 billion (95% uncertainty range: \$42.7–\$87.4 billion) from 2011 to 2020. More than half
323 (55%) of this expected cost is for service delivery, including costs for program management, training,
324 social mobilization, and surveillance. An additional 38% relates to vaccine and injection supplies and
325 the remainder (7%) represented supply chain costs. Figure 2 presents the routine and supplemental
326 immunization costs by component across the years. Examining the program costs per dose and per
327 surviving infant, service delivery costs remain the greatest component of costs across all country income
328 groupings (Table 4).

329

330 Thirty-two percent of the estimated total cost, equivalent to US\$19.8 billion, is forecasted to support the
331 full immunization programs for Ethiopia, India, Nigeria, and Pakistan alone—four countries with large
332 immunization target populations and substantial vaccine-preventable disease burden, including polio,
333 measles, and rubella.

334

335 3.1. Cost estimates for routine immunization:

336

337 Routine immunization programs for the decade are estimated to amount to 82% of the total costs of
338 immunization—approximately \$50.7 billion (\$34.2–\$73.2 billion). The majority of routine
339 immunization costs is due to service delivery at \$26.9 billion (\$15.8–\$43.2 billion; 53% of routine
340 immunization), with \$10.6 billion (\$6.2–\$16.8 billion) for immunization-specific personnel costs and
341 \$16.2 billion (\$9.6–\$26.5 billion) for shared personnel costs. Vaccine and injection supplies amount to
342 39% of routine immunization costs at \$19.7 billion (\$10.6–\$34.1 billion), whereas supply chain costs
343 amount to \$4.2 billion (\$3.3–\$5.2 billion), including \$0.5 billion (\$0.3–\$0.6 billion) for shared transport.
344 The total routine vaccine costs by vaccine and by GAVI eligibility status across the decade are shown in
345 Figure 3.

346

347 The 73 GAVI countries make up a majority of the total routine immunization costs at \$43.2 billion
348 (\$29.2–\$62.1 billion; 85% of routine immunization costs for 94 GVAP countries). Routine
349 immunization costs are estimated to increase by more than half (56%) from \$16.9 billion during the
350 period 2011–2015 to \$26.3 billion during 2016–2020 for GAVI countries. Similarly, the 21 non-GAVI
351 countries may face a 55% increase in costs between the same time periods. Among GAVI countries,
352 routine vaccine costs present the greatest increase of 66% – from \$5.9 billion to \$9.9 billion –
353 comparing the first half of the decade to the second half. Among the non-GAVI countries, routine
354 vaccine costs are projected to grow at 69%, from \$1.4 billion to \$2.4 billion.

355

356 Routine immunization costs are driven in large part due to seven vaccines – pentavalent, measles-
357 containing (measles, MR, and MMR), pneumococcal conjugate (PCV), oral polio (OPV), and rotavirus
358 vaccines – totaling \$41.6 billion (82% of routine costs). Large program costs associated with these
359 vaccines resulted from a combination of vaccine unit prices, service delivery costs and coverage levels.
360 Increasing costs across the decade are partly due to an expanding number of vaccine introductions

361 particularly of new and more expensive vaccines such as human papillomavirus (HPV) vaccine and
362 inactivated polio vaccine (IPV). The greatest numbers of these vaccine introductions are currently
363 planned for the year 2015, where 26% of vaccine introductions for GAVI 73 countries and 34% of
364 vaccine introductions for 21 non-GAVI countries are projected to occur in 2015. The largest vaccine
365 roll-out is for IPV, as all 94 countries in this analysis are projected to add a dose of IPV to their polio
366 vaccine schedule between 2014 and 2016 in preparation for the eradication of polio, planned for 2018
367 [6,41].

368

369 3.2. Cost estimates for supplemental immunization activities:

370

371 The total costs of SIAs against vaccine-preventable diseases including Japanese encephalitis (JE),
372 malaria, measles-containing vaccines, meningococcal conjugate A (MenA), OPV, typhoid, and yellow
373 fever, are estimated at \$11.1 billion (\$6.6–\$17.2 billion; 18% of total immunization costs) across 2011
374 to 2020. Of this total, 79% of the costs are for campaigns against polio and measles (including vaccines
375 for MR and MMR). In addition, 97% of the total SIA costs (\$10.8 billion; \$6.4–\$16.7 billion) are
376 projected for the 73 GAVI countries, while the remaining \$0.3 billion (\$0.2–\$0.5 billion) in campaigns
377 are projected to occur in 21 non-GAVI countries. The breakdown of total SIA costs by vaccine across
378 the decade is shown in Figure 4. The majority (64%) of total SIA costs are projected to be for
379 operational costs (\$7.0 billion; \$3.7–\$12.5 billion), with the remainder for costs of vaccines and
380 injection supplies (\$4.1 billion; \$2.2–\$7.1 billion).

381

382 3.3. Sensitivity and scenario analyses results:

383

384 Sensitivity analysis revealed that vaccine prices are the biggest driver of baseline estimates (total costs
385 may be 15% lower to 28% higher), followed by total doses (18% lower to 22% higher), service delivery
386 marginal cost per dose (11% lower to 24% higher), service delivery average cost per dose (6% lower to
387 16% higher), and SIA operational cost per dose (4% lower to 10% higher). Assumptions around supply
388 chain cost extrapolations were less influential on the total costs (see online supplement for a tornado
389 diagram).

390

391 Based on a scenario analysis, if all countries were to reach the GVAP goal of 90% routine immunization
392 coverage, the baseline costs of \$61.9 billion is expected to increase to \$62.7 billion (see Table 5). While
393 we might have anticipated a larger increase in costs for the 90% coverage scenario, the relatively small
394 (1.3%) increase is due to the large number of countries that are already projected to reach at least 90%
395 coverage by 2020 in GAVI's ADF v9 [4]. In the second scenario, if non-GAVI countries are to obtain
396 GAVI vaccine prices, total costs are projected to decrease to \$59.7 billion. As the price reduction
397 scenario only applies to 21 countries in the analysis, a \$2.2 billion difference in projected costs is within
398 expectations.

399

400 4. Discussion:

401

402 This costing analysis adds to the international knowledge base by estimating the global costs to reach the
403 GVAP goals across the Decade of Vaccines. By projecting the full costs of immunization programs, our
404 findings may aid to garner greater country and donor commitments toward preventing millions of deaths
405 by 2020 through more equitable access to existing vaccines for people in all communities. Beyond the
406 aggregate cost estimates, costs associated with vaccines, supply chain, and service delivery for both

407 routine immunization and SIAs lend an additional level of insight necessary for mobilizing and
408 effectively allocating resources for vaccine programs.

409

410 One of the key findings is that that more than half (53%) of total routine immunization costs are incurred
411 for service delivery. As service delivery costs have increasingly become the main driver of costs of
412 vaccine programs, additional consideration must be paid to financing operations and health systems
413 beyond the costs of vaccines. This shift can be explained by decreasing vaccine prices of newer vaccines
414 achieved through the collaboration of global partners such as the GAVI Alliance, combined with an
415 increasing need for health systems investment to reach higher coverage of vaccine programs [8].

416

417 Compared to the previous costing analysis conducted by Gandhi et al (2013), projected routine
418 immunization costs have increased marginally by \$4.4 billion based on a combination of greater
419 immunization coverage scale-up and decreasing vaccine price assumptions [24]. While the current
420 analysis relied on the latest GAVI demand forecast [8], the previous work relied on an earlier version
421 with different years in which countries are projected to introduce new vaccines and varying coverage
422 levels countries are estimated to reach [42]. A comparison to the previous costing analysis by Gandhi et
423 al. (2013) can be found in Table 6. Our analysis overcomes key limitations of the previous work by
424 providing a more detailed landscape of vaccination program cost drivers and additional sensitivity and
425 scenario analyses.

426

427 Our findings suggest that costs per program dose and costs per surviving infant are lowest for lower
428 middle-income countries (LMICs) rather than low-income countries (LICs). This can be explained by
429 the larger disease burden in LICs resulting in these countries introducing relatively more vaccines during
430 the decade compared to LMICs. In addition, LMICs may start to experience economies of scale with

431 increasing coverage, resulting in lower cost per program dose for supply chain and service delivery.

432 Costs are expected to be highest for UMICs with greater GNI per capita and high levels of vaccination

433 coverage. Moreover, we found cost per surviving infant to be relatively high for LICs due to higher

434 infant mortality, large number of SIAs, and high marginal costs for service delivery to reach DTP3

435 coverage levels above 80%, which half of the LICs reach.

436

437 Our estimates can be validated against cost per dose benchmarks from the literature. The supply chain

438 cost per dose was compared against a benchmark of \$0.40 per dose according to region, tier, and

439 percentage of urban population, where our results were reasonably aligned [43,44]. Service delivery cost

440 per dose was examined against the previous analysis, which used an incremental cost per dose of \$0.23

441 for childhood vaccines and \$1.30 for HPV vaccine. Our marginal costs per dose used in the current

442 analysis range from \$1.13 to \$2.13 according to DTP3 coverage level, where we observe greater costs to

443 reach higher coverage levels. The previous analysis also relied on an operational cost per dose of \$0.86

444 for SIAs, which are comparable to the SIA costs per dose in this analysis.

445

446 The greatest limitation of this analysis is the availability and quality of existing data. Since vaccine

447 prices for middle-income countries are not available outside of the GAVI price forecasts and PAHO

448 Revolving Fund price lists, our vaccine price projections for the 17 non-GAVI, non-PAHO countries are

449 a conservative estimate. Complete cMYP data were only available from 63 countries receiving support

450 for immunization from the GAVI Alliance. Country-level inconsistencies in cost definitions,

451 calculations, and validation methods in cMYPs may yield data quality constraints. In particular, the

452 estimate of marginal service delivery costs from cMYPs for countries above 80% DTP3 coverage may

453 still not fully encompass consideration for increasing costs of covering the hardest to reach children.

454 However, existing evidence supports the use of constant returns to scale when estimating marginal

455 service delivery costs for public health interventions [45,46]. In addition, utilizing cMYP data to
456 estimate costs for 21 higher-income countries has potentially underestimated service delivery costs in
457 those countries, producing a conservative estimate.

458
459 Despite these limitations, the results inform the costs necessary to support the Decade of Vaccines
460 across 94 countries to meet GVAP goals. This model was built to be updatable, where improved data
461 quality can only help to further inform resource mobilization efforts for vaccination programs. As the
462 model platform is built to also include financing projections, the analysis can further contribute to
463 estimations of the funding gap for vaccines to be used by global decision-makers.

464

465 Authorship:

466 AP, SO, and SG designed the study, developed the methodology, collected the data, performed the
467 analysis, and wrote the manuscript. For the supply chain component, BAN, JR, KMG, LAH, STB, and
468 BYL developed the methodology, collected the data, and performed the analysis. All authors contributed
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544 [document/715-public-sector-preferences-for-rtss/as01-malaria-vaccine-formulation-presentation-](http://www.technet21.org/index.php/documents/view-document/715-public-sector-preferences-for-rtss/as01-malaria-vaccine-formulation-presentation-and-packaging.html)
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592
 593

594 Table 1. Vaccine prices by country groupings

Vaccine	Low-high vaccine price per dose (US\$2010) between 2011 and 2020		
	GAVI Eligible	Non-GAVI Eligible	
	GAVI ^a [7]	PAHO [11-14]	Non-PAHO [15]
(<i>n</i>)	(<i>73 Countries</i>)	(<i>4 Countries</i>)	(<i>17 Countries</i>)
Tuberculosis (BCG)	0.09 – 0.10	0.10 – 0.16	0.10 – 0.16
Diphtheria-tetanus-pertussis (DTP)	0.15 – 0.22	0.15 – 0.23	0.15 – 0.22
Pentavalent (DTP–HepB–Hib combination)	1.63 – 2.43	2.13 – 2.98	2.16 – 4.06
Hepatitis B birth dose (HepB birth)	0.21 – 0.27	0.27 – 0.36	0.27 – 0.36
Human papillomavirus (HPV)	3.50 – 4.41	11.64 – 13.57	11.64 – 13.57
Japanese encephalitis (JE)	0.34 – 0.39	0.44 – 0.50	0.45 – 0.51
Malaria	4.26 – 4.85	5.44 – 6.30	5.62 – 6.40
Measles	0.24 – 0.30	0.31 – 0.39	0.31 – 0.39
Measles-rubella (MR)	0.47 – 0.54	0.62 – 1.08	0.63 – 1.08
Measles-mumps-rubella (MMR)	1.29 – 1.75	1.56 – 2.36	1.56 – 2.36
Meningitis A conjugate (MenA)	0.41 – 0.52	0.53 – 0.67	0.54 – 0.69
Pneumococcal conjugate (PCV)	2.60 – 6.79	12.77 – 14.52	12.77 – 14.52
Inactivated polio vaccine (IPV)	0.85 – 0.97	2.58 – 5.68	2.58 – 5.68
Oral polio vaccine (OPV)	0.12 – 0.13	0.12 – 0.21	0.12 – 0.21
Rotavirus (2-dose)	1.92 – 2.25	2.49 – 7.27	2.53 – 7.27
Rotavirus (3-dose)	2.81 – 4.85	3.65 – 5.09	3.70 – 5.09
Typhoid	2.21 – 2.91	2.88 – 3.78	2.92 – 3.84
Yellow fever	0.65 – 0.80	0.85 – 1.04	0.86 – 1.06

595 ^a See the online supplement for a full list of countries and groupings.

596 Table 2. Supply Chain Cost Estimation Process by Component: Mechanistic Model Equations and Inputs

Equation used to extrapolate costs from reference country to target country												
Transportation	(((m _t *Vaccine Regimen Volume)+ b _t)*SQRT(Target Country Area/Reference Country j Area)*(Target Country Gas Price/Reference Country j Gas Price))											
Storage	(((m _s *Vaccine Regimen Volume)+ b _s)*(Target Country Population/Reference Country j Population)*(Target Country Electricity Price/Reference Country j Electricity Price))											
Labor	(Reference Country j Labor Costs*(Target Country Population/Reference Country j Population)*(Target Country Hourly Wage/Reference Country j Hourly Wage))											
No. of Tiers in Supply Chain	Morphology of Supply Chain	Reference Country j Match for Supply Chain Category	m _t *	b _t	m _s *	b _s	HERMES 2011 Labor Cost	2011 Population	Area (sq km)	2011 Gas Price (per liter)	2011 Electricity Price (per kWh)	2011 Hourly Wage Rate
3 Levels	N/A	Benin	692	56,633	737	732,867	156,479	9,779,795	110,622	\$1.14	\$15.10	\$0.40
4 Levels	Bottom Heavy	Niger	7,426	129,243	3,851	416,363	374,116	16,511,462	1,266,700	\$1.10	\$13.20	\$0.40
4 Levels	Middle Heavy	Average of Bottom Heavy & Top Heavy	5,638	184,941	2,076	237,156	225,311	8,916,400	671,017	\$1.22	\$10.60	\$0.40
4 Levels	Top Heavy	Mozambique (Gaza Only)	3,849	240,639	300	57,949	76,505	1,321,338	75,334	\$1.35	\$8.00	\$0.40
5 Levels	N/A	India (Bihar Only)	3,783	836,794	2,131	53,495	131,128	103,804,639	94,163	\$1.20	\$16.60	\$0.47

597 *The slope is the increase in cost for a one unit increase in the volume of the vaccine regimen per child that is handled by the supply chain, measured in cubic centimeters (cc).

599 Table 3. Summary Measures of Estimated Routine Baseline Service Delivery Costs per Dose for 94 Countries (US\$2010)

	Immunization- specific personnel costs per dose	Shared personnel costs per dose	Non-personnel costs per dose	Total routine service delivery costs per dose
<i>Average (non-weighted)^a</i>	0.69	1.75	0.53	2.97
<i>Average (population weighted)^b</i>	0.32	0.74	0.21	1.27
<i>Median</i>	0.31	0.71	0.23	1.28
<i>Minimum</i>	0.05	0.16	0.05	0.28
<i>Maximum</i>	2.03	8.24	2.33	9.73
<i>Marginal (all coverage levels)^c</i>	0.43	0.64	0.13	1.20
<i><80% DTP3 coverage</i>	0.44	0.56	0.13	1.13
<i>>=80% DTP3 coverage</i>	0.46	1.52	0.15	2.13

600 ^a Analysis based on 63 cMYPs with baseline years ranging from 2004-2011; ^b Population weighted average costs are lower
601 than non-weighted average costs due to countries with large populations having lower costs; ^c Analysis based on 49 cMYPs
602 with baseline years 2009 or later.

603 Table 4. Costs per program dose and costs per surviving infant^a by income level^b across 2011-2020

	Low-income (LIC)	Lower middle-income (LMIC)	Upper middle-income (UMIC)
<i>Costs per program dose^c</i>			
Vaccine	\$0.99	\$0.78	\$1.61
Supply Chain	\$0.32	\$0.23	\$0.52
Service Delivery	\$1.43	\$1.26	\$1.51
Total	\$2.63	\$2.18	\$3.53
<i>Costs per surviving infant</i>			
Vaccine	\$30.20	\$22.94	\$46.00
Supply Chain	\$6.30	\$3.96	\$11.70
Service Delivery	\$43.74	\$37.13	\$43.11
Total	\$80.23	\$64.03	\$100.82

604 ^a Costs per program dose and costs per surviving infant are population-weighted by income level.
605 ^b LIC = GNI per capita < \$1,045. LMIC = GNI per capita between \$1,045 and \$4,125. UMIC =
606 GNI per capita > \$4,125.
607 ^c Program doses include administered doses, wastage doses, and buffer stock doses.

608

Table 5. Costing Scenario Analyses Comparison by Full Results, Difference, and Percentage Change							
Category ^a	Total Costs, Routine + SIA (US\$2010 billions)			Difference from Baseline (US\$2010 billions)		Percentage Change from Baseline (%)	
	Base	90%	Price	90%	Price	90%	Price
		Coverage	Reduction	Coverage	Reduction	Coverage	Reduction
LIC	21.13	21.28	21.13	0.16	0.00	0.73%	0.00%
LMIC	36.44	37.10	34.62	0.66	-1.82	1.80%	-5.00%
UMIC	2.38	2.39	2.03	0.02	-0.34	0.68%	-14.48%
GAVI	53.98	54.72	53.98	0.74	0.00	1.38%	0.00%
Non-GAVI	7.89	7.97	5.72	0.08	-2.17	1.05%	-27.47%
Total	61.87	62.69	59.70	0.83	-2.17	1.34%	-3.50%

609

^a Low-income country (LIC); Lower middle-income country (LMIC); Upper middle-income country (UMIC).

610 Table 6. Comparison to Gandhi et al. [24] Findings (US\$2010 billions)

	Gandhi et al ^a	Our analysis
Total Costs	57.5	61.9
Routine	49.4	50.7
Vaccine	24.0	19.7
Delivery ^b	25.4	31.0
SIA	8.1	11.1
Vaccine	2.5	4.1
Operational	5.6	7.0

611 ^a Key methodological differences with the Gandhi et al. analysis include the
612 following. Gandhi et al uses: (1) the GAVI Adjusted Demand Forecast version 4
613 (2011) for dose projections rather than the ADF v9 (2014); (2) constant prices
614 across the decades rather than prices that are projected to decrease; (3) a global
615 deflator for conversion to US\$2010 rather than local inflation based on
616 consumer price indices (CPI); (4) cMYPs for supply chain costs compared to
617 HERMES-based analysis; and (5) different cMYP data and methods used to
618 derive service delivery costs per dose.

619 ^b Routine delivery costs include both supply chain and service delivery.

Figure 1

Figure 1. DOVE/HERMES Supply Chain Cost Estimation Methods Flowchart

^a Reference countries include Benin, Niger, Mozambique (Gaza province), and India (Bihar state).

^b Because labor costs do not scale according to vaccine regimen volume, no linear equation was developed; instead, base labor costs are scaled directly by population and wage.

^c Each target country was matched with one of the four reference countries with the most similar supply chain structure, based on the number of tiers in the supply chain (3, 4, or 5) and by the relative distribution of storage locations (top heavy, middle heavy, or bottom heavy clusters, among countries with 4-tier supply chains), as detailed in the online supplement.

Figure 2

Figure 2. Total immunization program costs by component and by routine vs. SIA, 2011-2020.

Figure 3

Figure 3. Routine vaccine costs by vaccine type and by GAVI eligibility status, total over 2011-2020.
^a These represent full vaccine costs, not the incremental costs of introducing new vaccines.

Figure 4

Figure 4. Percentage of total SIA costs by vaccine for 94 GVAP countries, 2011-2020.