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Achieving immunization agenda 2030 coverage targets for 14 pathogens: Projected product and immunization delivery costs for 194 Countries, 2021–2030

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ABSTRACT

Understanding the level of investment needed for the next decade is vital to achieve the goal of Immunization Agenda 2030 (IA2030). Through the immunization funder perspective, this study estimates both global and regional economic resources required to achieve IA2030 coverage among 194 WHO member countries from 2021 to 2030, against 14 pathogens: Hepatitis B (Hep B), *Haemophilus influenzae* type b (Hib), Human papillomavirus (HPV), Japanese encephalitis (JE), Measles, Meningitis A (Men A), Streptococcus pneumoniae, Rotavirus, Rubella, Yellow Fever (YF), Diphtheria, Tetanus, Pertussis, and Tuberculosis.

The total cost of immunization program, routine vaccine, routine delivery, and non-routine costs (SIA and stockpile) were estimated using WHO coverage forecast for IA2030. Incremental costs of achieving IA2030 for all vaccines and cost per immunized child were also assessed. All costs were calculated for each income and regional level, as well as global level. Scenario analysis and sensitivity analysis were conducted to account for uncertainty in future vaccine pricing and delivery costs.

The total cost of immunization programs is $269.8 billion (95% confidence interval: $247.1 - $311.8), of which $152.8 billion is considered as routine vaccine cost, $114.9 billion is routine delivery cost. Non–routine cost for LICs and LMICs totaled $2.1 billion. The incremental cost of achieving coverage goals after 2020 is $89.9 billion ($27.7-$110.1), with upper-middle income countries requiring the largest increase in investment (56.2% of incremental costs). The average immunization cost per child across all countries is $192.6. Scenario analysis using the minimum and maximum vaccines price for fully self-financing countries resulted in total costs ranging from $193.6 and $552.2 billion.

The immunization program cost among 194 WHO member countries is expected to increase during this decade. The strategy for resource mobilization and increasing investment from country governments and donors are essential to achieving IA2030 coverage and ensuring sustainable immunization programs.

Introduction

In August 2020, the Seventy-Third World Health Assembly endorsed The Immunization Agenda 2030: A Global Strategy to Leave No One Behind (IA2030) in resolution WHA 72/(90) [1,2]. IA2030 defines an ambitious global vision and strategy for the decade 2021–2030 to enable "a world where every-one, everywhere, at every age fully benefits from vaccines for good health and well-being," [1]. IA2030 has been co-created and co-developed by all immunization stakeholders and aims to enhance country ownership in planning and implementation of immunization programs [2]. If fully implemented, IA2030 is expected to save over 50 million lives over the coming decade [3,4]. To achieve these health impacts, the global community needs to understand the level of investment needed for immunization programs during the next decade and develop effective strategies for resource mobilization and advocacy.

To facilitate such efforts, we estimated global and regional economic resources required to achieve aspirational coverage goals [3] for routine immunization and supplemental immunization activities (SIAs) from 2021 through 2030. This study builds on methods

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used in the Decade of Vaccines immunization costing study and return on investment analysis estimated costs of vaccines against ten pathogens in 94 LMICs [5,6]. This analysis considers the largest IA2030 cost drivers of vaccine product (costs of vaccines, injection supplies, wastage, buffer stock, freight) and immunization delivery costs (labor, storage, transportation, other capital costs, recurrent costs), and expands the scope to include all WHO member states and vaccines against 14 pathogens: Hepatitis B (Hep B), *Haemophilus influenzae* type b (Hib), Human papillomavirus (HPV), Japanese encephalitis (JE), Measles, Meningitis A (Men A), Streptococcus pneumoniae, Rotavirus, Rubella, Yellow Fever (YF), Diphtheria, Tetanus, Pertussis, and Tuberculosis. These costs correspond to the coverage estimates used in the recent study that modeled the impact of vaccination against 14 pathogens for IA2030. [3] These pathogens were selected based on assessment criteria encompassing IA2030 strategic priorities and availability of existing models and data [3].

Methods

The cost of achieving vaccine coverage goals outlined in IA2030 includes vaccine costs (costs of vaccines, injection supplies, wastage, buffer stock, freight), immunization delivery costs (labor, storage, transportation, other capital costs, recurrent costs), and stockpile costs. All costs are presented in 2020 USD. WHO regions [7], and World Bank income level classification [8] can be found in Appendix 1, along with Gavi eligibility and country transition [9].

This study was conducted from the immunization funder perspective, including government and donors such as Gavi, the vaccine alliance, and other development partners. This study does not include household cost such as traveling and transportation or loss of productivity time due to immunization.

Vaccine Costs.

We estimated the total number of doses for each vaccine by multiplying the country-specific coverage rate [3] outlined in IA2030 by vaccine-specific target population [10] and country-specific number of recommended doses for fully immunized child (excluding polio), and adjusting based on the wastage rate [11] and buffer stock rates [12]. For vaccine coverage, we applied the coverage forecast for IA2030 estimated in the modeling study by Carter et al. to calculate immunization costs for the year 2021 through 2030. This aspirational coverage rates were derived from IA2030 Impact Goal indicator 2.1, 2.2, and 3.1, of which country-specific achievements for DTP-contain vaccine-1 (DTPcv1) and subsequently DTPcv3 were approximated from 50 % reduction in zero dose children by 2030 [3]. Target population data were obtained from 2019 United Nation, World Population Prospects (UNWPP) [10]. Vaccine-specific assumptions for wastage and buffer stock rates can be found in Appendix 2. Vaccine costs were estimated by multiplying the number of doses of each vaccine (i), country (j) and year (k) by the price per dose. The number of doses was estimated separately for routine immunization and supplementary immunization activities (SIAs).

$$\textit{Number of doses}_{ijk} = \textit{Target population}_{ijk} \times \textit{Coverage rate}_{ijk} \times \textit{Number of recommended doses}_{ij} \times 1/(1 - \text{Wastage}) \times (1 + \textit{Buffer stock rate}_i)$$

We calculated vaccine costs by multiplying the number of doses with the vaccine price. Country-specific vaccine prices were determined based on Gavi-financing status, income level, and formulation. For Gavi-eligible countries, Gavi pricing were applied [13]. Countries that are a member of Pan-American Health Organization (PAHO), PAHO Revolving Fund was used [14]. LMICs that are non-Gavi or non-PAHO, we utilized UNICEF pricing [15]. Market Information for Access to Vaccines (MI4A) were applied to UMICs and HICs [16].

Under each data source, we applied the average price of vaccines across products and formulations, except for measles-containing vaccines (MCVs) and DTP-containing vaccines, for which formulation-specific average prices were used. Country vaccine formulations were extracted from WHO vaccine preventable disease monitoring system [17]. For Meningitis A, we utilized both Meningitis A vaccine pricing as well as other meningococcal vaccine due to the limitation of data available. For other multivalent vaccines, prices were allocated for each pathogen (Appendix 3).

Price forecasts were applied where available and assumed constant price after the latest year of available data throughout the remaining years, in accordance with Gavi's price forecast. Nevertheless, we conducted probabilistic sensitivity analysis and varied the percent change in vaccine price to account for the uncertainty in future price change. Additional costs of injection supplies were included based on the simple average of Gavi 2021 Public Price Forecast [13] and the PAHO Revolving Fund [14] for Gavi and non-Gavi countries, respectively.

$$\textit{Vaccine costs}_{ijk} = \sum_{k=2021}^{2030} \sum_{j=1}^{194} \sum_{i=1}^{12} (\textit{number of doses}_{ijk} \times \textit{price per dose}_{ijk})$$

Immunization Delivery Costs.

Delivery costs for vaccines include labor, transportation, fuel, cold chain equipment and maintenance. The full list of cost category and component included in each data source is available in Appendix 4. We estimated total immunization delivery costs by multiplying the country-specific delivery cost per dose by the total number of doses for each vaccine (i), country (j) and year (k).

$$\textit{Immunization delivery costs}_{ijk} = \sum_{k=2021}^{2030} \sum_{j=1}^{194} \sum_{i=1}^{12} (\textit{number of doses}_{ijk} \times \textit{delivery cost per dose}_{ij})$$

Estimates of routine delivery cost per dose were extracted from primary data sources, which were available for 63 LMICs. For LMICs with no direct estimates, we leveraged estimates from Portnoy et al. [18] which generated standardized delivery costs in 134 LMICs. For UMICs and HICs, we imputed delivery costs using a linear regression model. We conducted K-fold cross validation and applied Duan's smearing retransformation to determine the most well performing model by using combined dataset of delivery costs in LMICs and UMICs from IDCC [19], cMYP [20] and the Portnoy et al. model [18]. The final model used eight predictors to impute delivery cost per dose among UMICs and HICs. The initial list of predictors and sources used can be found in the Appendix 5.

$$\textit{Delivery Cost per dose}_i = Exp\left[\beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_3 + \beta_4 X_4 + \beta_5 X_5 + \beta_6 X_6 + \beta_7 X_7 + \beta_8 X_8 + \sum j \frac{e_j}{N}\right]$$

$X_1 =$ *Population* growth (annual %)

$X_2 =$ Total number of DTP3 doses delivered

$X_3 =$ GDP per capita

$X_4 = \textit{Poverty head count ratio at } 1.90 \textit{ a day} (2011 \textit{PPP}) (\%)$

$X_5 =$ Total number of births

$X_6 =$ DTP3 coverage rate (%)

$X_7 = \text{Electric power consumption (kWh per capita)}$

$X_8 = \text{Domestic general government health expenditure as \% GDP}$

Additionally, we validated the modeled estimates with the estimates found in published literature (Appendix 6). For countries with estimates available in the literature, we applied those delivery costs directly.

Delivery cost per dose were assumed to be the same across all vaccines. For multivalent vaccines, delivery cost per dose was apportioned equally to each pathogen contained in the vaccine to avoid double counting.

For vaccines delivered through SIAs, costs were only estimated in 59 LICs and LMICs for five vaccines, including Measles, Men A, YF, JE and HPV (multi-age cohorts) due to the limited availability of the SIA coverage data. We applied a simple average of the vaccine specific SIA delivery cost per dose from IDCC [19] and published literature. For HPV, we applied a simple average of delivery costs for MACs from a delivery cost database of estimates generated using the C4P tool [21].

Additionally, we also calculated the delivery cost for new vaccine introduction. The vaccine introductions and scale up are based on Gavi and UNICEF operational and strategic demand forecasts as well as the Gavi, PAHO, and UNICEF strategic and country vaccination plans. As the coverage increases from zero, then we considered the following year as the vaccine introduction year.

Due to limited data availability, vaccine introduction cost was only integrated for three vaccines – HPV, PCV and RV. To estimate the vaccine introduction cost, we calculated the mean incremental delivery cost estimates from IDCC and applied them to the introduction year only.

Stockpile costs.

The estimated costs of emergency vaccine stockpiles for Meningitis and yellow fever vaccines were included in this analysis based on Gavi Alliance Stockpile Forecasting v16.0 for 2021–2030.

Cost per child and cost per fully immunized child (excluding polio).

The cost per child and cost per fully immunized child (excluding polio) were calculated using a top-down approach using the target population and total vaccinated children as denominators, respectively. We assumed the standard immunization schedule includes vaccines against ten pathogens: measles, tuberculosis (BCG vaccine), diphtheria, tetanus, pertussis, S. pneumoniae, Hepatitis B, Hib, rubella, and rotavirus [22]. We calculated the cost per individual by pathogen and summed the results to estimate the total cost per fully immunized child (excluding polio).

We excluded regional vaccines (Men A, JE and YF) and HPV, which is used in adolescents and is not part of the infant routine immunization schedule, from the calculation. Additionally, we did not disaggregate vaccines into 1st and 2nd year of life as we did not have separate coverage estimates for DTP doses.

Scenario analysis.

Delivery cost per dose: Diminishing returns and constant returns to scale.

Under the base case scenario, we produced estimates based on an analysis by Ozawa et al. [23] that showed diminishing returns to scale for delivery costs as coverage increases (Appendix 7). At higher coverage levels, the diminishing returns assumption applies higher delivery costs per dose. Using the log-linear model, the delivery cost per dose per percent coverage change ranged from $0.09 -$1.40, with a mean cost per dose per percent coverage change of $0.66. Detailed model can be found in Appendix 7. Only the results of this scenario are presented as the primary results.

Additionally, we also estimated the incremental cost of achieving coverage goals of IA2030 for all vaccines which was calculated by comparing total costs of IA2030 to costs of immunization programs if coverage levels in 2020 are held constant over the decade.

$$IncrementalIA2030 = Totalcosts_{IA2030coverage} - Totalcosts_{2020coverage}$$

Fully Self-Financing Vaccine Pricing Scenarios.

We conducted additional analyses for fully self-financing countries. Of the 194 WHO member states, 73 are Gavi eligible countries. Sixteen of 73 Gavi countries are in the fully self-financing phase. Manufacturers still provide access to the same Gavi vaccine pricing for these fully self-financing countries. This access to vaccine prices under limited time and condition helps to ease the transition for these countries leading to improved sustainability for their immunization program [24].

For this scenario, we utilized the WHO MI4A database [16] on vaccine price for the 16 fully self-financing countries as if they do not have access for Gavi vaccine prices. We obtained all 2011–2020 price information that were not through UNICEF or PAHO procurement mechanism, including self-procurement, other pool procurement, and sub-regional pool procurement. We categorized the cost into minimum, maximum and average pricing for each vaccine type based on low, medium, and high volume purchased using the interquartile range of annual number of doses for each vaccine (Appendix 9). We assumed all prices were based on medium volume and used the average price as a base case. The two additional scenarios are MI4A at minimum and maximum price for all fully self-financing countries.

No Buffer Stock Scenario.

We conducted an additional analysis for the diminishing returns assumption when buffer stock is at 0 % instead of 25 %. The detailed results for both total and incremental costs can be found in Appendix 10.

All scenarios are conducted as follows:

1. Total costs with diminishing returns to scale
2. Incremental costs of IA2030 compared to 2020 coverage level with diminishing returns to scale
3. Total costs with constant returns to scale (Appendix 8)
4. Incremental costs of IA2030 compared to 2020 coverage level with constant returns to scale (Appendix 8)
5. Fully Self- Financing Vaccine Pricing
6. No Buffer Stock

Sensitivity analysis.

We conducted probabilistic sensitivity analyses (PSA) for all scenarios by varying five parameters simultaneously: country-specific routine immunization delivery cost per dose, vaccine-specific SIA delivery cost per dose and new vaccine introduction delivery cost, annual percent change in vaccine price, and stockpile costs. We used a uniform distribution for the annual percent change in vaccine price and stockpile cost per year (between ± 15 %), while a gamma distribution was applied to the other three parameters. We performed 10,000 Monte Carlo simulations to estimate the 95 % confidence intervals.

Results

We estimated the total costs of vaccines against 14 pathogens in 194 WHO countries between 2021 and 2030 to be $269.8 billion (95 % CI: $247.1 - $311.8). Routine vaccine costs comprise 56.6 % ($152.8 billion ($140.5 - $165.1)) of total costs and routine delivery costs comprise 42.6 % ($114.9 billion ($97.5 -$155.6)). Non-routine costs (SIA costs for 59 LMICs and Gavi stockpile costs) account for 0.8 % ($2.1 billion ($1.3 - $3.9)) of the total cost (Table 1). When stratified by income level, UMICs had the highest costs at $108.3 billion ($94.4 - $147.8) (40.2 %), followed by HIC, LMIC and LIC.

Table 1
Total costs and incremental costs, by income and regional level under diminishing returns scenario (95% confidence intervals in parentheses).

	Stratification	Total Cost Total Cost	Routine Vaccine Cost	Routine Delivery Cost	Non-Routine Cost*	Incremental Cost Total Incremental Cost	Routine Vaccine Cost	Routine Delivery Cost	Non-Routine Cost**
Income Level	**LIC (n = 34)** **SIA: n = 33**	$16.2B ($13.4B-$23.4B)	$6.5B ($5.9B-$7.1B)	$8.9B ($6.2B-$16.1B)	$802.2 M ($444.2 M-$1.7B)	$5.9B ($-2.3B-$11.3B)	$1.5B ($0.7B-$2.3B)	$4.4B ($-3.6B-$9.8B)	$0
	LMIC (n = 47) SIA: n = 26	$43.1B ($36.9B-$52.8B)	$19.4B ($17.9B-$21.1B)	$22.4B ($16.7B-$32.0B)	$1.3B ($879.5 M-$2.2B)	$18.3B ($4.3B-$24.0B)	$7.3B ($5.4B-$9.4B)	$10.9B ($-2.8B-$16.5B)	$0
	UMIC (n = 53)	$108.3B ($94.4B-$147.8B)	$74.5B ($68.5B-$80.4B)	$33.8B ($22.7B-$72.0B)	$0	$50.5B ($4.1B-$77.6B)	$30.2B ($23.3B-$37.3B)	$20.3B ($-25.6B-$46.6B)	$0
	HIC (n = 60)	$102.1B ($93.2B-$111.9B)	$52.3B ($48.0B-$56.7B)	$49.8B ($42.3B-$58.4B)	$0	$15.3B ($-1.1B-$24.1B)	$5.0B ($-1.3B-$11.7B)	$10.2B ($-4.3B-$17.3B)	$0
Regional Level	**EMRO (n = 21)** **SIA: n = 7**	$23.5B ($20.7B-$28.2B)	$12.9B ($11.8B-$13.9B)	$9.9B ($7.6B-$14.5B)	$630.7 M ($413.7 M-$1.2B)	$8.6B ($1.7B-$11.7B)	$4.6B ($3.2B-$6.0B)	$4.0B ($-2.6B-$7.0B)	$0
	AFRO (n = 47) SIA: n = 37	$30.9B ($25.8B-$41.1B)	$15.1B ($13.7B-$16.4B)	$14.8B ($10.2B-$25.1B)	$1.0B ($553.9 M-$2.2B)	$9.4B ($-2.3B-$17.4B)	$2.6B ($0.7B-$4.5B)	$6.8B ($-4.6B-$14.4B)	$0
	EURO (n = 53) SIA: n = 3	$50.9B ($45.7B-$57.4B)	$30.8B ($28.1B-$33.5B)	$20.1B ($15.8B-$26.0B)	$8.4 M ($7.5 M-$9.2 M)	$11.0B ($-0.2B-$15.7B)	$4.9B ($1.0B-$8.8B)	$6.1B ($-3.8B-$9.9B)	$0
	SEARO (n = 11) SIA: n = 7	$19.8B ($17.1B-$23.5B)	$9.4B ($8.6B-$10.1B)	$10.0B ($7.5B-$13.7B)	$375.8 M ($320.1 M-$471.5 M)	$10.5B ($3.9B-$11.9B)	$4.6B ($3.8B-$5.5B)	$5.9B ($-0.6B-$7.3B)	$0
	AMRO (n = 35) SIA: n = 1	$66.1B ($58.6B-$75.9B)	$34.8B ($32.1B-$37.6B)	$31.3B ($19.9B-$36.2B)	$8.6 M ($5.7 M-$15.7 M)	$10.0B ($-5.0B-$18.6B)	$3.0B ($-1.0B-$7.1B)	$7.0B ($-8.3B-$14.1B)	$0
	WPRO (n = 27) SIA: n = 4	$78.6B ($66.8B-$117.2B)	$49.8B ($45.9B-$53.9B)	$28.7B ($7.1B-$55.9B)	$26.3 M ($16.9 M-$49.4 M)	$40.4B ($-0.4B-$70.9B)	$24.4B ($19.9B-$29.1B)	$16.0B ($-26.7B-$45.0B)	$0
All countries (n = 194) **SIA: n = 59**		$269.8B ($247.1B-$311.8B)	$152.8B ($140.5B-$165.1B)	$114.9B ($97.5B-$155.6B)	$2.1B ($1.3B-$3.9B)	$89.9B ($27.7B-$110.1B)	$44.1B ($28.4B-$60.2B)	$45.9B ($-13.2B-$63.5B)	$0

*Stockpile costs could not be stratified by neither income level nor region. Therefore, the amount is only included for all countries in non-routine.
**Incremental costs calculation was based on routine coverage only; SIA was not included.

When classified by WHO regions, WPRO has the highest overall costs compared to other regions at $78.6 billion ($66.8 - $117.2) (29.1 %) while SEARO has the lowest cost at $19.8 billion ($17.1 - $23.5) (7.3 %). Detailed total and incremental costs categorized by income and region can be found in Table 1. For the total number of target population for each region and each income level, see Appendix 11.

The incremental cost of achieving IA2030 coverage for routine immunization compared to the 2020 coverage level increases significantly over the decade (Fig. 1). The incremental cost is highest among UMIC at $50.5 billion ($4.1 – $77.6) (56.8 %) followed by LMIC, HIC and LIC. At regional level, WPRO has the highest incremental cost at $40.4 billion (-$0.4 - $70.9) (44.9 %) while EMRO has the lowest cost at $8.6 billion ($1.7 - $11.7) (9.6 %) (Table 1).

As PCV and HPV vaccines are introduced in 56 and 42 more countries, they are expected to contribute the most to incremental costs. PCV is estimated to have the highest incremental cost with 57.6 % increase ($49.3 billion at the 2020 coverage level compared to $77.7 billion under IA2030 coverage), followed by HPV, which requires 108.5 % increase in costs to achieve IA2030 coverage ($13.93 billion to $27.7 billion) (Fig. 2).

Additionally, we assessed cost per child and cost per fully vaccinated child with standard schedule for children (excluding polio). The average cost per child is $192.62, with the cost per child increasing with income level. The incremental cost per child on average is $61.05 (Fig. 3). The UMIC income level and WPRO region have the highest incremental cost per child at $156.97 and $209.43, respectively. Detailed costing can be found in Appendix 12.

For total cost per fully vaccinated child using a standardized routine immunization schedule for children, the cost increases with the income level. When stratified by region, the EURO region has the highest cost per fully vaccinated child at $499.21 per fully immunized child (excluding polio), followed by AMRO at $458.43,

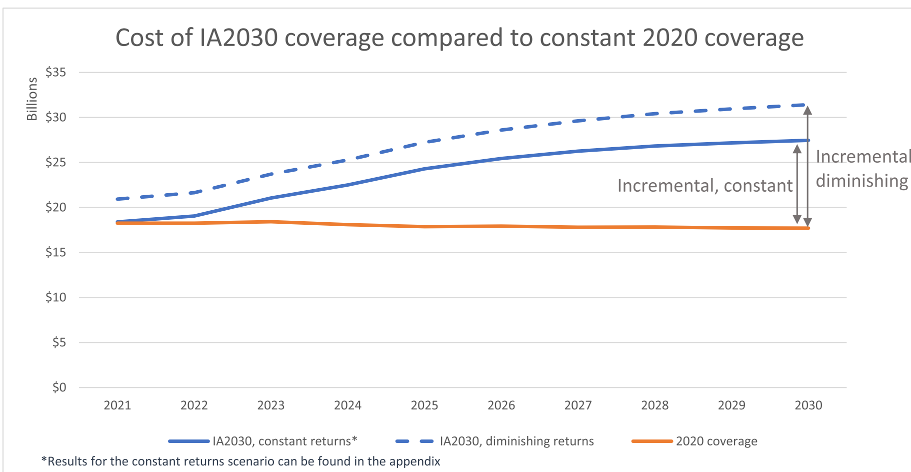

Fig. 1. Annual cost of IA2030 coverage compared to constant 2020 coverage level.

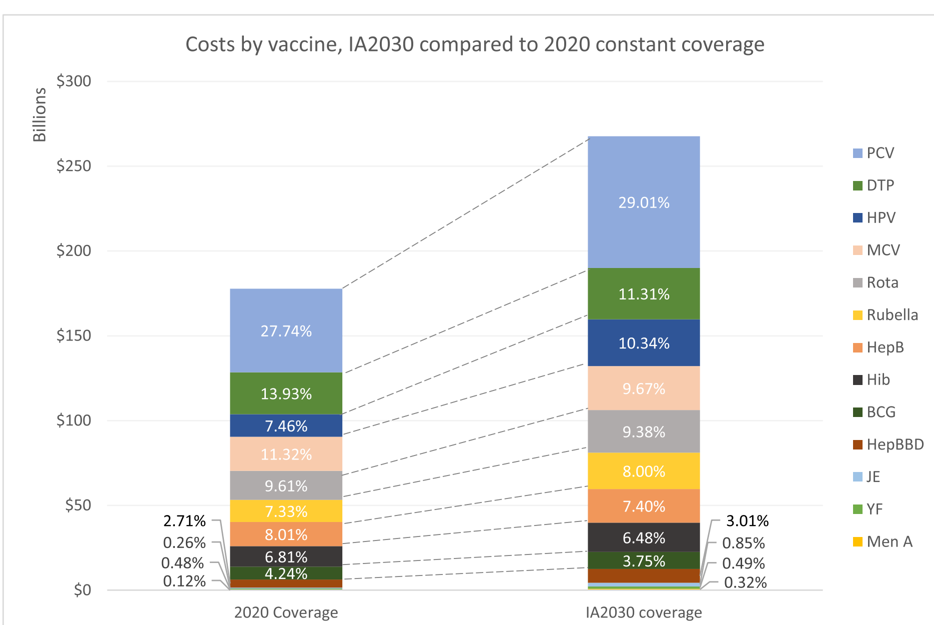

Fig. 2. Total costs by vaccine, 2020 coverage vs IA2030 coverage.

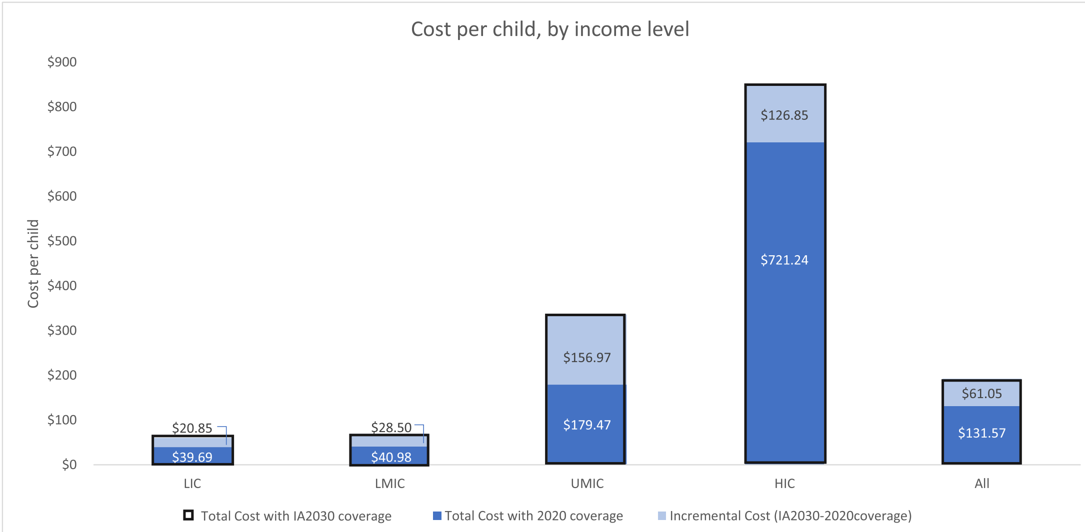

Fig. 3. Cost per child, by income level under diminishing returns to scale scenario.

WPRO at $376.80, EMRO at $141.79, AFRO at $81.59 and SEARO at $61.19. Detailed pathogen-specific cost per fully immunized child (excluding polio) can be found in Table 2.

Additional scenario analyses that explored higher and lower vaccine prices for fully self-financing countries had a large impact on the results. Using the MI4A minimum and maximum price, the total cost to achieve IA2030 coverage ranged from $193.6 to $552.2 billion, respectively. These costs mainly differ among UMIC and HIC (Appendix 9).

Discussion

The results from this analysis demonstrate that routine vaccine and delivery costs account for the majority (96.3 %) of the total costs for the next decade in 81 LICs and LMICs where the projected coverage and target population data for SIA were available.

When comparing the routine immunization vaccine and delivery costs across income groups, the largest proportion of the total costs (40.1 %) is attributed to UMICs due to a combination of larger birth cohorts (e.g. China) and higher vaccine prices. (Appendix 11) Across WHO regions, WPRO has the highest costs compared to other regions due to the same reason. Additionally, as countries become fully self-financing, vaccine prices could further drive the increase in the total resources required for the next decade.

The incremental cost scenario demonstrates the impact of new vaccine introduction and coverage improvement on the resource requirement. Since HPV and PCV contribute primarily to incremental costs due to their high vaccine price, it is important to continuously track and monitor the market landscape and country capacity for introducing these vaccines in the context of rapid roll-out of COVID-19 vaccines. Nevertheless, the negative lower bound for 95 % confidence interval in the incremental cost scenario means that there is a chance that the delivery cost and the price of these new vaccine could potentially decreases over the time.

The total cost per fully immunized child (excluding polio) is $60.54 for LICs and $69.48 for LMICs, which is comparable to the estimates from another study which estimates the average cost of fully vaccinating a child according to the standard schedule (excluding polio) as $58 per child (range US$37 – US$101) [22].

As many countries are transitioning and will no longer have the access to Gavi vaccine pricing, it is critical to understand the current financing gap. The average current immunization spending (Appendix 13), there remains a significant level of financing gap to reach IA2030 goal independently. If LICs were to fully self-finance for IA2030, based on our study, it would require a sixfold increase in domestic immunization expenditure. LMICs would need to increase 3.5 times and 1.8 times for UMICs. However, this study does not have sufficient data to forecast the spending for HICs. (Appendix 13). Given additional financial burden posed by new vaccine introductions, alternative financing strategies and global level coordination for access efforts will be needed to ensure the sustainability of the immunization programs.

There are several limitations in this analysis. First, the scope of analysis is limited to 14 pathogens for which IA2030 coverage scenario and vaccine impact estimates have been made available by Carter et al 2021. [3] Some vaccines included in the national immunization programs (including Polio and COVID-19 vaccines) were excluded from the analysis at this time due to limited data availability. Additional data on future vaccination coverage, vaccine prices and vaccination delivery strategies are essential to estimate the future costs of immunization programs for additional vaccines. Another limitation is the availability of delivery costs data. Given the uncertainty on country's decision for delivery strategies, we assumed uniform delivery cost per dose across all routine immunization vaccines. This implies that there was no distinction made between routine delivery via health facility and school for vaccine like HPV. This may underestimate the immunization delivery cost. Furthermore, this analysis focuses only on vaccine product and immunization delivery costs. For recurrent costs (Appendix 4), only the costs at the country level are included. Any limitations present in the underlying data sources have also been reflected in this analysis, including limited reliability from incomplete reporting or unclear estimation methods for country-level cMYP cost data [25],or heterogeneity with regards to data quality and categorization of cost components across empirical studies included in IDCC [26]. Future work should involve updated country-reported data based on the National Immunization Strategy costing application (NIS.COST) that has replaced cMYP costing tool, empirical evidence based on agreed-upon principles of estimation and reporting [27] and data on specific cost components (e.g. country-level VPD surveillance system) that have functional overlaps with other programs [28].

The scope excludes some areas of investment needed across IA2030 strategic priorities such as external funding requirement for vaccine-preventable disease (VPD) surveillance, research and

Table 2
Antigen-specific total and incremental cost per fully immunized child, regional level under diminishing returns scenario.

		Region	Antigen-specific cost per FIC Measles	Men A	HPV	PCV	Rota	YF	JE	BCG	DTP	Hep BBD	Hib	Rubella	Hep B	Cost per FIC standard schedule for children*
Total Cost	**Income Level**	**LIC**	$3.50	$5.51	$17.66	$20.41	$10.09	$4.05	$5.93	$5.19	$3.98	$2.89	$4.02	$5.94	$4.02	$60.04
		LMIC	$3.65	$6.07	$23.31	$23.64	$12.23	$5.04	$4.22	$5.87	$4.88	$3.04	$4.88	$5.84	$4.87	$66.67
		UMIC	$16.53		$104.41	$140.23	$19.86	$8.36	$12.70	$12.42	$60.53	$11.35	$23.27	$21.97	$26.87	$333.04
		HIC	$47.19		$188.29	$254.89	$146.29	$14.54	$45.56	$52.75	$73.96	$39.23	$71.80	$81.62	$72.35	$840.09
	Regional Level	**EMRO**	$7.87	$3.61	$55.76	$55.13	$17.63	$3.04		$9.17	$9.98	$7.51	$10.02	$14.46	$10.02	$141.79
		AFRO	$4.20	$5.95	$25.33	$26.80	$13.16	$4.73		$5.98	$6.51	$3.54	$6.47	$8.48	$6.47	$81.59
		EURO	$25.15		$140.29	$187.63	$61.43			$14.66	$57.27	$19.28	$45.62	$42.98	$45.19	$499.21
		SEARO	$2.94		$20.62	$20.97	$13.20		$4.09	$5.03	$4.01	$2.67	$3.87	$4.50	$4.00	$61.19
		AMRO	$33.59		$83.74	$145.59	$87.74	$7.74		$11.03	$38.61	$20.99	$38.08	$44.90	$37.89	$458.43
		WPRO	$16.28		$122.91	$159.89	$15.54		$13.85	$15.69	$76.22	$13.15	$26.60	$22.79	$30.65	$376.80
Incremental Cost	**Income Level**	**LIC**	$1.47	$4.24	$11.01	$4.87	$3.75	$2.07	$3.65	$1.86	$1.13	$2.57	$1.25	$2.82	$1.12	$20.85
		LMIC	$1.16	$4.52	$18.64	$11.01	$6.76	$1.43	$0.97	$2.00	$1.19	$1.76	$1.31	$2.12	$1.19	$28.50
		UMIC	$4.70		$73.85	$87.70	$5.82	$2.09	$12.70	$2.39	$12.88	$2.26	$17.54	$10.80	$12.88	$156.97
		HIC	$5.15		$25.29	$12.42	$34.64	$9.70	$45.56	$4.63	$6.51	$18.44	$7.76	$29.82	$7.49	$126.85
	Regional Level	**EMRO**	$2.08	$1.74	$44.85	$24.54	$2.75	$3.04		$2.41	$2.23	$2.17	$2.49	$4.59	$2.22	$45.48
		AFRO	$1.77	$4.62	$12.90	$4.66	$4.34	$1.74		$1.86	$1.34	$3.16	$1.48	$3.39	$1.33	$23.34
		EURO	$4.38		$57.29	$16.64	$20.60			$2.52	$7.64	$13.10	$9.11	$18.50	$8.10	$100.60
		SEARO	$0.95		$14.40	$16.43	$8.89		$1.33	$2.10	$1.26	$1.42	$1.44	$1.76	$1.26	$35.52
		AMRO	$4.62		$8.16	$8.11	$13.56	$2.03		$2.05	$6.05	$5.62	$7.16	$16.78	$6.51	$70.46
		WPRO	$4.14		$86.10	$125.52	$12.73		$12.91	$2.41	$14.45	$3.32	$21.17	$11.20	$14.50	$209.43

*Standard routine immunization schedule includes vaccines against 10 pathogens: measles, tuberculosis (BCG vaccine), diphtheria, tetanus, pertussis, *S. pneumoniae*, Hepatitis B, Hib, rubella, rotavirus.

development (R&D), technical assistance (TA), and incremental system strengthening (e.g., immunization information systems, immunization safety systems). Despite being a relatively smaller proportion of total costs, characterizing the remaining cost components remains an important area for future work.

Due to the COVID-19 pandemic, disruptions and total suspensions of immunization services delivery occurred in many countries in 2020 [29]. The number of doses for routine immunization in this study was calculated based on projected coverage data under the assumption that by 2030 we will reach aspirational goals set out in the Immunization Agenda 2030 [3]. The study did not capture any magnitude of actual disruption due to COVID-19 pandemic. As more data become available, future research could incorporate the pandemic's impact on new vaccine introductions and coverage rates.

Finally, there is limited evidence for the rate of diminishing returns to scale as vaccine coverage increases. While we use the latest available evidence for delivery costs associated with increasing coverage, more prospective studies will be needed to collect empirical evidence on costs required to deliver immunizations to harder-to-reach populations and their associated impact on vaccination coverage rates.

We acknowledge all the limitations stated above. This analysis may not fully resolve all the uncertainties, particularly in the future vaccine pricing, immunization delivery cost and the future trend of vaccine coverage in which may be affected by various exogenous factors. Nevertheless, this analysis provides essential information to understand the level of investment and resources needed, and for global decision makers to develop effective strategy for advocacy and resource mobilization.

Conclusion

The results from this analysis demonstrate the increases in immunization program costs from 2021 to 2030. This underlines the necessary investment for expanding access to vaccines among the WHO member states.

Data availability

Data will be made available on request.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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