ADVANCE MARKET COMMITMENT FOR PNEUMOCOCCAL VACCINES

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PREPARED BY THE AMC SECRETARIAT OF GAVI, THE VACCINE ALLIANCE

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Abbreviations

AMC	Advance Market Commitment
CDC	US Centers for Disease Control and Prevention
DTP	Diphtheria, tetanus, pertussis vaccine
EPI	Expanded Programme on Immunization
FCE	Full country evaluations
FOC	Firm order commitment
Gavi	Gavi, the Vaccine Alliance
Gavi Secretariat	Secretariat of Gavi, the Vaccine Alliance
IAC	Independent Assessment Committee
IPD	Invasive pneumococcal disease
IRC	Independent Review Committee
M&E	Monitoring and evaluation
PEF	Partners' engagement framework
PCV	Pneumococcal conjugate vaccine
PROWG	Pneumococcal & Rotavirus Operational Working Group
PSA	Provisional supply agreement
RFP	Request for proposals
UNICEF SD	UNICEF Supply Division
TPP	Target product profile
UNICEF	United Nations Children's Fund
VI-TAC	Vaccine Implementation Technical Advisory Consortium
WHO	World Health Organization
WUENIC	WHO/UNICEF Estimates of National Immunization Coverage

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Executive summary

The purpose of this report is to provide an update on the implementation activities of the Advance Market Commitment (AMC) for pneumococcal vaccines, including: supply and procurement; country demand; monitoring and evaluation (M&E); media and communications; and financial reporting. This is the twelfth and final Pneumococcal AMC Annual Report[i] and covers the period from **1 January to 31 December 2020**. The Pneumococcal AMC reached its conclusion on 31 December 2020, completing a decade of unprecedented progress in pneumococcal disease prevention, mainly fuelled by the expansion of routine immunisation in Gavi countries.

In the second half of 2021, an appendix to this report will be issued to reflect the 2020 WUENIC data scheduled to be published in July 2021, including PCV coverage achieved in 2020.

Supply and demand

The pilot AMC for pneumococcal vaccines completed its twelfth year of implementation in 2020. A total of 139 million doses of pneumococcal conjugate vaccine (PCV) were procured through the AMC in 2020, a 14% decrease from 2019 (161 million doses)[ii]. With the current eight supply agreements, the total contracted supply through 2029 amounts to 1.75 billion doses. Out of the US$ 1.5 billion AMC funds, the three suppliers that offer WHO-prequalified PCV have been allocated US$ 1.313 billion.

A new PCV, PCV10-5, manufactured by Serum Institute of India (SII), received prequalification from WHO on 19 December 2019. The IAC of the Pneumococcal AMC met virtually on 15 January 2020 and determined PCV10-5 eligible for the AMC. Demand for this new vaccine is starting to develop, with two countries having selected it, and is expected to gain momentum in the near future.

In terms of country demand, 86% of AMC-eligible countries (63 out of 73) had been approved to introduce PCV or to access the PCV price of the AMC to date. As of 31 December 2020, 60 countries have introduced these life-saving vaccines into their routine immunisation programmes. Bhutan was the most recent introduction, in the first quarter of 2019. Bhutan was the second formerly Gavi-supported country to fully self-finance a routine introduction of pneumococcal vaccine, after Mongolia. Three more countries followed with similar requests: in December 2019, Timor-Leste submitted a request to access the AMC price for routine introduction of PCV with a catch-up campaign (for children aged 1–5 years), for implementation in 2021 – the first request to mention PCV10-5 as a vaccine preference. Indonesia submitted a request in January 2020 to access the PCV AMC price to scale up PCV nationwide. Ukraine submitted a request in September 2020 for routine introduction starting in 2022. All three requests received approval in 2020, enabling countries to self-finance PCV introduction at the AMC price.

[i] *Previous Pneumococcal AMC Annual Reports can be found on the Gavi website: https://www.gavi.org/investing-gavi/innovative-financing/pneumococcal-amc*

[ii] *Total procured doses from the supply agreements that include countries that have access to AMC prices, in addition to Gavi-funded doses.*

Monitoring and evaluation (M&E)

The AMC continues to progress against selected indicators as shown in Table 1. It was estimated that more than 215 million children were immunised with AMC-supported PCV between programme start and the end of December 2019. The continued scale-up of PCV is estimated to have averted over 570,000 future deaths among children in Gavi-supported countries by the end of 2019.

Table 1. Selected non-confidential indicators for AMC progress tracking (calendar year view) in both AMC-eligible and Gavi-supported countries

	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
Objective 1: to accelerate the development of PCV that meet developing country needs												
Cumulative number of AMC-eligible TPP vaccines	0	2	2	2	2	2	2	2	2	2	2	3
Cumulative number of AMC-registered manufacturers that have made their registration public	0	4	4	4	4	4	4	4	4	4	4	4
Objective 2: to bring forward the availability of effective PCV for developing countries												
Annual number of doses of TPP vaccine procured under AMC by year (in millions)	0	7	36	58	58	100	133	164	156	149[iii]	161	139
Objective 3: to accelerate vaccine uptake by ensuring predictable vaccine pricing for countries and manufacturers												
Cumulative number of countries that have: applied for Gavi support for PCV	21	21	49	52	59	59	59	60	60	61	62	64
been approved	3	17	37	46	51	55	58	59	59	60	60	63
introduced TPP vaccines	0[iv]	1[iv]	16	24	38	46	54	57	58	59	60	60
PCV coverage[v]	0%	1%	5%	9%	19%	27%	36%	41%	44%	45%[vi]	49%	[vii]
Cumulative number of children vaccinated with PCV with Gavi support (in millions)	-	0.4	4	10	25	46	75	108	143	179	215	[vii]

Source: Gavi Secretariat

[iii] *The decrease was caused by a decline in demand from Nigeria, whose coverage rate has been lower than previously estimated.*

[iv] *In 2009, two countries introduced PCV that was not TPP-compliant; in 2011, they switched to a TPP-compliant vaccine.*

[v] *Indicator defined as the percentage of eligible population reached across 73 Gavi-supported countries.*

[vi] *The annual WUENIC update covers the whole time-series, so at times previous years' coverage figures change too.*

[vii] *Estimate not available as the impact of COVID-19 on PCV coverage and the number immunised with PCV is currently unknown. WUENIC coverage data and WHO-reported number of immunised for 2020 will be available in July 2021.*

PCV coverage performance at the country level continues to be tracked, using WHO/UNICEF Estimates of National Immunization Coverage (WUENIC) data, which are published annually in July for the previous year. Most countries have successfully introduced PCV into routine immunisation programmes, with PCV third-dose (PCV3) coverage tracking well against the third-dose coverage of diphtheria-tetanus-pertussis-containing vaccine (DTP3). Within two years of implementation, 46 of the 58 countries that had introduced PCV by 2017 had reached a coverage level of PCV3 amounting to at least 90% of their DTP3 coverage. Of the other 12 countries, 6 had reported PCV3 coverage of 81–90% of their DTP3 coverage within 2 years of introduction, 4 within 3 to 5 years of introduction (see Section 4, Figure 5), and 2 have had phased introductions (see Table 4).

The M&E framework established in 2007 includes a component for impact evaluations every four years from entry into the first AMC supply agreement to assess the achievements of the AMC and the association (and to the extent possible, causality) between the AMC intervention and observed outcomes. The first outcomes and impact evaluation of the AMC was completed in 2015, and the second outcomes and impact evaluation will be conducted in 2021, after the final year of the AMC pilot (refer to section 4.2).

In 2013, Gavi launched a set of FCEs in four countries (Bangladesh, Mozambique, Uganda and Zambia), with the aim of understanding the barriers to and drivers of immunisation. The introduction and implementation of PCV in the routine immunisation programmes (routinisation) of these four countries were evaluated as part of this project. The original FCE project contract ended in December 2016, and Phase 2 was approved in May 2017 in three countries (Mozambique, Uganda and Zambia). In May 2018, the Gavi Evaluation Advisory Committee (EAC) assessed the progress made in Year 1 of Phase 2 of the FCE project and decided to change the modalities of the FCE in line with the principle of country-led implementation. The FCE project, as originally designed, concluded in June 2018. Since then, the Gavi Secretariat has been engaging with country evaluation partners, where relevant, to scope specific evaluation priorities.

Gavi continues to fund special studies to assess the effectiveness and impact of PCV (refer to Annex 5). The aim is to help facilitate evidence-based decision-making in support of the introduction and continued implementation of PCV in developing countries.

Media and communications activities

Increasing AMC visibility through traditional, online and social media remained an important goal for Gavi's Communications team. The AMC was highlighted in both the printed and online versions of Gavi's 2019 Annual Progress Report (published in 2020). Further, the achievements of the Pneumococcal AMC were celebrated as a foundation for designing the next generation of effective financial tools for development: for example, the Gavi COVAX AMC Investment Opportunity was unveiled at Gavi's third replenishment, on the occasion of the Global Vaccine Summit, in the presence of 42 heads of state, including all 7 of the G7. The AMC has been featured prominently as an innovative financial mechanism that has quietly underpinned much of the Alliance's work.

Financial activities

From 1 January to 31 December 2020, Gavi disbursed US$ 356 million to UNICEF for the purchase of PCV. Of this amount, US$ 26 million was used to pay for the AMC-funded portion of the vaccine cost and thus came from the AMC funds. The remaining US$ 330 million was allocated from general Gavi funds to pay for the tail price portion of the vaccine purchase and related costs[viii].

Challenges and priorities ahead

The Pneumococcal AMC reached its conclusion on 31 December 2020, with 60 AMC-eligible countries having introduced PCV since 2010, and a further 3 countries approved to introduce PCV by 2022 by accessing the low AMC price(s) for pneumococcal vaccines. The AMC has ensured low, long-term and sustainable vaccine pricing for countries and manufacturers, and stimulated unprecedented demand for PCV in lower-income countries. Areas of priority for the Gavi Secretariat and Alliance partners to maintain this progress are: improving the balance of supply and demand; expanding tools for countries to assess new vaccine options; and securing continued access to low prices for Gavi-supported countries in the post-AMC PCV market.

One risk relates to country readiness to assess and switch to new PCV and presentations: the experience in 2020 was too short and impacted by COVID-19 events, yet the early signals point to slow adoption of innovation, which may limit the benefits of competition and increase exposure to supply disruptions. Furthermore, COVID-19 disruptions and vaccine production place pressure on manufacturing facilities, exposing supply to greater risk.

[viii] *Fulfilment costs are the extra costs incurred in supplying vaccines (estimated at US$ 0.08 per dose during the 2016–2020 period), in addition to the cost of the vaccine itself. These typically include the cost of syringes, safety boxes and freight.*

Background

An Advance Market Commitment (AMC) for vaccines aims to encourage the development and production of affordable vaccines tailored to the needs of developing countries. In June 2009, the Governments of Italy, the United Kingdom, Canada, the Russian Federation and Norway, along with the Bill & Melinda Gates Foundation, collectively pledged a total of US$ 1.5 billion to fund a pilot AMC against pneumococcal disease.

The overarching goal of the pilot AMC has been to reduce morbidity and mortality from pneumococcal disease, preventing hundreds of thousands of childhood deaths between 2010 and 2030. The objectives of the Pneumococcal AMC were to:

1. **accelerate the development of pneumococcal vaccines** that meet developing country needs (e.g. in terms of serotype composition and vaccine presentation) as specified in the TPP;
2. **bring forward the availability of effective pneumococcal vaccines** for developing countries by guaranteeing the initial purchase price for a limited quantity of new vaccines that represents value for money and incentivises manufacturers to invest in scaling up production capacity to meet developing country vaccine demand;
3. **accelerate vaccine uptake** by ensuring predictable vaccine pricing for countries and manufacturers, through binding commitments by participating companies to supply vaccines at low, long-term and sustainable prices; and
4. **test the effectiveness of the AMC mechanism** as an incentive for needed vaccines and to learn lessons for possible future AMCs.

Following the initiation of the Pneumococcal AMC in 2009, the first vaccines became available for procurement under the AMC terms and conditions, and the first roll-out occurred in Nicaragua in December 2010. As of December 2020, 63 of the 73 AMC-eligible countries had been approved to receive Gavi support for PCV introduction. Of this number, five countries are or will be self-funding PCV vaccination, and they will receive access to Gavi PCV AMC prices – the lowest in the world.

The purpose of this report is to provide an update on AMC implementation activities, including: supply and procurement; country demand; M&E; media and communications; and financial reporting. This is the twelfth Pneumococcal AMC Annual Report[ix] and covers the period from **1 January to 31 December 2020**.

The report was developed by the AMC Secretariat at Gavi, in collaboration with the World Bank and UNICEF. For more information about the AMC Secretariat, refer to Annex 1.

[ix] *Previous Pneumococcal AMC Annual Reports can be found on the Gavi website: http://www.gavi.org/library/gavi-documents/amc/*

1. Supply and procurement update

1.1 WHO recommendation and AMC-eligible pneumococcal vaccines

WHO recommends the inclusion of PCV in childhood immunisation worldwide[i]. For administration to infants, a 3-dose schedule administered either as 2 primary doses plus a booster (2p+1 schedule) or 3 primary doses (3p+0 schedule) are recommended. Primary vaccination can be initiated as early as at six weeks. WHO also states that, whenever possible, catch-up vaccination at the time of PCV introduction should be used to accelerate its impact on disease in children aged 1–5 years, particularly in settings with a high disease burden and mortality. Catch-up vaccination should be done with: a single dose of vaccine for children aged 24 months and older; and 1 or 2 doses in children aged 12–23 months. Gavi supports PCV for administration in infant routine immunisation programmes, with or without catch-up at introduction.

By 31 December 2020, three PCV, with a total of five different presentations, were available for procurement under the AMC. These three vaccines meet the criteria for TPP, which describe the minimum characteristics required for a pneumococcal vaccine to be eligible for AMC financing. The third and final manufacturer, Serum Institute of India (SII), received prequalification for its PCV in late December 2019 and started supplying to one Gavi country, Uzbekistan, in 2020.

1.2 Pneumococcal conjugate vaccine, 10-valent, 4-dose vial presentation by GSK

The 10-valent PCV (PCV10) is a liquid vaccine originally available in a 2-dose vial without preservative, produced by GlaxoSmithKline (GSK). It was launched in Europe in 2009; obtained WHO prequalification on 12 March 2010; and was deemed AMC-eligible on 16 April 2010 by the AMC IAC. GSK subsequently developed a 4-dose vial presentation of PCV10[ii], which includes a preservative, and was prequalified by WHO on 16 October 2017. It was deemed AMC-eligible on 17 October 2017 by the AMC IAC. The 4-dose vial presentation replaced the 2-dose vial, and all countries that had been using the PCV10 2-dose vial completed a switch to PCV10 4-dose vial or another product of their preference as of 2020. The PCV10 2-dose vial was available for shipment to countries until the end of 2019.

1.3 Pneumococcal conjugate vaccine, 13-valent, 1- and 4-dose vial presentation by Pfizer

The 13-valent PCV (PCV13) is a liquid vaccine in a single-dose vial, produced by Pfizer Inc. It obtained WHO prequalification on 22 August 2010 and was deemed AMC-eligible by the AMC IAC on 23 August 2010. In addition, Pfizer has developed a 4-dose vial presentation of PCV13, which also includes preservative. The 4-dose vial presentation obtained WHO prequalification on 14 July 2016 and was deemed AMC-eligible on 9 August 2016. The PCV13 single-dose vial presentation remains available.

1.4 Pneumococcal conjugate vaccine, 10-valent, 1- and 5-dose vial presentation by SII

The 10-valent PCV (PCV10) is a liquid vaccine available in a single-dose vial and in a 5-dose vial, produced by Serum Institute of India (SII). It obtained WHO prequalification on 19 December 2019 and was deemed AMC-eligible by the AMC IAC on 15 January 2020. The price of the 5-dose vial presentation currently available to Gavi countries is the lowest in the world. Both the single-dose and the 5-dose vial presentations have been available as a future option to Gavi countries since 2019, and three countries have selected it so far: Timor-Leste and Uzbekistan as a first preference, and Indonesia as a second preference. India is expected to use this locally produced vaccine to significantly scale up its PCV vaccination programme throughout the nation in 2021–2022: PCV10-5 received India's National Technical Advisory Group on Immunization (NTAGI)'s recommendation and was licensed for use in India in the third quarter of 2020.

1.5 Supply offers and agreements

Five Calls for Supply Offers under the AMC have been completed to date, resulting in eight supply agreements. The fifth and final Call[x] for Supply Offer was published in March 2020 and completed in April 2020. For a summary of the eight AMC supply agreements, refer to Annex 2. A summary of the supply commitments as of 31 December 2020 is shown in Table 2 below.

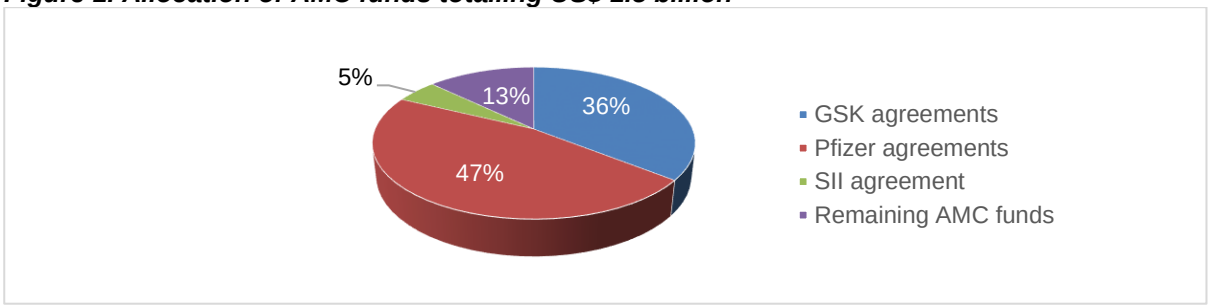
Table 2. Status of overall supply commitments, as of 31 December 2020

Manufacturer	Date of signature (week of)	Annual supply commitment (doses)	Tail price	Supply start date	AMC funds allocated
GSK	23 March 2010	30 million	US$ 3.50; reduced to US$ 3.05 from 2017*	2012	US$ 225 million
Pfizer	23 March 2010	30 million	US$ 3.50; reduced to US$ 3.40 mid-2013; US$ 3.30 from 2014**; US$ 3.05 from 2017***; US$ 2.95 from 2018****; US$ 2.90 from 2019*****	2013	US$ 225 million
GSK	12 Dec 2011	18 million	US$ 3.50; reduced to US$ 3.05 from 2017	2014	US$ 135 million
Pfizer	12 Dec 2011	18 million	US$ 3.50; reduced to US$ 3.40 mid-2013; US$ 3.30 from 2014*; US$ 3.05 from 2017***; US$ 2.95 from 2018****; US$ 2.90 from 2019*****	2014	US$ 135 million
GSK	22 July 2013	24 million	US$ 3.40; reduced to US$ 3.05 from 2017	2015	US$ 180 million
Pfizer	22 July 2013	26 million	US$ 3.40 in 2013; US$ 3.30 from 2014; US$ 3.05 from 2017***; US$ 2.95 from 2018****; US$ 2.90 from 2019*****	2016	US$ 195 million
Pfizer	5 April 2018	19 million	US$ 2.95 for 4-dose in 2018; US$ 2.90 from 2019*****	2018	US$ 142.5 million
SII	30 May 2020	10 million	US$ 2.00 for 5-dose; US$ 2.95 for 1-dose	2020	US$ 75 million

** Reduced tail price as announced in March 2016.*
*** Reduced tail price applied as per Pfizer's third supply agreement.*
**** Reduced tail price for MDV as announced in January 2017; tail price for SDV remains unchanged at US$ 3.30.*
***** Reduced tail price for MDV as announced in January 2018; tail price for SDV remains unchanged at US$ 3.30.*
****** Reduced tail price for MDV as announced in January 2019; tail price for SDV remains unchanged at US$ 3.30.*

The first price reduction achieved under the third set of supply agreements and the second tail price reduction from 2017 will likely contribute to savings totalling US$ 185 million and US$ 285 million respectively over the lifetime of the agreements. Pfizer's 2018 price reduction from US$ 3.05 to US$ 2.95 per dose will contribute additional savings of US$ 52.79 million over the duration of the existing four supply agreements. Another price reduction from Pfizer, from US$ 2.95 to US$ 2.90 per dose, will contribute further savings of US$ 22.9 million over the same period. In total, these price reductions will lead to savings amounting to US$ 546 million. The allocation of AMC funds is summarised in Figure 1 below.

Figure 1. Allocation of AMC funds totalling US$ 1.5 billion



1.6 Doses contracted to date

The number of doses on contract has increased since the 2013 supply agreements were signed, as additional doses were brought forward during the capacity development period in order to meet demand. The total contracted supply as of 31 December 2020 is summarised in Table 3 below.

Table 3. Total annual contracted supply, as of 31 December 2020 (in millions*)

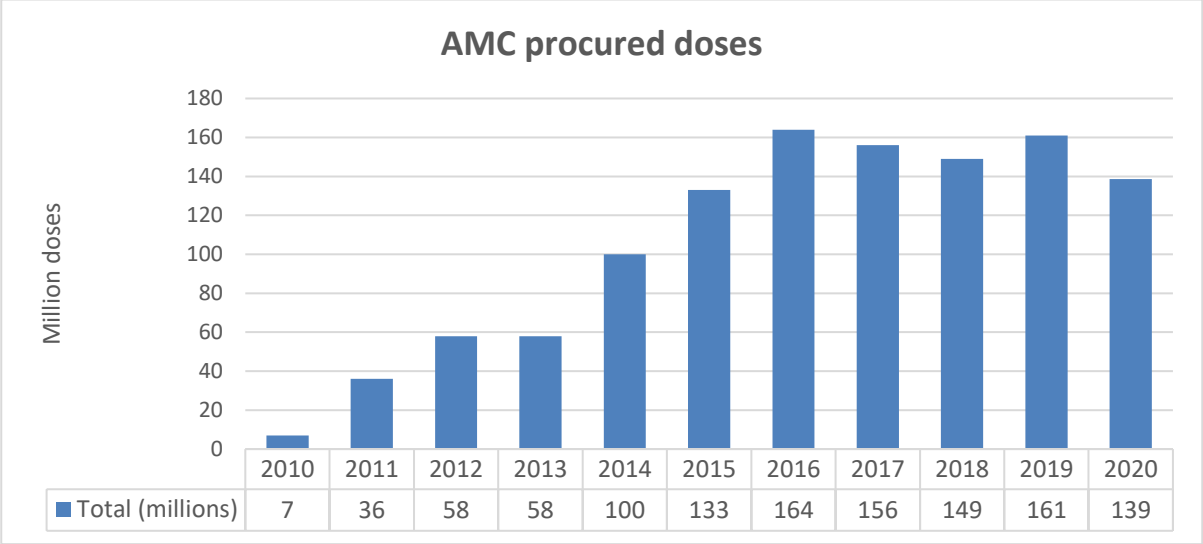
Year	2010	2011	2012	2013	2014	2015	2016	2017	2018-2020	2021	2022	2023	2024	2025-2029	Total
Doses contracted in 2010	5.5	28.9	54.0	53.5	45.9	40.6	57.7	60.0	60.0	54.9	19.0				**600.0**
Doses contracted in 2011			13.0	11.7	33.8	35.1	31.9	36.0	36.0	36.0	36.0	18.5			**360.0**
Doses contracted in 2013				3.0	9.0	43.8	44.6	80.3	50.0	50.0	50.0	57.9	11.4		**500.0**
Doses contracted in 2018									19.0	19.0	19.0	19.0	19.0	57.0	**190.0**
Doses contracted in 2020									10.0	10.0	10.0	10.0	10.0	50.0	**100.0**
GRAND TOTAL	**5.5**	**28.9**	**67.0**	**68.2**	**88.8**	**119.5**	**134.2**	**176.3**	**175.0**	**169.9**	**134.0**	**105.4**	**40.4**	**107.0**	**1,750.0**

Source: UNICEF SD
** Contracts are amended annually based on actual supply and demand to ensure that the total quantity in the supply agreements remains unchanged. Note: some numbers may appear not to add up due to rounding.*

1.7 Doses procured between 2010 and 2020

A total of 139 million doses of PCV were procured through the AMC in 2020. The total number of doses procured and delivered from 2010 to 31 December 2020 is summarised in Figure 2 below:

Figure 2. PCV procured volumes, 2010–2020 (in millions of doses)[xi]



It should be noted that special measures were undertaken with both suppliers in 2012 to ensure production at maximum capacity level in order to secure additional supply availability for 2013, when demand was projected to outpace supply. This resulted in early procurement of approximately 10 million additional doses in 2012 instead of in 2013; these doses were delivered during the first half of 2013 to minimise delays in country introductions. In 2016, to meet India's demand, 8.9 million additional doses were procured by pulling volumes from later years of the supply agreements; these doses were delivered in 2017. There were no India purchase orders (POs) issued in 2017 for delivery in 2018. This explains the decline in total volumes in comparison with the previous year. In 2018, one-off adjustments to the coverage estimates for Nigeria, driven by revised rates and stock updates, resulted in a significant reduction in the volume of doses needed for the year. In 2019, the volume requirements for Nigeria were restored to the normal trend and reflected an increase in procurement over the previous year. Stock adjustments in 2019 impacted 2020 PCV procurement with an overall reduction in volume, which was increasingly sharpened by COVID-19-related delays in the scale-up of PCV vaccination in Indonesia.

[xi] *Source: UNICEF SD. Note: the figure above indicates the number of doses placed on purchase orders during the respective years, including for delivery in a subsequent year.*

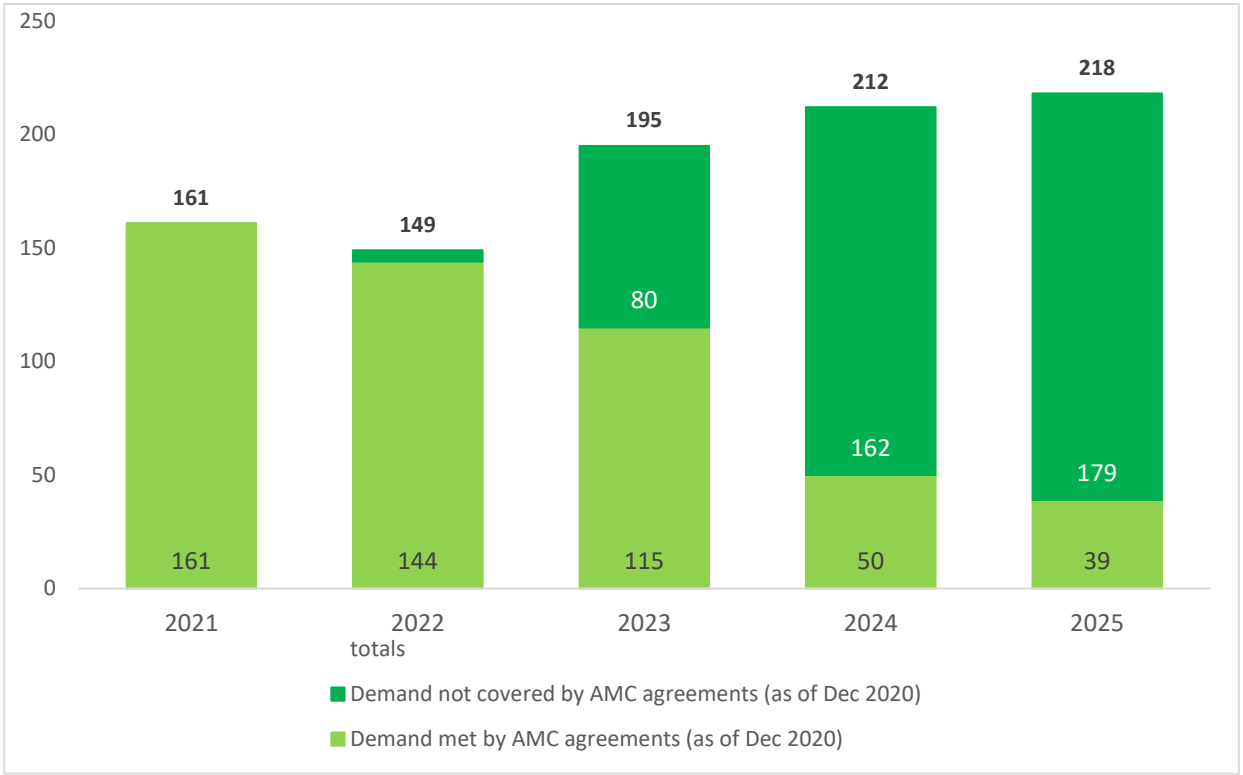
1.8 Strategic demand forecasts

In the last several forecasts, the long-term view of PCV demand has become relatively stable. The following demand forecast was developed, published and/or analysed in the reporting period:

- Demand forecasting for Gavi's v18.0 operational and financial forecast was completed in late 2020. This forecast represents the expected future demand through the AMC and UNICEF SD, as well as from self-procuring countries, such as India, through independent tenders. Assumptions include intensified scale-up of vaccination in India and Indonesia from 2021. The volumes associated with the v18.0 financial forecast were published on Gavi's website in January 2021.

The latest demand forecast is shown in Figure 3 below.

Figure 3. PCV demand forecast for Gavi73 (in millions of doses)[xii]



1.9 Availability of pneumococcal vaccines

There was sufficient supply of PCV for countries in 2020 with buffer capacity. The country presentation preferences were met with sufficient volumes of multi-dose and single-dose vial presentations. As part of the Healthy Markets Framework, PCV pricing demonstrated a positive trend with the entry of the first vaccine from a Developing Countries Vaccine Manufacturers Network (DCVMN) member, SII's PCV, at the price of US$ 2.00 per dose for its 5-dose vial presentation. The impact of the long-term supply agreement, signed under the fifth Call for Supply, is estimated to yield US$ 50–100 million in additional savings for Gavi and Gavi countries. Currently, sufficient manufacturing buffer capacity is expected due to the delay to 2021 of India's scale-up and the expected entry of another viable manufacturer within the Gavi 5.0 strategic period (2021–2025).

[xii] *Source: Gavi Base Demand Forecast v18, 2020*

Gavi and partners updated the PCV Supply and Procurement Roadmap to re-align on the target outcomes and action plans for the next two strategic periods, from 2021–2030, guided by the Healthy Markets Framework. Several uncertainties have the potential to impact supply and demand over the next ten years. These include:

- the preference among countries to change their product or presentation and the speed at which they wish to do so;
- PCV introduction timelines and scale-up plans of large countries eligible to access PCV at the price available through the AMC, such as India and Indonesia;
- the market entry of pipeline manufacturers and their achievement of production capacity targets; and
- possible schedule change from 3 doses to 1+1.

An action plan was agreed by Gavi stakeholders to focus on:

- mitigating potential supply risks related to premature manufacturer exits;
- supporting pipeline manufacturers to bring vaccines to market to ensure competitive market dynamics and sufficient buffer capacity;
- maintaining market health by ensuring country product and presentation preferences are grounded in evidence and consider supply availability and price; and
- driving continued price reductions to sustain PCV programmes.

For additional detail, refer to the public summary of the PCV Supply and Procurement Roadmap, available on the Gavi website.

1.10 AMC-registered manufacturers

Following the signature of AMC legal agreements on 12 June 2009, manufacturers can enter into an AMC Registered Manufacturer Agreement with Gavi and the World Bank. As part of the agreement, manufacturers formally agree to the AMC terms and conditions; accept to provide an annual update on expected timing for WHO prequalification and application for AMC eligibility; and recognise the role of the IAC in the determination of AMC eligibility. As described in the AMC procedures memorandum, manufacturers that are interested in participating in the AMC must submit to the AMC Secretariat an AMC Registered Manufacturer Application Package. This registration does not imply any commitment from manufacturers to participate in the AMC. It is, however, a prerequisite for taking part in UNICEF's Calls for Supply Offers.

Details about the registered manufacturers are confidential unless a firm agrees to have its registration made public. The list of AMC-registered manufacturers that have made their registration public is as follows:[iii]

- GSK Biologicals (Belgium)
- Panacea Biotec Ltd. (India)
- Pfizer Inc. (United States of America)
- Serum Institute of India (India)

To date, three of these manufacturers are producing WHO-prequalified, AMC-eligible PCV. Other pipeline manufacturers are not expected to have WHO-prequalified vaccines until 2021–2022. Gavi continues to actively monitor the pipeline development for other manufacturers.

2. Country demand and introductions overview

2.1 Gavi-supported countries approved for the introduction of PCV

As of 31 December 2020, 63 of the 73 AMC-eligible countries had been approved to receive Gavi support for PCV introduction. Of this number, five countries are or will be self-funding PCV vaccination, so they will receive access to AMC prices – the lowest in the world. Indonesia, Timor-Leste and Ukraine were approved in 2020 to access PCV at the AMC price and plan to introduce or scale up the vaccine by 2022.

2.2 Introduction of PCV in transitioned countries

In June 2010, the Gavi Board agreed that all countries eligible for Gavi support in 2003 would continue to have access to PCV under the terms and conditions of the AMC – even after transitioning out of Gavi support. As a result of this decision, fully self-financing[xiii] countries that have not yet been approved to receive Gavi support for pneumococcal vaccine have been able to apply for and introduce it under the terms and conditions of the AMC. To do so, they needed to: have achieved DTP3 coverage at or above 70% according to the latest WHO/UNICEF estimates; commit to procure through UNICEF; and self-finance the tail price component of the AMC price from the outset. Fully self-financing countries that have not applied despite being eligible to do so are Cuba[xiv], India[xv], Sri Lanka, and Viet Nam. Of note, in 2019–2020, it was agreed that India would be granted a set volume of Gavi-supported PCV doses in 2021, and India is expected to obtain a low PCV price in their national tender in 2021.

2.3 Pneumococcal vaccine introductions and product switches

As of 31 December 2020, 60 countries had introduced PCV supported by the AMC. The introductions that have taken place to date are listed in Table 4 below. In 2020, three countries switched vaccine product preference, driven by: a lower price (i.e. Uzbekistan); new National Immunization Technical Advisory Group (NITAG) recommendations (i.e. Pakistan); or the ceased production of PCV10 presentation in two-dose vials (i.e. Ethiopia). Counting these switches, of the 60 countries with Gavi-supported pneumococcal vaccines, 9 are using PCV10-4; 50 are using PCV13 in either the multi- or the mono-dose vial; and 1 is using PCV 10-5.

Table 4. Pneumococcal vaccine introductions to date[xvi]

Year	Country	Vaccine at launch	Status	Cumulative #
2009	Gambia	PCV7 (donation)	Switched to PCV13 in 2011	1
	Rwanda	PCV7 (donation)	Switched to PCV13 in 2011	2
2010	Nicaragua	PCV13	Introduced in December	3
2011	Guyana	PCV13	Introduced in January	4
	Yemen	PCV13	Introduced in January	5
	Kenya	PCV10	Introduced in January	6
	Sierra Leone	PCV13	Introduced in January	7

[xiii] *As per previous Gavi graduation terminology, graduating (accelerated transition) and graduated (fully self-financing) countries.*

[xiv] *Cuba is planning to introduce PCV7, hence it will not be able to access AMC products or prices.*

[xv] *India is in accelerated transition but can apply for the AMC tail price for the non-Gavi supported portion of PCV cost.*

[xvi] *Indonesia has been running a pilot in a few states, and hence reports 3% coverage, but has not yet formally introduced nationwide.*

	Mali	PCV13	Introduced in March	8
	Congo, Democratic Republic of	PCV13	Introduced in April (phased intro.)	9
	Honduras	PCV13	Introduced in April	10
	Central African Republic	PCV13	Introduced in July	11
	Benin	PCV13	Introduced in July	12
	Cameroon	PCV13	Introduced in July	13
	Burundi	PCV13	Introduced in September	14
	Ethiopia	PCV10	Introduced in October Switched to PCV13-4 in 2020	15
	Malawi	PCV13	Introduced in November	16
2012	Ghana	PCV13	Introduced in April* (joint intro. with rotavirus vaccine)	17
	Zimbabwe	PCV13	Introduced in June*	18
	Pakistan	PCV10	Introduced in October (phased intro.) Switched to PCV13-4 in 2020	19
	Congo, Republic of	PCV13	Introduced in October	20
	Madagascar	PCV10	Introduced in November	21
	Sao Tome and Principe	PCV13	Introduced in November	22
	Djibouti	PCV13	Introduced in December	23
	Tanzania	PCV13	Introduced in December* (joint intro. with rotavirus vaccine)	24
2013	Mozambique	PCV10	Introduced in April; switched to PCV13	25
	Uganda	PCV10	Introduced in April (phased intro.)	26
	Kiribati	PCV13	Introduced in May	27
	Angola	PCV13	Introduced in June	28
	Zambia	PCV10	Introduced in July (joint intro. with measles second dose)	29
	Sudan	PCV13	Introduced in August	30
	Moldova	PCV13	Introduced in October	31
	Lao People's Democratic Republic	PCV13	Introduced in October	32
	Burkina Faso	PCV13	Introduced in October (joint intro. with rotavirus vaccine)	33
	Senegal	PCV13	Introduced in November	34
	Mauritania	PCV13	Introduced in November	35
	Papua New Guinea	PCV13	Introduced in November	36
	Afghanistan	PCV13	Introduced in December	37
	Azerbaijan	PCV10	Introduced in December; switched to PCV13 in 2016	38
2014	Liberia	PCV13	Introduced in January	39
	Bolivia	PCV13	Introduced in January	40
	Togo	PCV13	Introduced in June (joint intro. with rotavirus vaccine)	41
	Niger	PCV13	Introduced in August (joint intro. with rotavirus vaccine)	42

	Armenia	PCV10	Introduced in September; switched to PCV13 in 2016	43
	Côte d'Ivoire	PCV13	Introduced in September	44
	Georgia	PCV10	Introduced in November	45
	Nigeria	PCV10	Introduced in December (phased intro.)	46
2015	Cambodia	PCV13	Introduced in January	47
	Nepal	PCV10	Introduced in January	48
	Solomon Islands	PCV13	Introduced in February	49
	Bangladesh	PCV10	Introduced in March (joint intro. with inactivated polio vaccine)	50
	Guinea Bissau	PCV13	Introduced in June	51
	Lesotho	PCV13	Introduced in July	52
	Eritrea	PCV13	Introduced in August	53
	Uzbekistan	PCV13	Introduced in November Switched to PCV10-5 in 2020	54
2016	Kyrgyzstan	PCV13	Introduced in March	55
	Mongolia	PCV13	Introduced in June (2 districts)	56
	Myanmar	PCV10	Introduced in July	57
2017	India	PCV13	Introduced in May (phased intro.)	58
2018	Haiti	PCV13	Introduced in October	59
2019	Bhutan	PCV13	Introduced in January	60

** Ceremonial launch; national introduction in the following month.*

2.4 Future pneumococcal vaccine introductions

Four introductions or nationwide scale-ups of PCV vaccination are expected by 2022: Indonesia, Timor-Leste and Ukraine are now approved to introduce or scale up PCV with the AMC price. India is expected to scale up PCV nationwide in 2021.

Out of the 73 AMC-eligible countries, only 10 have not been granted pneumococcal vaccine support through the AMC: Chad, Comoros, Cuba, Democratic Republic of Korea, Guinea, Somalia, South Sudan, Sri Lanka, Tajikistan and Viet Nam. Of these, four countries were ineligible for support until the Gavi Board removed the AMC application requirement, effective June 2020, to have achieved DTP3 coverage at or above 70%. Tajikistan expressed interest to apply for support to introduce PCV (without catch-up) in 2022. Comoros, Guinea and Somalia had expressed political will to move forward with planning an application for PCV support, and there is an expectation that these applications will be submitted in Gavi's 2021–2025 strategic period. Gavi will continue to support health system and routine immunisation strengthening in these countries to ensure adequate readiness to introduce PCV and other vaccines in the future. Three of these countries have already transitioned out of Gavi support (Cuba, Sri Lanka and Viet Nam).

2.5 Coordination and support for pneumococcal vaccine introductions and implementation

With the introduction of the partners' engagement framework (PEF) for the 2016–2020 strategic period, Gavi strengthened its coordination mechanisms with partners to ensure more effective and efficient technical support to countries. The PEF structure – split between foundational support, targeted country assistance and strategic focus areas – ensured that Alliance resources, including technical assistance, were better targeted to address key bottlenecks at the country level.

At the global level, the PROWG was established in 2011 with the aim of facilitating effective partner coordination, including country communication and operational decision-making. The PROWG has been instrumental in creating favourable conditions for Gavi-supported countries to successfully apply, introduce and sustain use of pneumococcal and rotavirus vaccines, as per Gavi's mission and the AMC goals and objectives.

The PROWG members represent WHO, UNICEF SD, UNICEF Programme Division, PATH, Johns Hopkins University (JHU), Clinton Health Access Initiative (CHAI), CDC and the Gavi Secretariat. The working group meets periodically by teleconference to discuss the following key topics, among others:

- monitoring the progress of implementation, such as reports of faster (or slower) uptake of the vaccine post-launch;
- assessing need for vaccine product switches in response to supply shortage risks;
- determining technical assistance needs and mobilising relevant resources to ensure successful application, programme planning and implementation; and
- gathering lessons learned and analysing experiences to optimise and improve future introductions.

For a list of current PROWG members, refer to Annex 3.

At the country level, programmatic challenges post-introduction have been gathered through post-introduction evaluations (PIEs), which measured the overall impact of new vaccine introductions on a country's national immunisation programme. A PIE focuses on a range of programmatic aspects, such as: pre-introduction planning; vaccine storage and wastage; logistics of administering the vaccine; and community receptiveness. It is used to rapidly identify problem areas needing correction within the immunisation programme (either pre-existing or resulting from the introduction of a new vaccine) and provide valuable lessons for future vaccine introductions. PIEs were conducted as standalone assessments or as part of comprehensive reviews of the Expanded Programme on Immunization (EPI).

Five countries[xvii] have conducted PIEs for PCV. The PIEs carried out have concluded that, due to high demand, PCV introduction is generally successful and that high coverage is reached within a short period. Some of the issues identified include cold chain and vaccine management, training, reporting and monitoring. The Gavi FCEs have also provided relevant lessons learned regarding routine introductions of PCV[xviii].

2.6 Global Action Plan for the Prevention and Control of Pneumonia and Diarrhoea

In 2013, WHO/UNICEF published the integrated Global Action Plan for the Prevention and Control of Pneumonia and Diarrhoea (GAPPD)[iv]. GAPPD proposes a cohesive approach to ending preventable pneumonia and diarrhoea deaths. Furthermore, it provides a roadmap for national governments and their partners to plan and implement integrated approaches for the prevention and control of pneumonia and diarrhoea. GAPPD brings together critical services and interventions, including immunisation, to create healthy environments; promotes practices known to protect children from disease; and ensures that every child has access to proven and appropriate preventive and treatment measures.

[xvii] *Burkina Faso, Côte d'Ivoire, Eritrea, Kyrgyzstan and Nigeria.*

[xviii] *See Section 4.3 for more information.*

Gavi has supported the advancement of GAPPD. With the increase in PCV introductions, there has been a unique opportunity to strengthen the integration of service delivery and help improve the coverage of other important interventions. Since 2014, Gavi required countries applying for PCV support to describe the status of implementation of other complementary interventions for disease prevention and control, and explain how they could leverage the opportunity of a new vaccine introduction to strengthen an integrated approach. This was not designed to raise the requirements for proposal approval but, rather, as an opportunity to prompt countries' consideration and planning of comprehensive disease prevention and control at the time of proposal development.

3. AMC Independent Assessment Committee

The IAC has been in place for the duration of the AMC and will be called upon one last time in 2021 to review this report. The IAC served a number of key functions. Most importantly, it had the mandate to review and approve the TPP and thereby the minimum technical requirements that candidate products must meet to be eligible for AMC funding[xix]. In addition, the IAC established when and if an adjustment of the present long-term price of vaccines is necessary.

The IAC members represent expertise in: public health; health economics; vaccine business development; vaccine industry economics; contract law; public-private finance; and clinical performance and delivery systems. As expressed in the IAC charter and bylaws, the initial term of up to six years of IAC members was subject to reappointment and could only be renewed once. The membership of three IAC members had been pending revision in 2018, and one member resigned effective 2018.

In June 2018, a call for nominations of new IAC members was circulated, and a sufficient number of candidacies were received to replace potentially all members whose terms had expired. The candidates were assessed in September 2019 by the IAC Selection and Oversight Panel, and four new members were appointed on 1 November 2019:

William (Bill) Hausdorff
Lead, Public Health Value Proposition, PATH, Washington, DC, USA

Evans Mpabalwani
Paediatrician and Clinical Virologist, Ministry of Health, Zambia

Giorgi Pkhakadze
Professor, School of Public Health, David Tvildiani Medical University (DTMU), Georgia

Piers Whitehead
Chief Executive Officer, SeromYx Systems, Cambridge, MA, USA

For a list of all active IAC members, refer to Annex 4.

[xix] *Also see section 3.2 of the 2010 AMC Annual Report: http://www.gavi.org/funding/pneumococcal-amc/*

4. Monitoring and evaluation (M&E)

In 2007, the United Kingdom's Department for International Development (DFID) and the Canadian International Development Agency (CIDA) commissioned a monitoring and evaluability assessment study on behalf of the AMC for Pneumococcal Vaccines Donor Committee. The study proposed an M&E framework, including four key components:

- annual monitoring to be implemented by the AMC Secretariat;
- a baseline study to establish the context (industry and country situation) at the beginning of the intervention and to develop proposed counterfactuals (two counterfactuals were proposed to estimate what would happen if no AMC were to be implemented and to measure incremental impact of the AMC initiative on the vaccine market and on pneumococcal disease and mortality);
- an independent process and design evaluation to assess the AMC implementation process and the efficiency and effectiveness of the AMC design; and
- impact evaluations every four years from entry into the first AMC supply agreement to assess the achievements of the AMC and the association (and to the extent possible, causality) between the AMC intervention and observed outcomes.

Annual monitoring is carried out by the AMC Secretariat, and an Annual Report has been published on the Gavi website each year since 2010. The baseline study was completed in 2010 and is available on the Gavi website. The AMC process and design evaluation were carried out in 2012. Upon recommendation of the Gavi Evaluation Advisory Committee (EAC), and following consultations with AMC stakeholders in 2013, the first impact evaluation of the AMC was completed in 2015 instead of in 2014 (for more information, refer to section 4.2).

4.1 Programme performance reporting

Gavi's 2016–2020 strategy did not define targets for PCV coverage and instead included a composite indicator tracking overall coverage of all vaccines in Gavi's portfolio. Pneumococcal vaccine coverage in Gavi-supported countries continues to be closely monitored through a comprehensive PCV results framework.

By the end of 2019, weighted PCV3 coverage in the original 73 Gavi-supported countries was 49%, based on WUENIC data published in July 2020[v] – an increase of 3 percentage points in relation to 2018[xx]. The corresponding DTP3 coverage in the same group of countries, which includes countries that have not yet introduced PCV, is 81%. In the subset of Gavi-supported countries that introduced the vaccine prior to 2017 (57[xxi]), weighted average PCV3 coverage has reached 76%, only 1% behind the DTP3 coverage of 77%.

In the large majority of Gavi-supported countries that have introduced PCV3 (85%), PCV3 coverage amounted to more than 90% of the coverage levels for DTP3[xxii]. Across all 60 Gavi countries that introduced PCV, the PCV3 coverage at 56% trails behind DTP3 (80%). India has introduced in 2017 and is expected to fully scale up in 2021–2022. Actual 2020 data will become available in July 2021 and will be published as an appendix to this report in the second half of 2021.

[xx] As per WUENIC data published in July 2020, Gavi73 weighted average PCV3 coverage was 45% in 2018 and 49% in 2019.

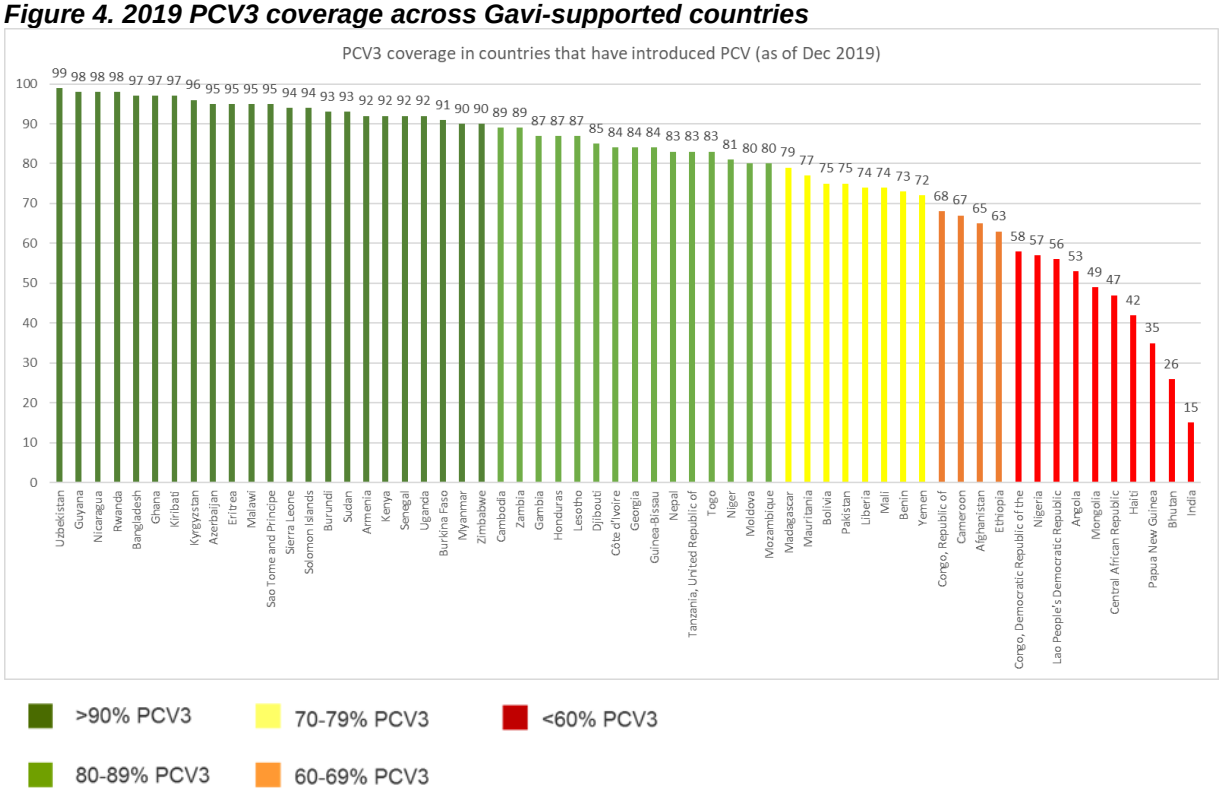
[xxi] Kyrgyzstan and Mongolia were excluded because PCV coverage during the year of introduction (2016) was 0% in both countries.

[xxii] Among the countries that have not achieved 90% of DTP3 coverage, three recently introduced PCV (Bhutan in 2019, Haiti in 2018 and India in 2017).

A few countries have opted to administer the third dose of PCV at a later time. This includes: Nepal, which moved the administration to 9 months[xxiii] (together with the first dose of measles vaccine); Bangladesh, which initially administered the third dose at 18 weeks; and Moldova, where the vaccine is provided at 12 months. In Bangladesh, a decision from the National Committee for Immunization Practices in January 2017 subsequently moved PCV third-dose administration to 14 weeks.

In Nepal, the novel schedule was introduced to avoid administering the second dose at the same time as inactivated polio vaccine (IPV) and is not in line with WHO recommendations (which recommends at least 8 weeks between first and second dose in the 2p+1 schedule). Immunogenicity studies in Nepal showed that the immune response after the second dose given at 10 weeks was lower; however, these differences disappeared after a booster dose was administered[xxiv]. In complement, there is an ongoing study comparing invasive pneumococcal disease (IPD) pre- and post-introduction in the same population.

Figure 4. 2019 PCV3 coverage across Gavi-supported countries

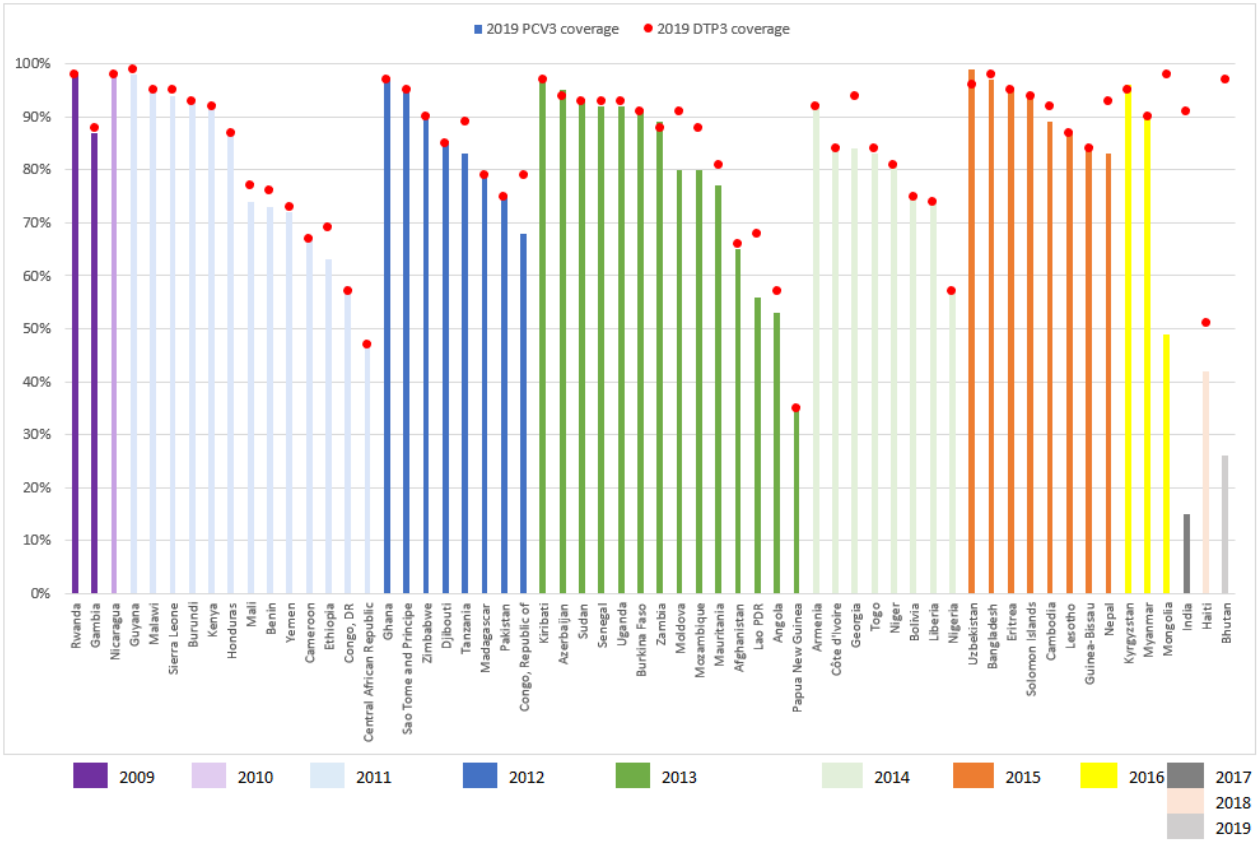


[xxiii] *Nepal has currently a 2+1 schedule (6 weeks, 10 weeks and a booster at 9 months).*

[xxiv] Kandasamy R, Gurung M, Thorson S, et al. Comparison of two schedules of two-dose priming with the ten-valent pneumococcal conjugate vaccine in Nepalese children: an open-label, randomised non-inferiority controlled trial. *Lancet Infect Dis.* 2019; 19: 156–64.

Figure 5 below shows PCV3 coverage in 2019 (WUENIC July 2020 data) according to the year of PCV introduction into routine immunisation, versus the 2019 DTP3 coverage (WUENIC July 2020 data). Countries that introduced in 2017, 2018 and 2019 may not have had sufficient time to ensure routinisation of the third dose of PCV prior to data collection.

Figure 5. PCV and DTP third-dose coverage by year of PCV introduction



4.2 AMC outcomes and impact evaluation

In 2015, as stipulated in the AMC M&E framework, the Gavi Secretariat commissioned The Boston Consulting Group to conduct an outcomes and impact evaluation. The purpose was to assess the extent to which the pilot AMC had achieved its stated objectives and the overarching goal of reducing morbidity and mortality from pneumococcal disease. The evaluation also captured lessons learned in the pilot and recommendations for future impact evaluations of the AMC.

The report was published on the Gavi website in early 2016[vi]. The Gavi Secretariat prepared a management response to the findings and recommendations, which is publicly available on the Gavi website together with the report. The Gavi EAC also submitted an independent assessment of the quality and usefulness of the report.

The second outcomes and impact evaluation will be commissioned in 2021. Building on previous M&E work, this evaluation will be retrospective, covering the entire period of the pilot AMC mechanism implementation (2009–2020), in order to document lessons learned and improve the design of potential future AMCs.

4.3 Full country evaluations

In 2013, Gavi launched a set of evaluations to better understand and quantify the barriers to and drivers of immunisation programme improvements, with particular emphasis on Gavi's contribution. Four countries are involved in the FCE project: Bangladesh, Mozambique, Uganda and Zambia. Local research institutions in all four countries partnered with the Institute for Health Metrics and Evaluation (IHME) and PATH to collect and evaluate information, data and evidence, including information about the introduction and routinisation of PCV, to help improve their immunisation programmes. The original FCE project contract ended in December 2016.

Based on multiple stakeholder consultations at the country and global levels, the Gavi EAC agreed on a two-year continuation (2017–2019) of the FCE project (Phase 2), with targeted priorities by country in Mozambique, Zambia and Uganda, including country-specific evaluation questions proposed by national stakeholders. In May 2018, the Gavi EAC assessed the progress made in Year 1 of Phase 2 of the FCE project and made the decision to change the modalities of the FCE in line with the principle of country-led implementation. The FCE project as designed was stopped in June 2018, and the Secretariat has been engaging with country evaluation partners, where relevant, to scope specific evaluation priorities.

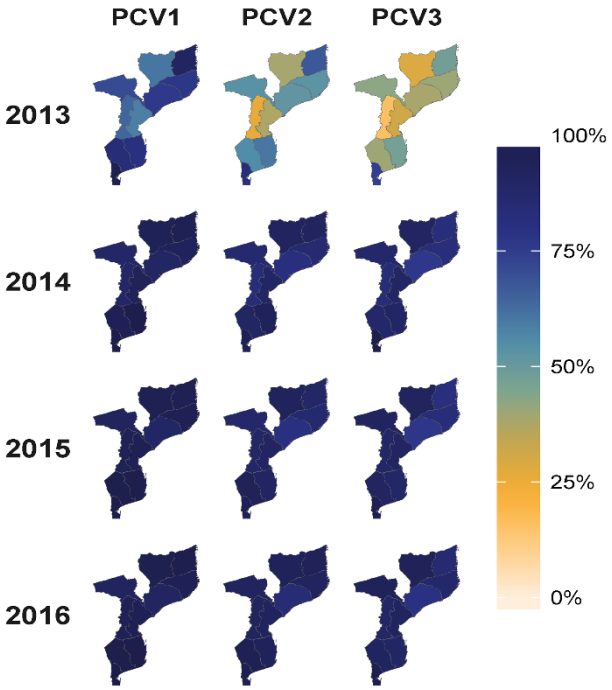
Previous Gavi FCE reports (2013, 2014 and 2015) evaluated the introduction and routinisation of PCV in Mozambique, Uganda and Zambia, as well as the joint launch of PCV and inactivated polio vaccine (IPV) in Bangladesh (Table 5). The 2016 report continued to monitor the routinisation of PCV in all four countries and presented findings of the impact of PCV on pneumococcal disease burden, based on studies in Mozambique and Bangladesh.

Table 5: Timeline of PCV introductions in Gavi FCE countries (2013–2016)

	Bangladesh	Mozambique	Uganda	Zambia
2013		PCV introduction (April 2013)	PCV introduction in one district (April 2013)	PCV introduction (July 2013)
2014		PCV routinisation	PCV national roll-out and routinisation	PCV routinisation
2015	PCV introduction (March 2015)	PCV routinisation	PCV routinisation	PCV routinisation
2016	PCV and IPV routinisation	PCV routinisation	PCV routinisation	PCV routinisation

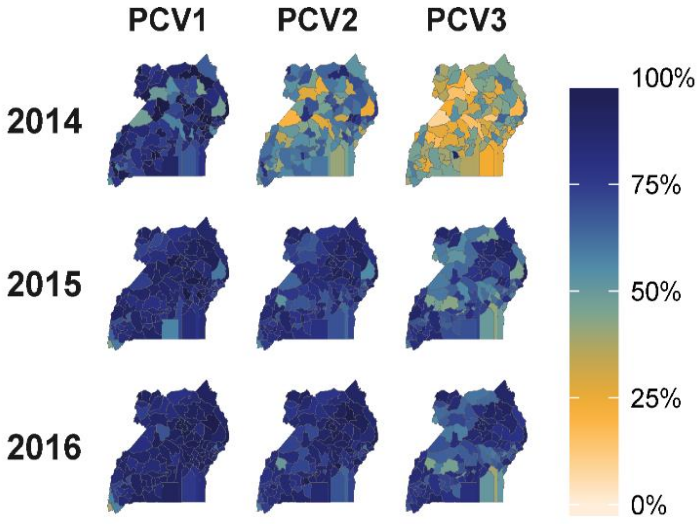
Evaluation findings indicated variable success in the FCE countries' ability to routinise PCV in 2016, as shown in the coverage maps below. A review of EPI health management information system (HMIS) data in Bangladesh, where PCV was introduced in March 2015, showed that PCV third-dose coverage amounted to 93% – just 4 percentage points below coverage with the third dose of pentavalent vaccine.

Figure 6. PCV coverage in Mozambique



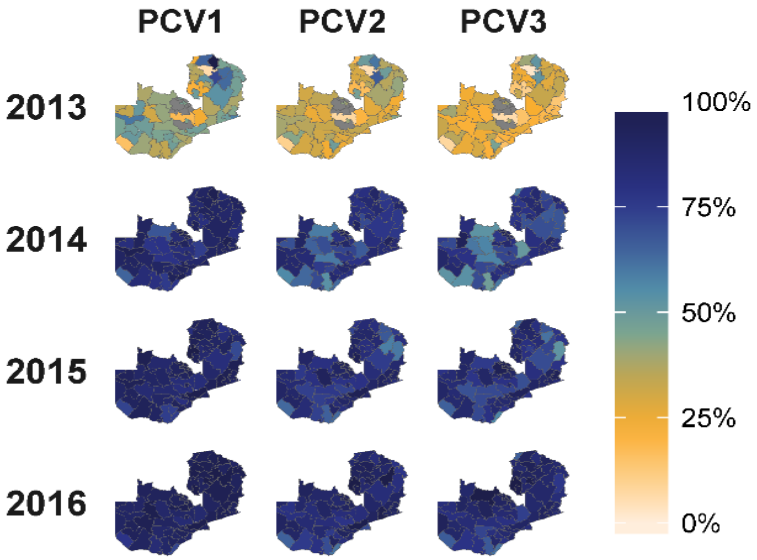
In Mozambique, PCV was introduced in April 2013 and was quickly integrated into the routine EPI system, as illustrated in the coverage maps in Figure 6.

Figure 7. PCV coverage in Uganda



Uganda, which rolled out PCV nationally in 2014, experienced challenges in the routinisation of the vaccine in the first two years – mainly driven by vaccine stock-outs. The issues were covered in detail in the 2015 FCE report. However, the PCV/pentavalent ratio improved significantly in 2015 and 2016. This improvement coincided with strategic interventions by the Uganda National Expanded Programme on Immunization (UNEPI) and partners, including a scale-up of the Reach Every District micro-planning strategy and training of health workers on data quality improvement by dedicated teams throughout the country. The 2016 evaluation findings suggested that the discrepancy in delivery between PCV and pentavalent vaccines may be due to reporting issues at the facility level. Because pentavalent vaccine is a performance indicator for facilities in Uganda, it may have been better recorded than PCV. This potential root cause highlighted data quality issues in administrative and HMIS data, and suggested that a population-based coverage survey or data quality audit would be necessary to confirm the discrepancy. Based on subnational data collection, no stock-outs of PCV were observed in facilities visited in 2016.

Figure 8. PCV coverage in Zambia



In Zambia, where PCV was introduced in 2013, two factors may have accounted for the reported undercoverage of PCV: (1) supply-side challenges causing stock-outs; and (2) data quality issues.

As part of the FCE project, pneumococcal vaccine impact was assessed in two countries: Mozambique and Bangladesh. The assessment included: pre- and post-introduction nasopharyngeal carriage surveys; case-control studies; and time series analyses of surveillance data on IPD and X-ray confirmed pneumonia.

In Mozambique, evidence gathered from vaccine effectiveness studies suggests that the introduction of PCV in 2013 has reduced nasopharyngeal carriage of vaccine-type pneumococcus, as well as the incidence of vaccine-type IPD and pneumonia[xxv].

[xxv] Sigauque B, Moiane B, Massora S, et al. Early Declines in Vaccine Type Pneumococcal Carriage in Children Less Than 5 Years Old After Introduction of 10-valent Pneumococcal Conjugate Vaccine in Mozambique. *Pediatr Infect Dis J*. 2018; 37: 1054-1060.

More specifically, the nasopharyngeal carriage study aimed to estimate the effects of PCV10 introduction on pneumococcal nasopharyngeal carriage among HIV-infected and HIV-uninfected children. The study involved carriage surveys pre- (October 2012–March 2013) and post- (first round October 2014–April 2015; second round October 2015–May 2016) PCV introduction. Based on this study, a direct effect of the vaccine on PCV10 serotype-specific (VT) pneumococcal carriage was observed at the first round (within 18 months) and second round (within 30 months) after PCV introduction.

- A 44% (95% CI 33, 59) reduction in vaccine serotype (VTS) pneumococcal carriage was observed in HIV-uninfected children receiving three doses, and a 70% reduction (95% CI: 57-78) was observed at the second round.
- A 60% (95% CI 25, 95) reduction in VTS pneumococcal carriage was observed in HIV-infected children receiving three doses at the first round, and no additional decline was observed at the second round.
- There was also an early signal of an indirect effect among HIV-infected children, with a 31% reduction (95% CI: 11, 46) among HIV-infected children receiving no PCV doses.
- As expected, there was also an increase in pneumococcal carriage of non-PCV10 VTS, including serotypes in PCV13 (i.e. 19A).

Findings from the pneumococcal impact study in Bangladesh suggest some reductions in both the overall transmission of pneumococci and serotypes included in the vaccine (VTS) as measured through population-based nasopharyngeal carriage surveys pre- and post-vaccine introduction. During the pre-vaccine period (before March 2015), a total of 1,901 specimens were collected and processed among different age groups. In the post-vaccine period, a total of 2,060 specimens were collected. There were observed reductions of approximately 25% in vaccine-type pneumococcal carriage among children who were age-eligible for PCV but no change among age-ineligible children. There were increases in non-vaccine serotypes of 17%–20% among age-eligible children.

The reduction in carriage in Mozambique has been accompanied by a reduction in vaccine-type IPD. Based on a Bayesian regression discontinuity design of surveillance data from the Manhiça Demographic Surveillance System (DSS), it was estimated that there was a significant (94%) reduction in vaccine-type IPD (95% UI: 65.8, 99; Figure 9), although the number of IPD cases each month is small. There was also a significant reduction in X-ray confirmed pneumonia (85%, 95% UI: 64.3, 93.7; Figure 10). There was a nonsignificant change in non-vaccine-type IPD (16.3%, 95% UI: -55.4, 203.4; Figure 11).

Figure 9: Reduction in vaccine-type IPD over time in Manhiça DSS

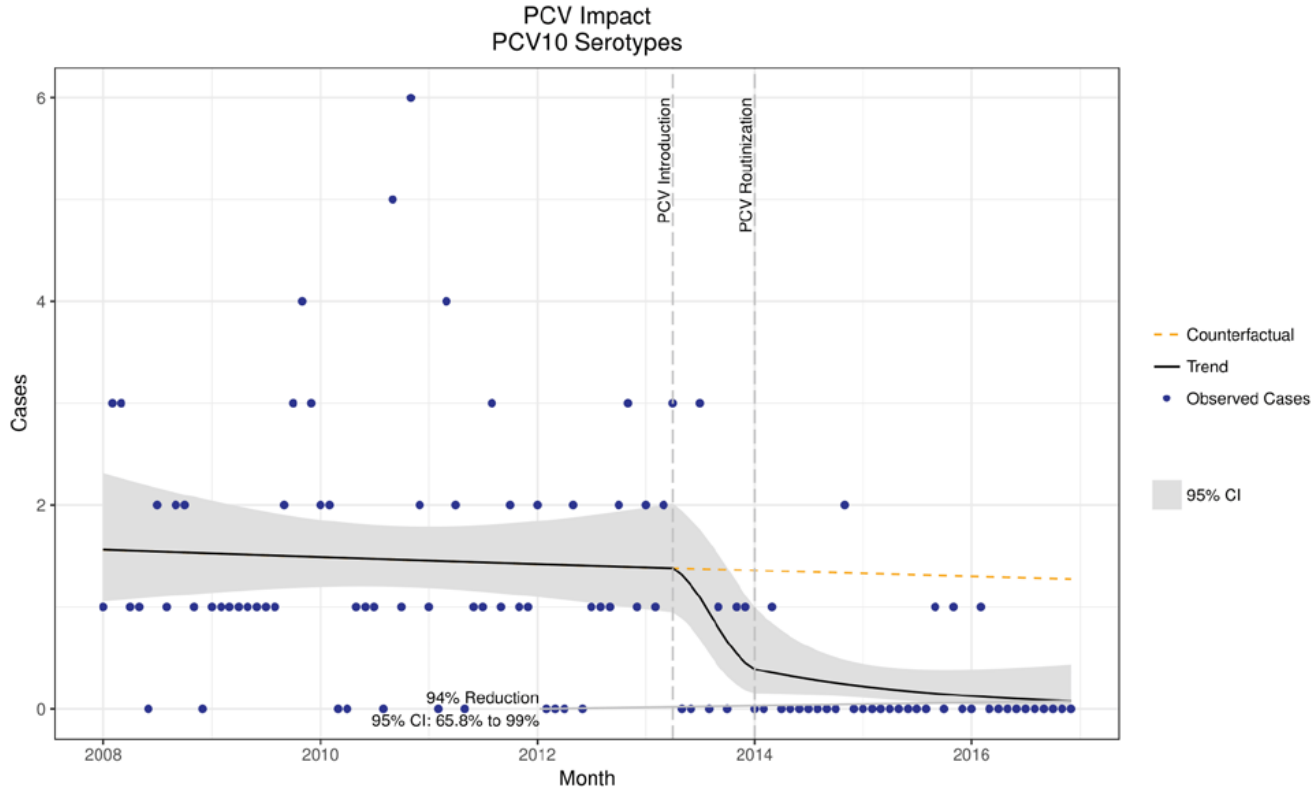


Figure 10: Reduction in X-ray confirmed pneumonia over time in Manhiça DSS

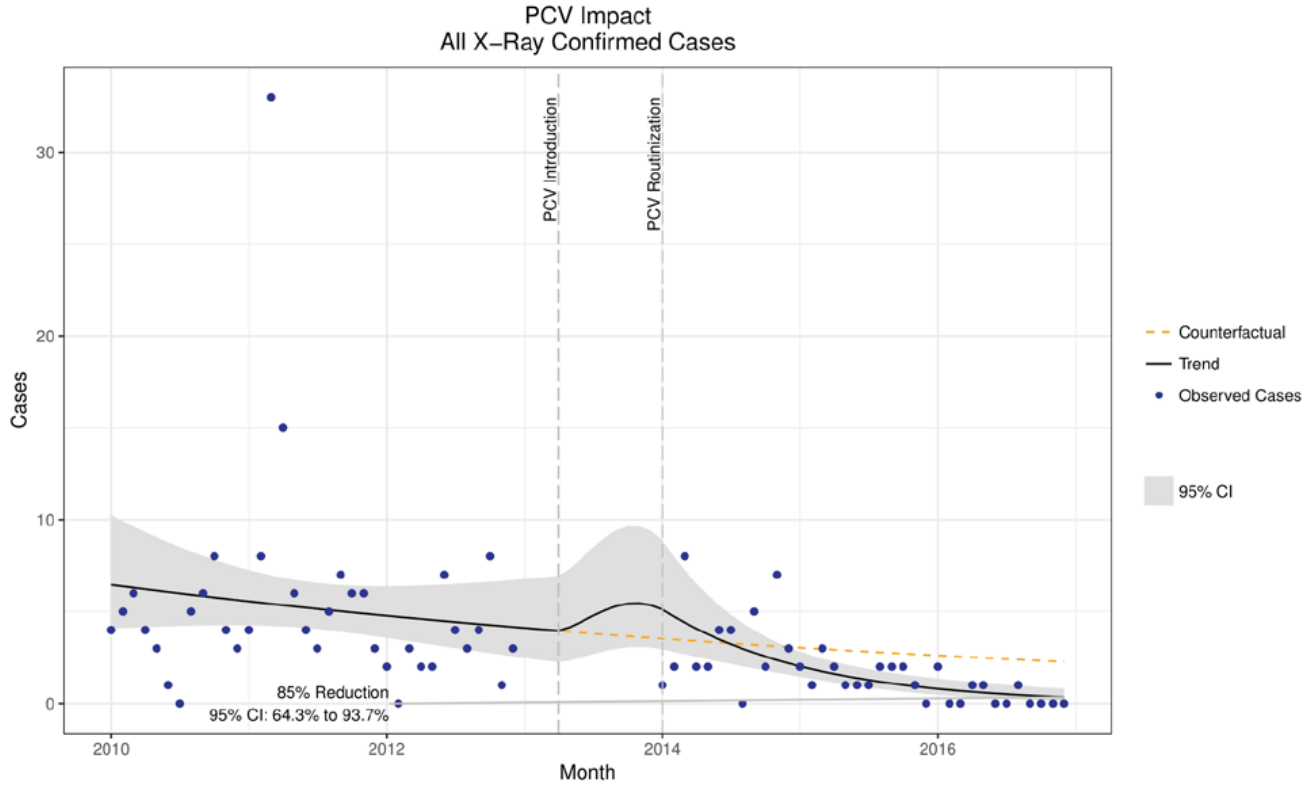
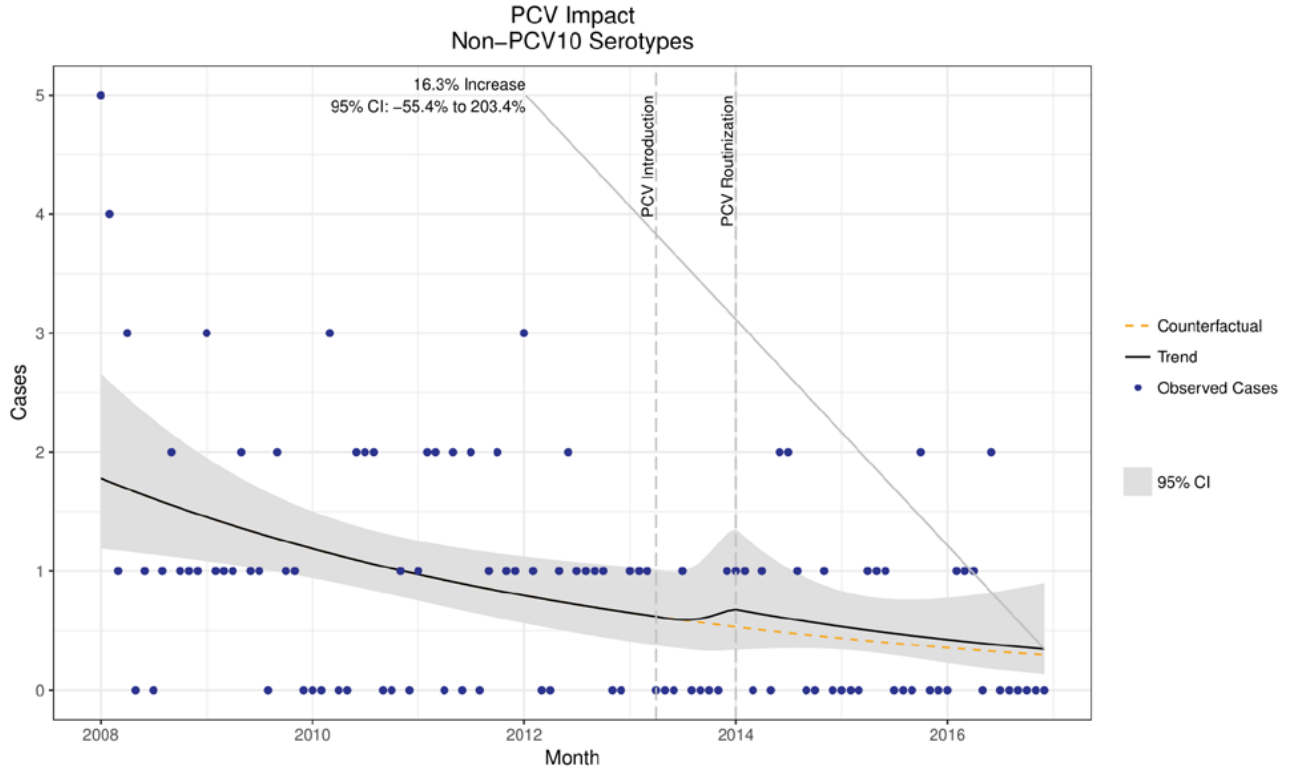


Figure 11: Change in non-vaccine-type IPD over time in Manhiça DSS



The high effectiveness noted in the vaccine effectiveness studies on vaccine-type pneumococcal disease is consistent with the high coverage of the vaccine achieved in Manhiça district (small-area estimates of vaccine indicate that coverage of three-dose PCV in Manhiça district was 89.3%, 95% UI: 85.1, 93.4 in 2016). The high coverage was the result of the rapid routinisation of PCV nationwide, which has been maintained to the present date (for further details, refer to Finding 1 in the 2016 FCE cross-country report). This provides evidence that the high coverage of PCV nationally in Mozambique (88.0%, 95% UI: 86.0, 90.1 in 2016) has led to considerable reductions in vaccine-type pneumococcal disease. Given the similar results seen in reducing pneumococcal disease in other studies in Africa and elsewhere, scale-up of PCV has also likely led to reductions in pneumococcal disease in the other three FCE countries. These findings also highlight the missed opportunities for health impact due to suboptimal coverage of these vaccines, particularly at the subnational level (Figures 6–8).

The 2016 report includes a number of key recommendations for the Alliance and for the four FCE countries. As in previous years, the four countries and Alliance partners will continue to implement the key evaluation recommendations in order to address PCV-related implementation bottlenecks and improve programme performance.

The final report is available on the Gavi website, along with an Alliance management response (document jointly developed by Gavi Secretariat and Alliance partners to provide contextual information on ongoing efforts and future actions identified to address the key findings and recommendations), in line with previous Pneumococcal AMC Annual Reports[vii].

4.4 Estimates of the impact of pneumococcal vaccination

In 2011, a multidisciplinary group with expertise in mathematical modelling was established by Gavi and the Bill & Melinda Gates Foundation to estimate the impact of vaccination in 73 Gavi-supported countries. In January 2017, this was formalised into a modelling consortium, the Vaccine Impact Modelling Consortium, which is managed by a secretariat based at Imperial College London. The consortium aims to foster a community that will continue to increase the quality and robustness of vaccine impact estimates. The consortium continues to base their approach on the methodologies adopted previously by Gavi and the Bill & Melinda Gates Foundation.

Based on the most recent WUENIC, PCV is estimated to have averted over 570,000 future deaths in Gavi-supported countries by the end of 2019. Prior to the COVID-19 pandemic, projections based on the operational forecast version 17 (completed in late 2019) estimated the number to reach over 700,000 by the end of 2020. Currently, the impact of the pandemic on immunisation services and PCV vaccinations is uncertain. The July 2021 WUENIC update will provide a clearer view of the possible disruptions and the effects on coverage and estimated impact.

4.5 Other special studies on PCV impact

In addition to support for surveillance, Gavi funds a number of special studies to help facilitate evidence-based decision-making for vaccine introduction and impact monitoring to support sustained implementation of pneumococcal vaccines in lower-income countries. Studies assess the impact of PCV on health and economic outcomes, and monitor potential changes in pneumococcal serotype epidemiology. For the status of the historical and ongoing studies and key findings, refer to Annex 5.

The earliest assessments in Gavi countries were supported under the Pneumococcal vaccines Accelerated Development and Introduction Plan (PneumoADIP) and Vaccine Implementation Technical Assistance Consortium (VI-TAC) grant. These included pneumococcal vaccine effectiveness and impact studies in Kenya and South Africa, and economic impact evaluations of pneumococcal vaccines in Ghana and the Gambia, concluded in 2015. The PCV impact study in Kenya will continue through 2021 to monitor potential changes in the epidemiology of pneumococcal disease, including serotype epidemiology.

These Gavi-funded special studies yielded important findings that continue to develop the PCV evidence landscape and to inform policies. Health economic analyses from the Gambia have demonstrated that PCV is likely to be both cost-effective and cost-saving, and to reduce the substantial economic burden borne by families of children with disease. Evidence is also being collected on some novel PCV dosing schedules (for example in Nepal, mentioned in Section 4.1) to determine the most effective schedules to reduce pneumococcal disease burden. In addition to a comprehensive dosing landscape analysis (published in 2014[xxvi]) and peer-reviewed publications on vaccine impact in the Gambia, in 2014 the Kenya and South Africa effectiveness studies produced several key publications highlighting their results. This included herd protection with reductions in transmission of the disease by reducing nasopharyngeal colonisation of vaccine-serotype strains in both vaccinated and unvaccinated individuals, as well as reductions in antibiotic-resistant strains of the disease in very young children. Overall, findings illustrate PCV effectiveness against vaccine-specific serotypes, as well as protection against IPD among children for vaccine and non-vaccine serotypes. Results from South Africa have shown that routine use of PCV is effective against presumed bacterial pneumonia at a

[xxvi] http://journals.lww.com/pidj/toc/2014/01002

magnitude similar to that measured in randomised controlled trials. Results from the Gambia indicated that cases of childhood IPD are reduced by more than half with the introduction of PCV.

In June 2013, Gavi issued an RFP for the "Evaluation of PCV Effectiveness in Asia" to assess the impact of PCV among Gavi-supported countries in Asia that had introduced the vaccine at an early stage. On the recommendation of an adjudication committee, Gavi commissioned three service providers (Aga Khan University, Murdoch Children's Research Institute and University of Oxford) to conduct PCV impact studies in Pakistan, Nepal and the Lao People's Democratic Republic. These studies are assessing a range of outcomes, including disease effects (e.g. IPD, hospitalised pneumonia, serotype-specific disease impact), effects on agent transmission (nasopharyngeal carriage), antibiotic resistance, economic benefits and long-term sequelae. Data collection for these studies began in late 2013 and early 2014. The study in the Lao People's Democratic Republic concluded in 2018, and findings suggest that PCV13 is effective at preventing the severe pneumonia cases that may not be treated effectively in low- and middle-income countries (LMIC), where supplemental oxygen is often unavailable outside urban hospitals (for more detailed results, refer to Annex 5). During 2020, data collection and analysis for ongoing studies was impacted by the COVID-19 pandemic. Some of these studies have been extended through 2021 to ensure study objectives can be met. The Nepal study site has been extended through to the end of 2021 to allow for additional long-term monitoring of serotype epidemiology and impact, and due to the impact of COVID-19. A fourth study, to assess the impact of phased PCV introduction on the incidence of radiological pneumonia in Mongolia, began data collection in 2015. This study has also been extended until the end of 2021 .

Gavi contracted CDC to assist Burkina Faso in assessing the impact of PCV introduction on pneumococcal meningitis and potential changes in circulating strains. The study was extended until mid-2021 to continue monitoring of serotype 1.

As mentioned previously, pneumococcal vaccine effectiveness and impact studies were conducted in Bangladesh and Mozambique as part of the FCE work, which ended in 2016. This included population-based assessment of changes in agent transmission and impact of PCV on IPD and X-ray confirmed pneumonia in Mozambique.

5. Media and communications

Increasing the visibility of the Pneumococcal AMC through traditional and new media, including social media, has remained an important goal for Gavi's Communications team.

5.1 Communications overview 2020

On World Pneumonia Day 2020, Gavi highlighted the AMC and its impact through its social media channels, as well as through AMC-related content.

The AMC was also highlighted in both the printed and online versions of Gavi's 2019 Annual Progress Report (published in 2020). Further, the achievements of the Pneumococcal AMC were celebrated as a foundation for designing the next generation of effective financial tools for development: for example, the Gavi COVAX AMC Investment Opportunity was unveiled at Gavi's third replenishment, on the occasion of the Global Vaccine Summit, in the presence of 42 heads of state, including all 7 of the G7. The AMC has been featured prominently as an innovative financial mechanism that has quietly underpinned much of the Alliance's work.

Gavi continued to highlight and explain the AMC in relevant communications materials throughout 2020. In addition to sharing updated material, Gavi ensured that appropriate speaking points were incorporated into the speeches of Alliance spokespeople at relevant events.

5.2 Communications outlook for 2021

2021 will see Gavi's Communications team plan and implement its communications strategy to fund the Gavi COVAX AMC. Gavi's previous experience with innovative financing mechanisms, such as the Pneumococcal AMC, are a messaging point. The Pneumococcal AMC's success and impact will continue to be built into press releases, speeches, op-eds, features and reports to ensure visibility. In the second half of 2021, when an appendix to this report will be issued to reflect the 2020 WUENIC data scheduled to be published in July 2021, Gavi will promote the report and its annex through its website and social media channels.

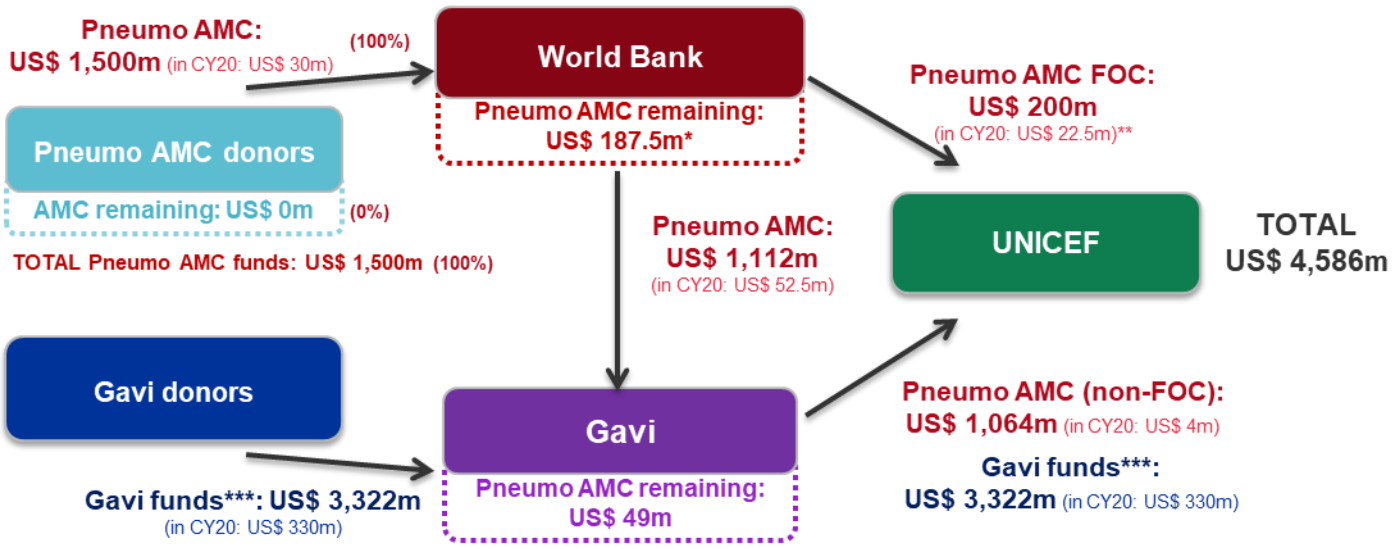
6. Financial activities

The financial structure of the AMC remains unchanged from previous years. It is composed of the six AMC donors (Bill & Melinda Gates Foundation, Canada, Italy, Norway, Russian Federation and United Kingdom), the World Bank, Gavi, UNICEF, Gavi-supported countries and eligible vaccine manufacturers. For a detailed description of the AMC financial structure (including the FOC), refer to the AMC Annual Report covering the period from 12 June 2009–31 March 2010 (pages 28–29).

In summary, the process works as follows: the AMC donors, which have entered into grant agreements with the World Bank totalling US$ 1.5 billion, make annual payments to the World Bank. In turn, the World Bank holds the funds in trust for Gavi on behalf of the donors and confirms quarterly to Gavi the amounts being held for the AMC. To access these funds, Gavi submits a Quarterly Funding Request to the World Bank for vaccine purchase payments in the upcoming quarter. The request is based on the most recent demand forecast and on the quarterly Cash Management Plan submitted by UNICEF to Gavi.

Prior to procuring vaccines from AMC-eligible vaccine manufacturers, UNICEF sends a cash disbursement request for the necessary AMC and Gavi funds, upon receipt of which Gavi transfers the requested funds into a Gavi-held procurement bank account. These funds can only be withdrawn from the account by UNICEF. Gavi-supported countries are obliged to co-finance the pneumococcal vaccine, in accordance with Gavi's standard co-financing policy. Countries make their co-finance payments directly to UNICEF.

Figure 12. Summary of AMC financial process flow and funds disbursed (inception to 31 December 2020)



Note: CY20 is Calendar Year 2020.

** Of the US$ 187.5 million Pneumococcal AMC funds remaining unutilised at the World Bank at the close of the Pneumococcal AMC on 31 December 2020, US$ 177.5 million will be redirected for use in the Gavi COVAX AMC in January 2021, and US$ 10 million will be redirected for use in Gavi core programmes, as agreed with the Pneumococcal AMC donors.*

*** US$ 22.5 million was paid directly to Gavi, which subsequently transferred these funds into Gavi's "UNICEF procurement account".*

**** Allocated from general funds to pay for tail price portion of vaccine and related fulfilment costs.*

Source: Gavi Secretariat. Note: some numbers may appear not to add up due to rounding.

For details, refer to sections 6.1–6.3 below.

6.1 AMC donor funds: inflow to the World Bank

The six donors are categorised into two groups. The first group, known as "fixed-schedule donors" (the Bill & Melinda Gates Foundation, Italy and the Russian Federation) make annual payments to the World Bank in accordance with predetermined payment schedules set out in the individual grant agreements. The second group of donors, known as "on-demand donors" (Canada, Norway and the United Kingdom), make payments in response to requests from the World Bank based on forecasts received from Gavi to meet specific funding needs. The three fixed-schedule donors have pledged a total of US$ 765 million to the AMC. The three on-demand donors have pledged US$ 735 million (see Table 6). These pledges combined bring the total available AMC funds to US$ 1,500 million – funds that are dedicated solely to the procurement of pneumococcal vaccine.

Donor contribution receipts

As of 31 December 2020, the World Bank had received a total of US$ 1,500 million from AMC donors (as shown in Table 6 below). Accordingly, all donors paid the total amounts that they had committed to pay under their respective grant agreements.

Table 6. Grant receipts from AMC donors, as of 31 December 2020 (in US$ millions)

	Contribution Amount	Paid-in Amount	Remaining Balance
Fixed Schedule Donors			
Italy	635	635	-
Russia	80	80	-
Bill & Melinda Gates Foundation	50	50	-
sub-total:	**765**	**765**	-
On Demand Donors			
UK	485	485	-
Canada	200	200	-
Norway	50	50	-
sub-total:	**735**	**735**	-
Total	**1,500**	**1,500**	-

Source: The World Bank

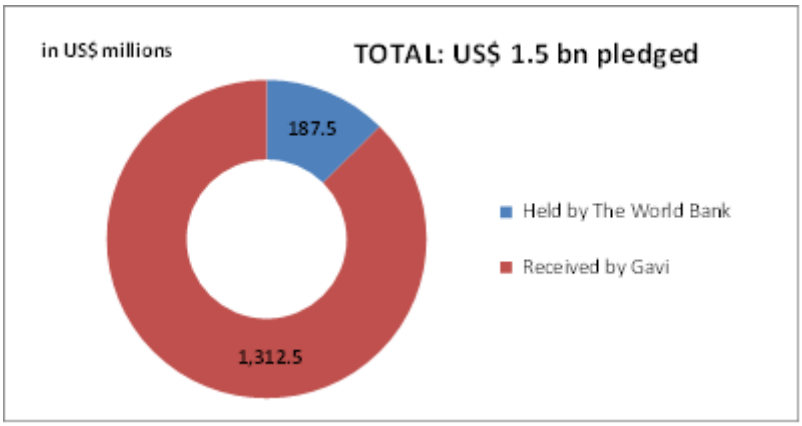
The World Bank has recorded the AMC donor funds in its financial statements as designated assets, with a corresponding liability to provide the funds to Gavi for the purchase of pneumococcal vaccines subject to the terms and conditions of the AMC. To enhance the predictability of AMC funding, the World Bank committed to transfer funds to meet the AMC-funded portion of the vaccine price, upon request from Gavi in accordance with the AMC terms and conditions and with the schedule of donor payments, whether or not donors actually pay on schedule or default. The World Bank also provides financial management and administrative services with respect to donor contributions and AMC disbursements[xxvii].

[xxvii] *As agreed between stakeholders, from 2016 onwards any shortfall in investment income to cover these administrative fees, beyond the amount provided by the UK per its AMC grant agreement, will be covered by Gavi.*

6.2 AMC donor funds: outflow from the World Bank

As of 31 December 2020, of the total US$ 1,500 million pledged under the AMC, the World Bank had disbursed US$ 1,312.5 million (US$ 1,112.5 million to Gavi and US$ 200 million to Gavi's "UNICEF procurement account" relating to the FOCs). Of the US$ 1,312.5 million disbursed, US$ 75 million was disbursed to Gavi during 2020[xxviii]. This leaves a balance of US$ 187.5 million held by the World Bank (see Figures 12 and 13).

Figure 13. Status of AMC donor funds, as of 31 December 2020 (in US$ millions)[xxix]



Source: Gavi Secretariat

6.3 Disbursement of AMC donor funds to UNICEF

During 2020, US$ 356 million was disbursed to UNICEF for the purchase of pneumococcal vaccines. Of this amount, US$ 26 million pertains to the AMC-funded portion of the vaccine purchase. The remaining US$ 330 million was allocated from general Gavi funds to pay for the tail price portion of the vaccine purchase and related fulfilment costs[xxx]. Total funds include the transfers relating to the AMC-funded portion of the minimum purchase obligation (i.e. FOC) on the eighth supply agreement amounting to US$ 22.5 million (see Figures 12 and 14).

To date, eight supply agreements have been signed under the Pneumococcal AMC. As of 31 December 2020, AMC funding allocated under all of these agreements was fully disbursed, except for US$ 49 million remaining under the eighth supply agreement. These funds are expected to be disbursed during the 2021–2022 period.

[xxviii] *This amount includes US$ 22.5 million for the full portion (years 1–3) of the AMC FOC requirement under the new supply agreement signed in the second quarter of 2020. Given the required sequencing of FOC payments prior to supply agreement signature, Gavi requested the International Bank for Reconstruction and Development (IBRD) to transfer these AMC funds via the regular Quarterly Funding Request process and subsequently transferred the funds directly into the FOC account.*

[xxix] *Of the US$ 187.5 million unutilised at the close of the Pneumococcal AMC on 31 December 2020, US$ 177.5 million was transferred to Gavi on 13 January 2021 for use in the Gavi COVAX AMC, as agreed with Pneumococcal AMC donors. The remaining US$ 10 million will be redirected for use in Gavi core programmes.*

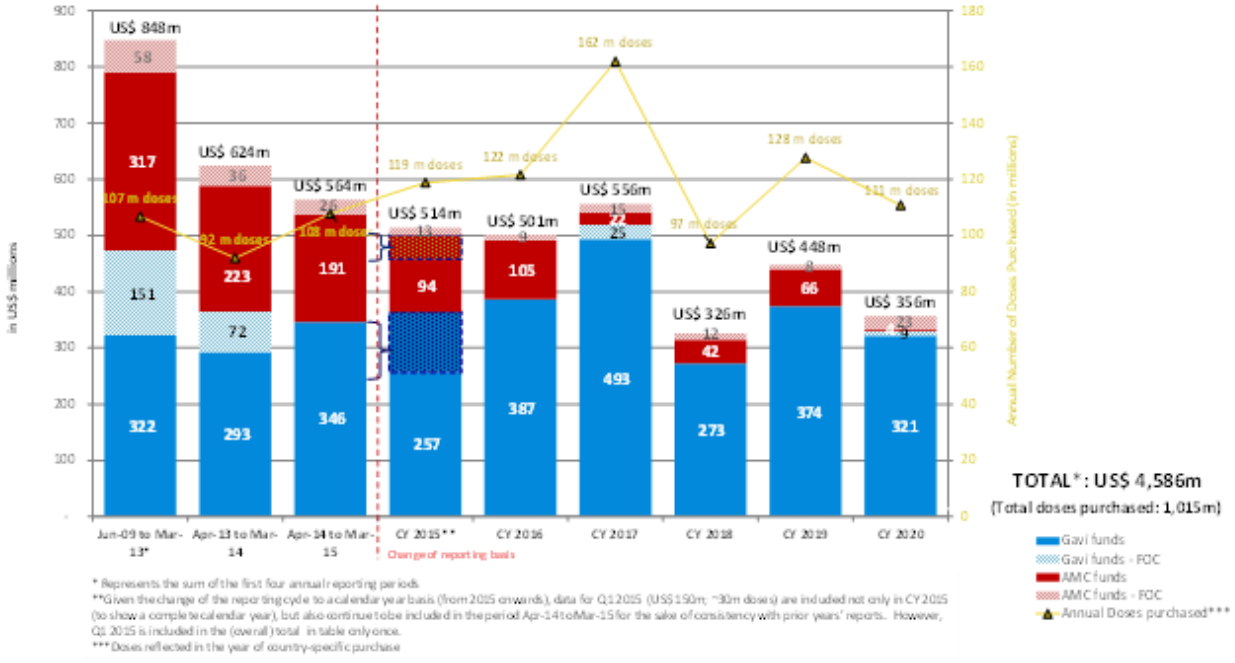
[xxx] *Fulfilment costs are the extra costs incurred in supplying vaccines (estimated at US$ 0.08 per dose during the 2016–2020 period), in addition to the cost of the vaccine itself. These costs typically include the cost of syringes, safety boxes and freight.*

As of 31 December 2020, a total of US$ 457 million had been transferred to Gavi's "UNICEF procurement account" regarding the FOCs for the eight signed supply agreements. Of this amount, US$ 256 million represents the Gavi-funded portion of the FOCs, and US$ 200 million represents the AMC-funded portion of the FOCs. Of the US$ 457 million transferred, all has been utilised except US$ 21.5 million remaining for the eighth supply agreement (comprised of US$ 12.5 million for AMC-funded portion and US$ 9 million for the Gavi-funded portion).

Figure 14. Total cash disbursements to Gavi's "UNICEF procurement account" (inception to 31 December 2020, in US$ millions)

In US$ millions

Funding Source	Jan-09 to Mar-13	Apr-13 to Mar-14	Apr-14 to Mar-15	CY 2015** Q1	CY 2015** Q2-Q4	CY 2015** Total	CY 2016	CY 2017	CY 2018	CY 2019	CY 2020	TOTAL	of which: AMC/Gavi	of which: FOC	of which: Non-FOC
AMC Funds - FOC	58	36	26		13	13	9	15	12	8	23	200	1,264	200	
AMC Funds	317	223	191	43	94	137	105	22	42	66	4	1,063			1,063
Gavi Funds - FOC	151	72	-	-	-	-	-	25	-	-	9	256	3,322	256	
Gavi Funds	322	293	346	107	257	364	387	493	273	374	321	3,065			3,065
TOTAL:	848	624	564	150	364	514	501	556	326	448	356	4,586		457	4,129



Source: Gavi Secretariat. Notes: (1) for each successive reporting period, the total number of doses purchased has increased relative to the amount of funds disbursed, due to an increasingly higher proportion of doses being procured under the Gavi-funded tail price only; (2) the spike in purchases at the end of 2017 is primarily attributed to an increase in volume in the fourth quarter of 2017 as part of an agreement with one manufacturer to secure a reduced tail price; and (3) some numbers may appear not to add up due to rounding.

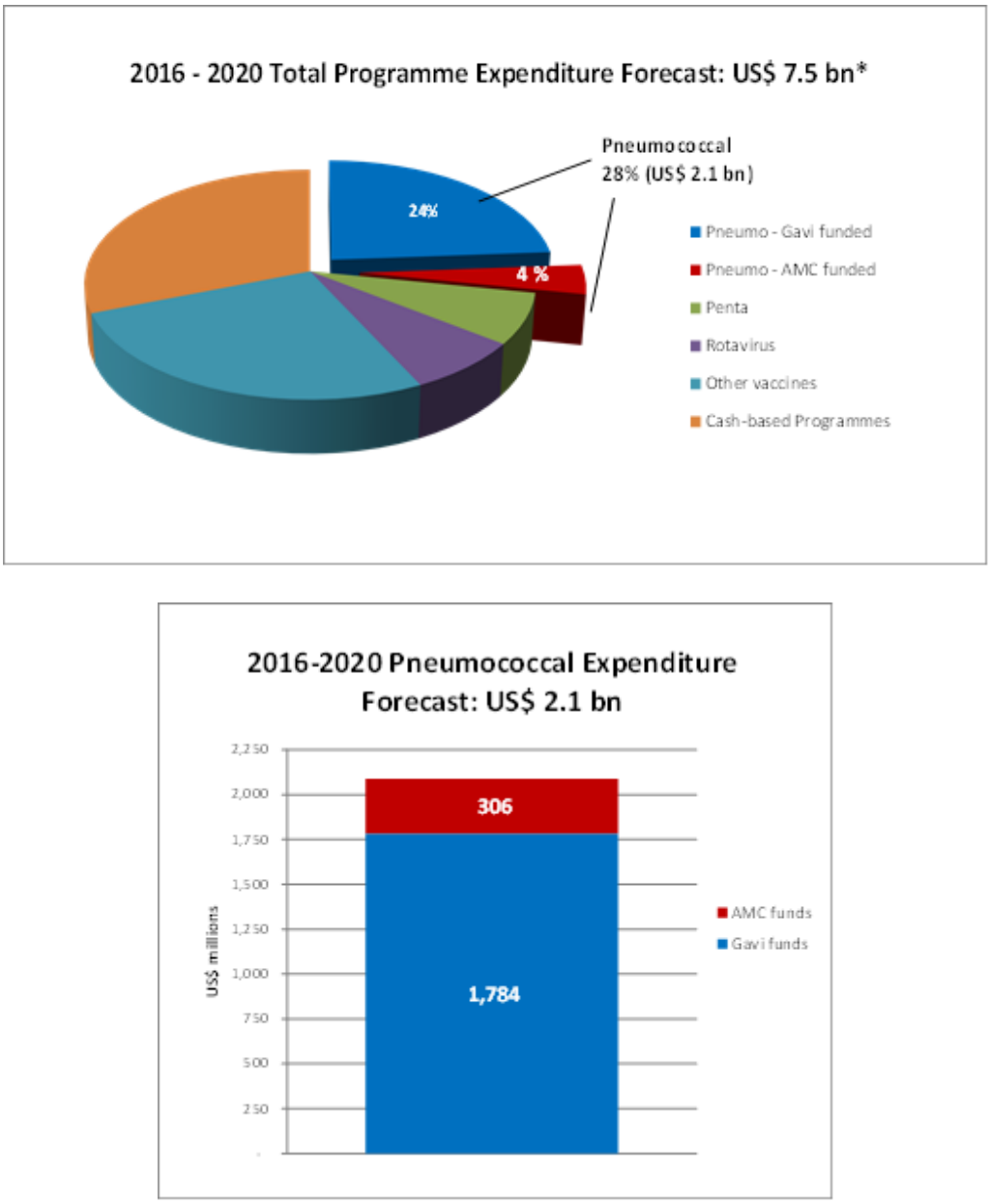
6.4 The AMC and Gavi's long-term financial forecast

At the December 2020 Gavi Board meeting, a report was presented on Gavi's long-term financial forecast[xxxi]. Total programme expenditures were projected to be US$ 7.5 billion[xxxii] for the 2016–2020 period, of which pneumococcal vaccine expenditures were anticipated to amount to US$ 2.1 billion, representing approximately 28% of total programmatic expenditures (see Figure 15 below).

[xxxi] *December 2020 Board report titled "Financial update, including forecast."*

[xxxii] *Does not include expenditures related to partners' engagement framework (PEF), the Gavi Secretariat or the Coalition for Epidemic Preparedness Innovations (CEPI).*

Figure 15. AMC within total Gavi forecasted expenditure, 2016–2020



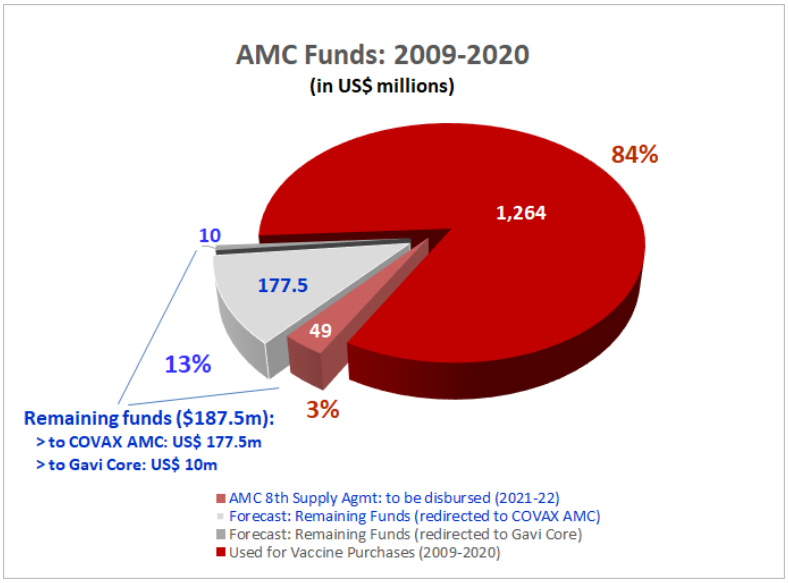
Source: Gavi Secretariat

The financial forecast also highlighted that a total of US$ 187.5 million of Pneumococcal AMC funds would remain unutilised at the close of the Pneumococcal AMC on 31 December 2020, of which $177.5 will be redirected for use in the Gavi COVAX AMC[xxxiii], and US$ 10 million will be redirected for use in Gavi core programmes, as agreed with the Pneumococcal AMC donors. Regarding the US$ 75 million of AMC funds allocated under the eighth supply agreement signed in 2020, AMC stakeholders agreed that the World Bank would disburse the full amount to Gavi before the end of 2020, given that the Pneumococcal AMC would

[xxxiii] *At the time this report was published in 2021, US$ 177.5 million had been transferred to Gavi on 13 January 2021 for use in the Gavi COVAX AMC.*

officially conclude at the end of the year. Subsequently, Gavi would disburse these funds to UNICEF, based upon demand needs during the 2020–2022 period[xxxiv].

Figure 16. Latest forecast of AMC funds needed, as presented at the December 2020 Gavi Board meeting (in US$ millions)



Source: December 2020 Board report titled "Financial update, including forecast"

7. Challenges and future priorities

The implementation of the pilot Pneumococcal AMC has been very successful, with high demand and uptake at the country level. As the mechanism closed, challenges remain nonetheless: ensuring low, long-term and sustainable vaccine pricing for countries and manufacturers, as well as a proper balance between supply and demand, is key as countries transition out of Gavi support and start to fully self-finance their own PCV programmes.

Moving forward, to continue building on the progress achieved by the Pneumococcal AMC, priorities for Gavi include: strengthening country decision-making processes and the capacity to make evidence-based policy decisions that take into account value for money considerations; supporting remaining countries to introduce PCV with Gavi support in the context of relative trade-offs and alternative investments; and continuing to nurture the learning agenda by measuring impact of new PCV and different schedules.

7.1 Supporting country introductions and product switches

The Vaccine Alliance has focused its efforts on ensuring that technical assistance is provided where appropriate to ensure high-quality decision-making and implementation of product switches. Alliance partners will continue to closely monitor country introduction status and coordinate technical assistance activities, with

[xxxiv] *Of the US$ 75 million disbursed from the World Bank to Gavi during 2020, US$ 22.5 million FOC funds were subsequently transferred by Gavi into the FOC account, while US$ 3.6 million non-FOC funds were transferred directly to UNICEF, leaving a balance of US$ 49 million AMC funds at Gavi as of 31 December 2020.*

the aim of identifying and resolving issues with the support of partners at the country level. Lessons drawn from these contexts can inform future pneumococcal vaccine introductions, as well as the roll-out of other vaccines.

For countries that have already introduced and are aiming to switch to a different product, Gavi and its partners will continue to monitor and support the operational and strategic aspects of the switches. In doing so, they will pay particular attention to the programmatic challenges, and encourage an informed and evidence-based switch request from countries.

7.2 Strengthening health systems and routine immunisation to ensure high coverage

Maintaining, restoring and strengthening PCV immunisation to address vaccination gaps in countries that experienced disruption of immunisation services due to the COVID-19 pandemic continues to be a key priority, particularly with regard to the countries that remain Gavi-eligible.

In addition, PCV implementation will continue to be closely monitored to identify issues in coverage performance in specific countries and/or settings.

7.3 Ensuring sustainability for transitioning and transitioned countries

Through the result of its final Pneumococcal AMC tender in 2020, the AMC procurement mechanism has achieved a tail price reduction of 43% compared with the initial tail price cap of US$ 3.50 per dose. This is a very favourable outcome with a new low-priced vaccine at US$ 2.00 per dose. One Gavi country switched to this lower-priced product in 2020 (Uzbekistan), and another selected it for introduction in 2022 (Timor-Leste). Broader uptake of this vaccine product is expected to happen from 2021 onwards. A first non-AMC PCV tender will be launched to cover the demand of Gavi countries beyond contracted volumes due to the expiring long-term supply agreements and for additional volumes needed for SII due to an expected increase in switch dynamics. The resulting vaccine price may still be challenging for sustainable pneumococcal vaccination, especially as countries continue to transition out of Gavi support. As outlined in the PCV Supply and Procurement Roadmap, a key priority objective is to further reduce the weighted average price.

Demonstrating the impact of PCV is also key to ensuring sustainability of pneumococcal vaccine programmes after transition. The Alliance's focus on gathering evidence on vaccine effectiveness and impact will continue through Gavi-supported special studies. An AMC outcomes and impact evaluation to assess the achievements of the AMC pilot will be commissioned in 2021.

7.4 Managing supply and demand

Thanks to the AMC, manufacturers have entered into ten-year supply agreements, which is unique for a Gavi-supported vaccine. This provided assurance that manufacturers would invest in scaling up production capacity and that supply would be available to meet long-term demand from countries. Not only did this long-term demand visibility attract incumbent suppliers to significantly scale up their production facilities, but also it incentivised pipeline manufacturers to continue prioritising their PCV trials. Hence, with the current supplier base encompassing three prequalified manufacturers, the supply capacity largely exceeds the forecasted demand. The Alliance's Market Shaping teams will carefully monitor switch dynamics that may lead to a reshuffling of market shares in the coming years.

Conclusion

Country demand for PCV has been unprecedented, with more than 86% of the 73 Pneumococcal AMC-eligible countries approved for support and 60 country introductions completed as of 31 December 2020. Third-dose PCV coverage increased by 4 percentage points from 2018 to 2019, reaching 49% in 2019. Vaccine impact estimates also suggest 570,000 future deaths had been averted through PCV use in Gavi supported countries by the end of 2019.

Despite this unparalleled success, as countries enter the pathway to transition out of Gavi support, programme sustainability and higher levels of healthy market dynamics are areas of increased focus for the Alliance. Gavi will continue to support this transition pathway in order to ensure that the PCV programme, as well as other vaccine programmes, are programmatically and financially sustained in future years.

Annex 1 – Membership of the AMC Secretariat in 2020

Team	Staff member
Vaccine Implementation	**Veronica Denti** Senior Programme Manager
Resource Mobilisation	**Sebastian Meaney** Head, UK Strategy
Finance	**Eric Godfrey** Senior Manager, Financial Forecasting & AMC
Monitoring & Evaluation	**Hope Johnson** Director, Monitoring & Evaluation
Communications	**Olly Cann** Director, Communications
Market Shaping	**Edward Baker** Senior Specialist, Strategy Development & Tenders **Markus Beck** Senior Manager, Strategy Development & Tenders
Legal	**Hélène Gaudin de Villaine** Associate Legal Counsel

Source: Gavi Secretariat, as of 31 December 2020

Annex 2 – Summary of previous calls for offers

7.5 First AMC supply agreements

The first procurement cycle for the supply of PCV under the AMC was initiated with the issuance of a Call for Supply Offers on 4 September 2009. UNICEF SD received four offers in response to this first call. In March 2010, UNICEF SD entered into provisional supply agreements (PSAs) with two manufacturers: GlaxoSmithKline Biologicals (GSK) and Pfizer Inc. – the only companies whose Product Summary File had been accepted by WHO for prequalification review. Each manufacturer committed to supply 30 million doses annually, with GSK starting in January 2012 and Pfizer Inc. in January 2013, and continuing for 10 years. Consequently, 15% of AMC funds were allocated to each manufacturer under this procurement round.

In addition to the above-mentioned PSAs, GSK and Pfizer agreed to provide in total 7.2 million, 24.2 million and 20 million doses in 2010, 2011 and 2012, respectively, as part of the AMC Capacity Development Period3F[xxxv]. Both suppliers subsequently communicated the ability to increase such early supplies, should there be demand; based on demand, quantities on contracts were increased by 7.8 million doses in 2011 and 4 million doses in 2012. The total quantities on these contracts with each supplier remain 300 million doses each; only the distribution over the years has changed.

Both GSK's and Pfizer's products received WHO prequalification in 2010 and were deemed AMC-eligible by the AMC IAC on 16 April 2010 and 23 August 2010, respectively. This was communicated to suppliers with a copy to UNICEF on 6 May 2010 and on 23 August 2010. As a result, the PSAs automatically turned into effective supply agreements, allowing the procurement of those two vaccines.

7.6 Second AMC supply agreements

Following the publication of Strategic Demand Forecast v3.0 in March 2011, Gavi, in consultation with UNICEF, decided to issue a new Call for Supply Offers for the procurement of PCV, which was published on 8 April 2011, with a maximum target of 74 million doses by 2016. UNICEF SD received four offers by 6 May 2011.

In the week beginning 12 December 2011, UNICEF, as procurement agency on behalf of Gavi, confirmed the entry into new supply agreements with GSK and Pfizer Inc. Per the timeline set out in the AMC legal agreements, the supply agreements should have been finalised by 9 September 2011. However, UNICEF SD and Gavi agreed to delay the procurement timeline in order to be able to take into account any new demand recommended for approval by the IRC following the May 2011 round in the award recommendations.

Both GSK and Pfizer Inc. started supplying 18 million doses annually (annual supply commitment) from 2014 for a period of 10 years, up to a maximum of 180 million doses. The tail price for this agreement is US$ 3.50. Consequently 9% of the AMC funds are allocated to each of the two manufacturers under this agreement, according to the AMC terms and conditions. The total doses awarded to GSK and Pfizer Inc. under both supply agreements amount to 48 million annually.

As part of the supply agreements, manufacturers agreed to provide in total 30 million doses in 2012 and 2013 as part of the AMC Capacity Development Period.

[xxxv] The capacity development period is defined as the period during which suppliers develop dedicated manufacturing capacity to serve Gavi-eligible countries under their respective supply agreements.

UNICEF opted not to award the full quantities of the Gavi Strategic Demand Forecast for 2016 in response to this second tender. In order to: incentivise manufacturers to accelerate the development of new vaccines; contribute to the creation of a healthy market with multiple suppliers; and enhance the possibility to access lower tail prices through future offers, quantities were reserved for award at a later point in time. It should be noted, however, that 100% of the quantities offered for supply in 2012–2013 in response to tenders were contracted. Furthermore, UNICEF considered that the unexpected ramp-up of demand led to a faster than expected commitment of the AMC funding and that it would be prudent to pause to allow for a discussion with AMC stakeholders before proceeding to commit more than 50% of AMC funding at this early stage.

Fifty-two percent of the AMC funds corresponding to US$ 780 million remained unallocated following the completion of the second Call for Supply Offers and were available for successive rounds of calls for offers.

7.7 Third AMC supply agreements

Following the publication of the third Call for Supply Offers on 27 August 2012, Gavi announced two new supply agreements for the supply of PCV under the AMC. These new supply agreements include the first decrease to the AMC tail price, as well as additional short-term supply to support the accelerated introduction in a number of countries.

On 24 July 2013, UNICEF, in its capacity as Gavi's procurement agency, confirmed its entry into new supply agreements with GlaxoSmithKline Biologicals (GSK) and Pfizer Inc.

GSK started supplying 24 million doses annually (Annual Supply Commitment) from 2015 for a period of 10 years. Consequently, 12% of the AMC funds are allocated to this manufacturer under this agreement, according to the AMC terms and conditions. The tail price for this agreement is US$ 3.40 from 2013 and US$ 3.05 from 2017. The total doses awarded to GSK under its three supply agreements amount to 720 million.

Pfizer started supplying 26 million doses annually (Annual Supply Commitment) from 2016 for a period of 10 years. Consequently 13% of the AMC funds are allocated to this manufacturer under this agreement, according to the AMC terms and conditions. The tail price for this agreement is US$ 3.40 in 2013; US$ 3.30 from 2014; US$ 3.05 from 2017 for the multi-dose vial only; US$ 2.95 for the multi-dose vial only from 2018 onwards; and US$ 2.90 for the multi-dose vial only from 2019 onwards. The total doses awarded to Pfizer under its three supply agreements amount to 740 million.

In addition, Pfizer agreed that the reduced tail prices outlined above can be applied to all doses remaining to be procured under its first and second supply agreements. To access Pfizer's reduced tail price, Gavi provided a financial guarantee for the tail price component, equivalent to 80% of the total contracted quantities in the period 2013–2015. The standard AMC commitments of 20%, 15% and 10% in the first three years of each supply agreement counted towards the financial guarantee. It was also agreed to accelerate the procurement of doses at US$ 7.00 under the new supply agreement to ensure that all doses at that price were procured before 2016. As part of these supply agreements, GSK and Pfizer Inc. agreed to provide a total of 42 million doses during the AMC capacity development period.

UNICEF opted not to award the full quantities of the Gavi Strategic Demand Forecast for 2017 in response to this third tender and only awarded quantities to meet the approved demand. Quantities were reserved for award at a later point in time, in order to: incentivise manufacturers to accelerate the development of new

vaccines; contribute to the creation of a healthy market with multiple suppliers; and enhance the possibility of accessing lower tail prices through future offers.

Twenty-seven percent of the AMC funds corresponding to US$ 405 million remained unallocated and were available for later calls for offers.

7.8 Fourth AMC supply agreements

Following the publication of the fourth Call for Supply Offers on 6 June 2017, Gavi announced one new supply agreement for the supply of PCV under the AMC. This new supply agreement included another decrease to the AMC tail price for the multi-dose vial, as well as additional short-term supply to support an increase in demand triggered primarily by India's decision to introduce PCV in a number of low-income states through Gavi catalytic support limited in both time and value, expected to span 2017–2019 and consistent with the Gavi Board decisions on support for India.

On 5 April 2018, UNICEF confirmed its entry into a new supply agreement with Pfizer Inc. Pfizer started supplying 19 million doses annually (Annual Supply Commitment) from 2018 for a period of 10 years. Consequently, 9.5% of the AMC funds were allocated to this manufacturer under this agreement, according to the AMC terms and conditions. The tail price for this agreement is US$ 2.95 for the 4-dose vial presentation from 2018 onwards and $2.90 for the 4-dose vial presentation from 2019 onwards. The total doses awarded to Pfizer under its four supply agreements amount to 930 million. In addition, Pfizer has agreed that the tail price outlined above can be applied to all doses (supplied in a 4-dose vial) remaining to be procured under its first, second and third supply agreements.

UNICEF has opted not to award the full quantities of the Gavi Strategic Demand Forecast for 2020–2021 in response to this fourth tender and has only awarded quantities to meet the approved demand. Quantities have been reserved for award at a later point in time in order to: incentivise manufacturers to accelerate the development of new vaccines; contribute to the creation of a healthy market with multiple suppliers; and enhance the possibility of accessing lower tail prices through future offers.

7.9 Fifth AMC supply agreements

Following Indonesia's request in January 2020 to access PCV supply through the Pneumococcal AMC, the demand increase for the following five years was enough to trigger the final AMC Call for Supply Offers (AMC-5). UNICEF and Gavi reviewed the market context, particularly the prequalification of the first PCV from a DCVMN manufacturer and decided to go ahead with AMC-5 tender.

The fifth Call for Supply Offers was open from 14 February through 6 March 2020. The tender evaluation and awards were completed by 23 April, and the final supply agreement was executed on 30 May 2020. The timely turnaround for AMC-5 was critical for the AMC stakeholders' decision on how best to utilise the remaining AMC funds.

The outcome of AMC-5 was an unprecedented low tail price of US$ 2.00 per dose, 30% lower than the lowest tail price prior to that. SII was awarded an AMC subsidy of US$ 75 million for the supply of 100 million doses over a ten-year period (2020 through 2029). PCV supply through the AMC-5 Supply Agreement started rolling out in September 2020, with Uzbekistan, a fully self-financing country, receiving the first shipments. The remaining 12.5% of the Pneumococcal AMC funds were mostly redirected to the Gavi COVAX AMC following this final Call for Supply Offers.

Annex 3 – Membership of the PROWG in 2020

The Pneumococcal & Rotavirus Operational Working Group (PROWG) is a sub-team of the Vaccine Implementation Management Team. Members in 2020 were as follows:

Organisation	Members
Gavi Secretariat	**Veronica Denti** Senior Programme Manager, Vaccine Implementation, Vaccines & Sustainability **Markus Beck** Senior Manager, Market Shaping, Vaccines & Sustainability
UNICEF Supply Division (SD)	**David K. Mutuerandu** Contracts Manager, Vaccine Introductions Unit, Vaccine Centre **Abraham Kofi Ntow** Contract Specialist, Vaccine Introductions Unit, Vaccine Centre
WHO	**Jenny Walldorf** Immunization, Vaccines and Biologicals, IVB/EPI **Alejandro Ramirez Gonzales** Immunization, Vaccines and Biologicals, IVB/EPI
CDC	**Terri Hyde** Team Lead, Vaccine Introduction Team, Global Immunization Division **Heidi Soeters** Epidemiologist, Vaccine Introduction Team, Global Immunization Division **Jacqueline Tate** Rotavirus Epidemiology Team Lead, Division of Viral Diseases **Tamara Pilishvili** Pneumococcal Disease and Vaccine Policy Lead, Division of Bacterial Diseases
PATH	**Allison Clifford** Senior Communications Officer, Center for Vaccine Innovation and Access **Laura Kallen** Scientific Communications Officer, Center for Vaccine Innovation and Access
JHU/RAVIN	**Molly Sauer** Deputy Director, Policy, Advocacy & Communications, International Vaccine Access Center
CHAI	**Chand Mehta** Program Manager, Vaccine Markets **Laure-Anais Zultak** Associate, Global Vaccines Delivery
UNICEF Programme Division	**Godwin Mindra** Senior Immunisation Specialist, Health Section **Ben Hickler** Communication for Development (C4D) Specialist, Routine Immunisation and New Vaccines, Health Section

As of 31 December 2020

Annex 4 – Membership of the Independent Assessment Committee in 2020

Claire Broome (Chairperson)
Adjunct Professor, Division of Global Health, Rollins School of Public Health, Emory University, Atlanta, Georgia, USA

George Amofah
Part-Time Lecturer, School of Public Health, University of Ghana, Legon; Retired Deputy Director General, Ghana Health Service

Bernard Fanget
CEO, Bernard Fanget Consulting; and VP R&D and Pharmaceutical Development, Neovacs, France

William (Bill) Hausdorff
Lead, Public Health Value Proposition, PATH, Washington, DC, USA

Mary Kitambi
Public Health Specialist, Ministry of Health and Social Welfare, Tanzania

Evans Mpabalwani
Paediatrician and Clinical Virologist, Ministry of Health, Zambia

Giorgi Pkhakadze
Professor, School of Public Health, David Tvildiani Medical University (DTMU), Georgia

Halvor Sommerfelt
Professor of Epidemiology, Centre for International Health, and Director, Centre for Intervention Science in Maternal and Child Health (CISMAC), University of Bergen, and Senior Consultant, Norwegian Institute of Public Health, Norway

Piers Whitehead
Chief Executive Officer at SeromYx Systems, Cambridge, MA, USA

Source: Gavi Secretariat, as of 31 December 2019

Annex 5 – Summary of Gavi investments in targeted assessments

Gavi annually invests approximately US $12 million in targeted assessments (note: excludes malaria vaccine pilots and country implementation research) across the vaccine portfolio to: inform evidence-based decision-making; document programme outcomes and impact; and generate lessons to inform programme improvements from a subset of settings (predominantly through primary data collection). The table below summarises recent Gavi-commissioned investments assessing PCV.

5.1 ONGOING STUDIES	
5.1.1 Pneumococcal Conjugate Vaccine Impact Study (PCVIS) in Kilifi, Kenya, co-funding surveillance and impact assessment activities London School of Hygiene and Tropical Medicine (2012–2021)	
Objective(s)	• Measure the impact of PCV10 use in Kenya
Finding(s)	• Since its introduction in 2011, PCV10 has reduced the incidence of vaccine-type invasive pneumococcal disease by over 90% in children aged under 5 years. Herd effects of the vaccine were also demonstrated by significant declines in PCV10-type IPD in unvaccinated age groups with estimated reductions of 100%, 74% and 81%, in those <2 months, 5–14 years and ≥15 years, respectively. There was no significant change in the incidence of non-PCV10 type IPD, suggesting no replacement disease. • Hospitalisations for clinical pneumonia had been declining progressively prior to PCV introduction but fell an additional 27% with the introduction of PCV10. The incidence of X-ray confirmed pneumonia fell by 48%. • Introduction of PCV10 with a catch-up campaign in this developing country setting has led to a 92% reduction in carriage of vaccine-serotype pneumococci in children <5 years, as well as reductions in unvaccinated older children (74%) and adults (81%). • After Kenya's transition from Gavi support, the average cost per disability-adjusted life years (DALYs) averted was US$ 153, which falls well below the WHO cost-effectiveness threshold of GDP per capita, or US$ 1,445.
5.1.2 Impact of PCV on disease, nasopharyngeal carriage, and health economics in Nepal Oxford University (2013–2021)	
Objective(s)	• Measure the health impact of PCV use in Nepal • Determine the costs of pneumococcal disease and the potential financial risk protection PCV can provide for families • Determine the immunogenicity of Nepal's accelerated PCV dosing schedule as compared to the WHO-recommended schedule
Finding(s)	• The proportion of children hospitalised with pneumonia who are carrying vaccine-type pneumococcus has nearly halved since PCV introduction in 2015; there have also been significant reductions in pneumococcal carriage among healthy children since vaccine introduction. • Retrospective administrative data from Patan Hospital, where data on all hospital admissions was collected, shows that before vaccine introduction, pneumonia, meningitis and sepsis accounted for a significant number of childhood admissions; data collection for the post-introduction period is ongoing. • Nepal's novel schedule with the second primary dose given at 10 weeks showed inferior immunogenicity to the recommended schedule with the second dose at 14 weeks for some serotypes; however, the differences observed after the primary series are not likely to be clinically important because all serotypes reached the immunogenicity threshold that confers protection against disease and because differences are substantially diminished after the booster dose. Results suggest the accelerated

	schedule may be used by programs if there are barriers to implementation of the standard schedule and contributed to a revision of WHO dosing recommendations in 2017. • The average cost per episode of disease ranged from approximately US$ 160 for pneumonia to US$ 370 for meningitis, which translates to 25–50% of the median per capita annual income of US$ 670 in Nepal. • The cost of hospitalised pneumococcal disease per 100,000 children aged 1–59 months ranged from US$ 73,000 to US$ 156,000; about a third of costs were incurred prior to hospitalisation; primary caregivers lost 11 days of wages for pneumonia and meningitis and 17 days for sepsis. • Using the conventional definition of "catastrophic expenses," a single case of hospitalised pneumonia was considered catastrophic for about 10% of all households studied, and for approximately 40% of households in the poorest income quintile, suggesting that PCV's potential financial risk protection is likely to benefit the poorest and most vulnerable families.
5.1.3 Impact of PCV on hospitalized pneumonia and nasopharyngeal carriage in Mongolia Murdoch Children's Institute (2013–2021)	
Objective(s)	• Measure the health impact of PCV use in Mongolia
Finding(s)	• Before vaccine introduction, preliminary analysis shows the majority (76%) of pneumococci present in the nasopharynx in children hospitalised with pneumonia belonged to serotypes covered by PCV13. • Preliminary analysis of the pre-introduction carriage survey among healthy children found 61% aged 12–23 months were carrying pneumococci, of which 43% were vaccine-type. • One year after PCV introduction, vaccine-type carriage declined by approximately half in both 5–8 week infants and children aged 12–23 months. Non-vaccine type carriage increased 1.5 fold in the 12–23 month age group.
5.1.4 Evaluating the impact of PCV in Burkina Faso US Centers for Disease Control and Prevention (2013–2021)	
Objective(s)	• Measure the health impact of PCV use in Burkina Faso
Finding(s)	• After four years of PCV13 use in Burkina Faso, rates of vaccine-type meningitis are significantly lower in all age groups. The largest decrease was observed among children younger than one year (65%-84% decline), but rates also declined by more than 60% in those too old to be vaccinated, suggesting the vaccine offers significant indirect protection. • The impact on serotype 1 is still in question since the incidence was stable over the period from 1 year pre-PCV through the post-PCV years. This supports evidence from earlier PCV licensure trials that showed lack of serotype 1 efficacy, suggesting that serotype 1 disease outbreaks may continue even in settings of prolonged vaccine use. • In older children and adults, serotype 1 continues to be the main cause of pneumococcal meningitis, with little appreciable reduction in disease rates. • Incidence of non-PCV13 type meningitis among children aged under 5 years was stable for the first 2 years post-PCV but increased 26% in the third post-PCV year, suggesting some serotype replacement may be occurring.

5.2 COMPLETED STUDIES	
5.2.1 Impact of PCV introduction on hospitalised pneumonia, IPD and nasopharyngeal carriage in Lao PDR Murdoch Children's Institute (2013–2018)	
Objective(s)	• Measure the health impact of PCV use in Lao PDR
Finding(s)	• PCV was effective against severe pneumonias requiring oxygen supplementation; this significant finding suggests that the vaccine is effective at preventing cases that may not be treated effectively in low- and middle-income countries, where supplemental oxygen is often unavailable outside urban hospitals. • PCV significantly decreased vaccine-type carriage in healthy children aged 12–23 months by 23% in the first 3 years since PCV introduction; there was no significant decrease in unimmunised infants (aged 5–8 weeks), suggesting no meaningful indirect effects during this early stage of PCV use.
5.2.2 Impact of PCV-10 on Invasive Pneumococcal Disease (IPD) in Lower Sindh, Pakistan Aga Khan University (2013–2017)	
Objective(s)	• Measure the health impact of PCV use in Pakistan • Estimate coverage • Evaluate the success of a portfolio of interventions designed to increase coverage
Finding(s)	• With low vaccine coverage, estimated efficacy of PCV10 against vaccine-type IPD was 82% for children who were fully vaccinated. While these results are not statistically significant, they suggest that a large impact may be expected when higher coverage is achieved. • The average cost of illness for pneumococcal meningitis at US$ 340 per patient per episode was much higher than that for pneumonia at US$ 160; however, with a GNI per capita of less than US$ 6,000, both syndromes represent significant costs to the health system and households. • After the implementation of new quality improvement measures to improve vaccination rates in low-coverage areas during the roll-out of PCV, coverage increased only marginally (e.g. Penta3 increased from 22% to 39%) and remained low (<40% fully immunised) through the duration of the study. • Vaccine-type colonisation steadily decreased in vaccine-age-eligible children after PCV introduction in the rural site and was ~50% lower 3 years after introduction compared to pre-PCV levels. But at the urban site, the evidence of a decline was less clear: colonisation decreased from pre-PCV to year 3 post-PCV by only 25%; and in year 2 of the PCV programme, the vaccine-type colonisation rate was higher than in the pre-PCV period. These findings in the urban site are suggestive of low vaccine coverage, as was observed in the coverage surveys.
5.2.3 Evaluating the impact of PCV on nasopharyngeal carriage, IPD and X-ray confirmed pneumonia in Mozambique IHME (2013–2016)	
Objective(s)	• Assess impact of PCV10 on the burden of pneumococcal meningitis in children less than 5 years of age at the three largest hospitals in Mozambique
Finding(s)	• Introduction of PCV10 immunisation resulted in rapid decline of pneumococcal meningitis in children aged under 5 years in Mozambique. • Among HIV-uninfected children receiving three doses, a 44% (95% confidence interval [CI]: 33, 59) reduction in VTS pneumococcal carriage was observed at the first round and a 70% reduction (95% CI: 57-78) at the second round. In HIV-infected children receiving three doses, a 60% (95% CI: 25, 95) reduction was observed at the first round, and no additional decline was observed at the second round. There was also an early signal of an indirect effect among HIV-infected children, with a 31% reduction (95% CI: 11, 46) among HIV-infected children receiving no PCV doses. This decline was accompanied by substantial changes in the pattern of circulating pneumococcal

	serotypes. As expected, there was also an increase in pneumococcal carriage of non-PCV10 VTS, including serotypes in PCV13 (i.e. 19A). • Significant reduction in vaccine-type IPD of 94% (95% CI: 65.8, 99). There was also a significant reduction in X-ray confirmed pneumonia (85%, 95% CI: 64.3, 93.7). At this point, we did not observe evidence of serotype replacement, with a non-significant change in non-vaccine-type IPD (16.3%, 95% CI: -55.4, 203.4).
5.2.4 Impact of PCV on nasopharyngeal carriage in Bangladesh IHME (2013–2016)	
Objective(s)	• Assess impact of PCV on nasopharyngeal carriage among infants in Bangladesh
Finding(s)	• Observed 25% reduction in vaccine-type carriage among children age-eligible for PCV but no change among the age-ineligible children. • There were increases in non-vaccine serotypes of 17–20% among age-eligible children.
5.2.5 PCV13 Effectiveness in South Africa Grant A11 (2012–2015)	
Objective(s)	• Measure the impact of PCV use in South Africa, in the context of switch from PCV7 to PCV13
Finding(s)	• PCV13 was 85% effective against vaccine-type disease among HIV-uninfected children and 91% effective among HIV-infected children • PCV13 effectiveness against the 6 serotypes not in PCV7 was 92% among HIV-negative children. The PCV13 vaccine effectiveness for PCV7 serotypes among malnourished children who were HIV-negative was 90%.
5.2.6 Landscape analysis of PCV dosing (analysis updated in 2016-2017 with funding by the Bill & Melinda Gates Foundation: PCV Review of Impact Evidence (PRIME)) VI-TAC Special Studies (2009–2013)	
Objective(s)	• Review existing literature and conduct analyses on collected data that can support evidence-based decision-making on the use of the three WHO-recommended PCV schedules: 1) three primary doses plus a fourth booster dose (3+1); 2) three primary doses without a booster dose (3+0); and 3) two primary doses plus a third booster dose (2+1)
Finding(s)	• The available literature shows that each of the three recommended PCV schedules showed significant reductions in pneumococcal disease, however varying study designs and epidemiologic settings made direct comparison of impact between schedules difficult; thus, the choice of schedule used in a PCV program should balance programmatic considerations and local epidemiology, with the primary goal of maximising coverage.
5.2.7 Effectiveness of PCV7 against IPD and presumed bacterial pneumonia in South Africa VI-TAC Special Studies (2009–2013)	
Objective(s)	• Measure the impact of PCV use in South Africa
Finding(s)	• Routine PCV 2+1 schedule (novel at the time) in setting with high pneumococcal transmission schedule was 78% effective against IPD for HIV-uninfected children but significantly lower (12% effective) among HIV-infected children; this may indicate the benefit of a booster dose for HIV+ children on this schedule. • In the matched case-control study, PCV7 was 39% effective in preventing probable bacterial pneumonia (PBP).

5.2.8 Pneumo/Rota time series in South Africa VI-TAC Special Studies (2009–2013)	
Objective(s)	• Measure the impact of simultaneous PCV and Rotavirus vaccine use in South Africa
Finding(s)	• Among HIV-uninfected children aged under 5 years, PCV13 reduced all cause pneumonia by up to 39% each year following introduction; this translated to 7–9 prevented hospitalisations for every 1,000 children vaccinated.
5.2.9 PCV Impact in The Gambia PneumoADIP Special Studies (2004–2013)	
Objective(s)	• Measure the impact of PCV use in the Gambia
Finding(s)	• The incidence of vaccine type IPD decreased 82% in children aged 2–23 months after vaccine introduction; incidence of all IPD decreased by 55% in the 2–23 month age group. This was due to an 82% (64%–91%) reduction of serotypes covered by PCV13. • PCV13 had a moderate impact on radiological pneumonia (23% decline after introduction) in children aged 2–11 months. The vaccine substantially reduced the severest forms of disease, pneumococcal and hypoxic pneumonia, by 58% and 57%, respectively. After vaccine introduction, there was a modest, non-significant increase in pneumonia due to non-PCV13 serotypes, indicating little to no serotype replacement.
5.2.10 Economic impact of PCV in The Gambia VI-TAC Special Studies (2009–2013)	
Objective(s)	• Measure the cost and economic impact of PCV use in the Gambia
Finding(s)	• The total incremental cost for transition to pentavalent and introduction of PCV together in the Gambia in 2009 amounted to US$ 1,616,943 or US$ 24.22 per fully immunised child, over 85% of which was the cost of vaccines. Savings from the switch from tetravalent to pentavalent vaccine slightly offset the large additional cost of introducing PCV. • The average costs to families of pneumococcal disease in the Gambia, including out-of-pocket costs and lost income, is substantial at US$ 15–144 per case (up to 29 times the average daily household expenditure in the country).
5.2.11 Cost-effectiveness of PCV10 catch-up in Kenya PneumoADIP Special Studies (2004–2013)	
Objective(s)	• Model the impact and cost-effectiveness of PCV catch-up campaigns among under-one year olds, under-two year olds (current WHO recommendations) and under-five year olds, in Gavi-eligible countries
Finding(s)	• Preliminary results suggest that catch-up campaigns not only lead to more rapid reduction in the IPD burden but also increase efficiency of the vaccine schedule in the first years after vaccination through rapid establishment of herd protection. • Any catch-up campaign in the first years after introduction, particularly among under-two and under-five year olds, is likely to prevent a high number of IPD cases for comparatively fewer extra vaccine doses than routine immunisation; more targeted campaigns aimed at under-one year olds achieve additional direct benefits but fewer indirect benefits.

5.2.12 Economic value of vaccination in India PneumoADIP Special Studies (2004–2013)	
Objective(s)	• Evaluate the potential health impact and costs averted through immunisation with three vaccines – Hib, PCV, RV vaccines • Generate new evidence on the health and economic benefits of these vaccines at the national level & in four states in India (Bihar, Delhi, Maharashtra, and Tamil Nadu), specifically in three categories: (i) death & cases averted; (ii) disease costs averted; and (iii) productivity loss averted
Finding(s)	• By introducing and scaling up coverage of Hib, PCV and RV, India could save over US$ 1 billion each year in economic benefits and avert more than 90,000 needless child deaths each year. • An estimated US$ 1 billion or 88% of the total amount of cost savings would be attributable to lost productivity due to premature pneumococcal death; another US$ 112.8 million, or 10% of the total cost, would be due to costs related to loss of productivity due to disability as a result of these diseases. • Treatment costs of Hib, pneumococcal and rotavirus gastroenteritis would account for US$ 8.4 million (US$ 4–12million) or <1% of the total costs of these diseases. Finally, caretaker productivity loss from seeking care would represent US$ 1.5 million (US$ 1–4.9 million).

Sources

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