ADVANCE MARKET COMMITMENT FOR PNEUMOCOCCAL VACCINES

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PREPARED BY THE AMC SECRETARIAT OF GAVI, THE VACCINE ALLIANCE

Contents

Abbreviations

AMC	Advance Market Commitment
AMP	Agence de Médicine Préventive
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 & evaluation
PEF	Partners' engagement framework
PCV	Pneumococcal conjugate vaccine
PROWG	Pneumococcal & Rotavirus Operational Working Group
PSA	Provisional supply agreement
PSF	Product summary file
RFP	Request for proposals
SD	Supply Division (UNICEF)
SDF	Strategic demand forecast
SDS	Strategic demand scenarios
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 Advance Market Commitment (AMC) implementation activities, including supply and procurement, country demand, monitoring and evaluation, media and communications and financial reporting. This is the tenth pneumococcal AMC Annual Report[i] and covers the period from **1 January to 31 December 2018**.

Supply and demand

The pilot AMC for pneumococcal vaccines completed its tenth year of implementation in 2018. A total of 149 million doses of pneumococcal conjugate vaccine (PCV) were procured through the AMC in 2018, a 4% reduction from 2017 (156 million doses)[ii]. This was caused by a decline in demand from Nigeria, driven both by accumulation of stock and changes in actual coverage rates, compared with those previously reported. With the current seven supply agreements, the total contracted supply through 2027 amounts to 1.65 billion doses. Out of the US$ 1.5 billion AMC funds, the two suppliers that offer prequalified PCV have been allocated US$ 1.238 billion. This means that 17.5% of the total AMC funding remains available.

In terms of country demand, 82% of AMC-eligible countries (60 out of 73) had been approved to introduce pneumococcal vaccines to date. As of 31 December 2018, 59 countries have included these life-saving vaccines into their routine programmes. One country, Haiti, did so during this reporting period (1 January to 31 December 2018). In addition, Bhutan was approved to access the AMC price for PCV and is expected to introduce the vaccine in Q1 2019. Bhutan will be the second formerly Gavi-supported country to fully self-finance a routine introduction with pneumococcal vaccine, after Mongolia.

Monitoring and evaluation

AMC continues to progress against selected indicators as shown in Table 1. It is estimated that more than 143 million children were immunised with AMC-supported pneumococcal vaccines between programme start and the end of December 2017. By the end of 2018, this figure is projected to have reached more than 149 million (actual 2018 data will become available in July/August 2019). The continued scale-up of PCV is expected to result in over 700,000 prevented deaths by 2020.

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

	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Objective 1: to accelerate the development of pneumococcal vaccines that meet developing country needs.										
Cumulative number of AMC eligible target product profile (TPP) vaccines	0	2	2	2	2	2	2	2	2	2

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

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

	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Cumulative number of AMC-registered manufacturers who have made their registration public	0	4	4	4	4	4	4	4	4	4
Objective 2: to bring forward the availability of effective pneumococcal vaccines 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]
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
been approved	3	17	37	46	51	55	58	59	59	60
introduced TPP vaccines	0[iv]	1[iv]	16	24	38	46	54	57	58	59
PCV coverage*	0%	1%	5%	9%	19%	28%	35%	41%	43%	n/a**
Cumulative number of children vaccinated with Gavi support (in millions)	-	0.5	4	10	26	48	76	109	143	n/a**

Source: Gavi Secretariat

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

*** WUENIC coverage data and WHO-reported number of immunised for 2018 will be available in July 2019*

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 their routine systems, with PCV third-dose (PCV3) coverage tracking well against the third-dose coverage of diphtheria-tetanus-pertussis vaccine (DTP3). Within two years of implementation, 41 of the 54 countries that introduced PCV in 2015 had reached a coverage level of PCV3 amounting to at least 90% of their DTP3 coverage. Of the other 13 countries, 10 had a reported PCV3 coverage of 81–90% of their DTP3 coverage within two years of introduction (see Section 4, Figure 5).

In 2013, Gavi launched a set of full country evaluations (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 approved in May 2017 in three countries (Mozambique, Uganda and Zambia). In May 2018, the Gavi Evaluation Advisory Committee 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, stopped in June 2018. Since then, the Secretariat has been engaging with country evaluation partners, where relevant, to scope specific evaluation priorities.

[iii] *The decrease was caused by a decline in demand from Nigeria, whose coverage rate has been lower than previously estimated, due to a recent survey with new information*

[iv] *Two countries introduced PCV in 2009, but with a vaccine that was not TPP compliant. They have since switched to a TPP vaccine in 2011.*

Gavi continues to fund special studies demonstrating the effectiveness and impact of PCV. The aim is to help facilitate evidence-based decision-making in support of the introduction and continued implementation of pneumococcal vaccines in developing countries through the AMC.

Media and communication activities

Increasing AMC visibility through traditional, online and social media remains an important goal for Gavi's Communications team. This multi-platform approach continues as 59 countries have now introduced pneumococcal vaccines into their national immunisation schedules. The AMC was highlighted in both the printed and online versions of Gavi's Annual Progress Report, as well as Gavi's Mid-Term Review Report. At the Mid-Term Review itself, the AMC was featured prominently in a special session on innovative solutions and was celebrated both for its past success and as a foundation for designing the next generation of effective financial tools for development.

In October 2018 the Gavi media team issued a press release announcing the introduction of PCV into Haiti's routine immunisation programme, securing positive coverage in the Miami Herald, amongst other international news outlets.

Financial activities

From 1 January to 31 December 2018, Gavi disbursed US$ 326 million to UNICEF for the purchase of pneumococcal vaccines. Of this amount, US$ 53 million was used to pay for the AMC-funded portion of the vaccine cost and thus came from the AMC funds. The remaining US$ 273 million was allocated from general Gavi funds to pay for the tail price portion of the vaccine purchase and related costs[v].

Challenges and priorities ahead

With 60 AMC-eligible countries approved for PCV and 59 already having introduced it since 2010, moving forward Gavi will focus on supporting countries that have not yet applied for support for routine immunisation and catch-up vaccination with pneumococcal vaccine through the AMC. For countries that have introduced, the priorities remain to sustain PCV implementation and improve coverage, support product and presentation switches and measure the impact of PCV, especially as countries start to transition out of Gavi support. Reducing the price of pneumococcal vaccines and ensuring a proper balance between supply and demand remain key areas of focus, in addition to preparing for the expected availability of a new prequalified vaccine before the end of 2020.

[v] 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

Advance Market Commitments (AMC) for vaccines aim 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, Norway and 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 is to reduce morbidity and mortality from pneumococcal disease, preventing an estimated seven million childhood deaths by 2030. The objectives of the pneumococcal AMC are 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 target product profile (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. To date, 82% of the 73 AMC-eligible countries have submitted applications to Gavi for financial support and been approved for pneumococcal vaccine introduction.

The purpose of this report is to provide an update on AMC implementation activities, including supply and procurement, country demand, monitoring and evaluation, media and communications and financial reporting. This is the tenth pneumococcal AMC Annual Report[vi] and covers the period from **1 January to 31 December 2018**.

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

[vi] *Previous AMC Annual Reports can be found on the AMC 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 that the inclusion of pneumococcal vaccines be given priority in childhood immunisation programmes worldwide, especially in countries with an under-five mortality rate above 50 per 1,000 live births[1]. For administration to infants, three primary doses (3p+0 schedule) or, as an alternative, two primary doses plus a booster (2p+1 schedule) are recommended. Primary vaccination can be initiated as early as at six weeks. Gavi currently supports PCV for administration in infant routine immunisation programmes.

WHO also states that catch-up vaccination can be conducted as part of a pneumococcal vaccine introduction to accelerate herd protection and thereby increase the impact of PCV on disease burden and carriage[2]. The SAGE Working Group on PCV reviewed the effectiveness of catch-up vaccination leading to an updated recommendation in October 2017, which states that '"*Catch-up vaccination as part of PCV introduction will accelerate both direct and indirect protection and therefore accelerate PCV impact on disease, particularly in case of high VT*[vii] *carriage prevalence and disease burden in children aged* ***1 to 5 years old"****,* thus expanding the age range of the target population recommended for catch-up vaccination.

Furthermore, the revised recommendation provides more guidance on the dose schedule: "*Catch-up vaccination with PCV can be done with 1 dose of vaccine for those initiating vaccine at age 24 months and older. For those who are 12-23 months at the time of first vaccination some programs have used 2 PCV doses separated by at least 8 weeks, and others have used 1 dose. For those initiating vaccination at age 6 months or under, a 3 dose regimen should be offered. For infants aged 7-11 months, some programmes have used 2 doses, and others have used 3 doses. If there is limited availability or capacity for catch-up immunization, the youngest children should be prioritized to receive catch-up doses of PCV because of the higher pneumococcal disease risk."*[viii]

In June 2018, the Gavi Board approved a proposal to support PCV catch-up vaccination for countries that have not yet introduced the vaccine. Guinea, the Democratic People's Republic of Korea and Tajikistan are expected to introduce PCV in the near future, and will thus be the first to potentially benefit from this change in Gavi's programmatic support.

By 31 December 2018 two types of pneumococcal conjugate vaccine (PCV), with a total of three different presentations, were available for procurement under the AMC. These two vaccines meet the criteria for TPP, which describe the minimum characteristics required for a pneumococcal vaccine to be eligible for AMC financing. One additional manufacturer is expected to start offering a WHO-prequalified pneumococcal vaccine by 2020.

[vii] *Streptococcus pneumoniae vaccine serotypes (VT)*

[viii] *http://www.who.int/immunization/sage/meetings/2017/october/4_PCV_WG_MERGED_Evidence_to_Rec__SEPT_26.pdf?ua=1 page 62*

1.2 Pneumococcal conjugate vaccine, 10-valent

The 10-valent PCV (PCV10) is a liquid vaccine originally available in a 2-dose vial without preservative, produced by GlaxoSmithKline. 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 Independent Assessment Committee (IAC).

GlaxoSmithKline (GSK) subsequently developed a 4-dose vial presentation of PCV10[3], which includes a preservative and was prequalified by WHO on the 16th October 2017. It was deemed AMC-eligible on the 17th October 2017 by the AMC IAC. The 4-dose vial presentation is replacing the 2-dose vial, and thus, all countries that are currently using PCV10 2-dose vial will need to switch to PCV10 4-dose vial or another product of their preference. The PCV10 2-dose vial will continue to be available for countries until the end of 2019.

1.3 Pneumococcal conjugate vaccine, 13-valent

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 to the above single-dose vial, 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 Supply offers and agreements

There have been four completed calls for supply offers for supply of PCVs under the AMC to date. The fourth and last call for supply offers was published on 6 June 2017 and completed on 5 April 2018. A summary of the four AMC supply agreements can be found in Annex 2. A summary of the supply commitments as of 31 December 2018 is shown in Table 2 below.

Table 2. Status of overall supply commitments, as of 31 December 2018

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 Inc.	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*** and 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 Inc.	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**; $2.95 from 2018*** and $2.90 from 2019****	2014	US$ 135 million
GSK	22 July 2013	24 million	US$ 3.40; reduced to US$ 3.05 from 2017	2015	US$ 180 million
Pfizer Inc.	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*** and US$2.90 from 2019****	2016	US$ 195 million
Pfizer Inc.	5 April 2018	19 million	US$2.95 for the 4-dose vial in 2018 and US$2.90 from 2019****	2018	US$ 142.5 million

**Reduced tail price as announced on March 2016*

***Reduced tail price for MDV as announced in January 2017; tail price for SDV remains unchanged at US$ 3.30*

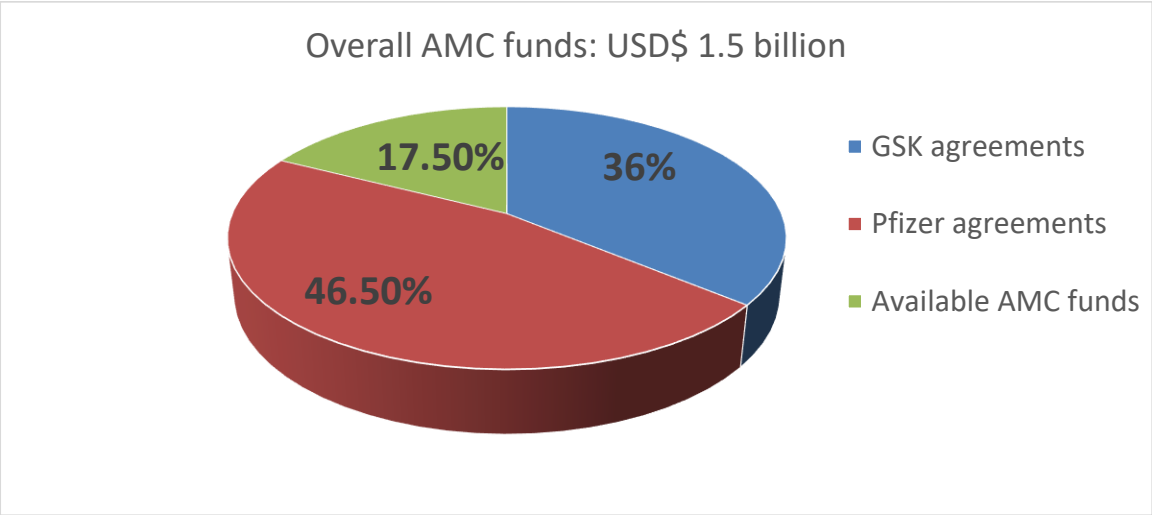
**** Reduced tail price for MDV as announced in January 2018; tail price for SDV remains unchanged at US$ 3.30*

***** 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 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 recent 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.

Figure 1. Allocation of AMC funds



1.5 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. Table 3 summarises the total contracted supply, as of 31 December 2018.

Table 3. Total annual contracted supply, as of 31 December 2018 (in millions*)

Year	2010	2011	2012	2013	2014	2015	2016	2017	2018-2020	2021	2022	2023	2024	2025-2027	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	19	19	19	19	57	**190.0**
Grand Total	**5.5**	**28.9**	**67.0**	**68.2**	**88.8**	**119.5**	**134.2**	**176.3**	**165.0**	**159.9**	**124.0**	**95.4**	**30.4**	**57**	**1,650.0**

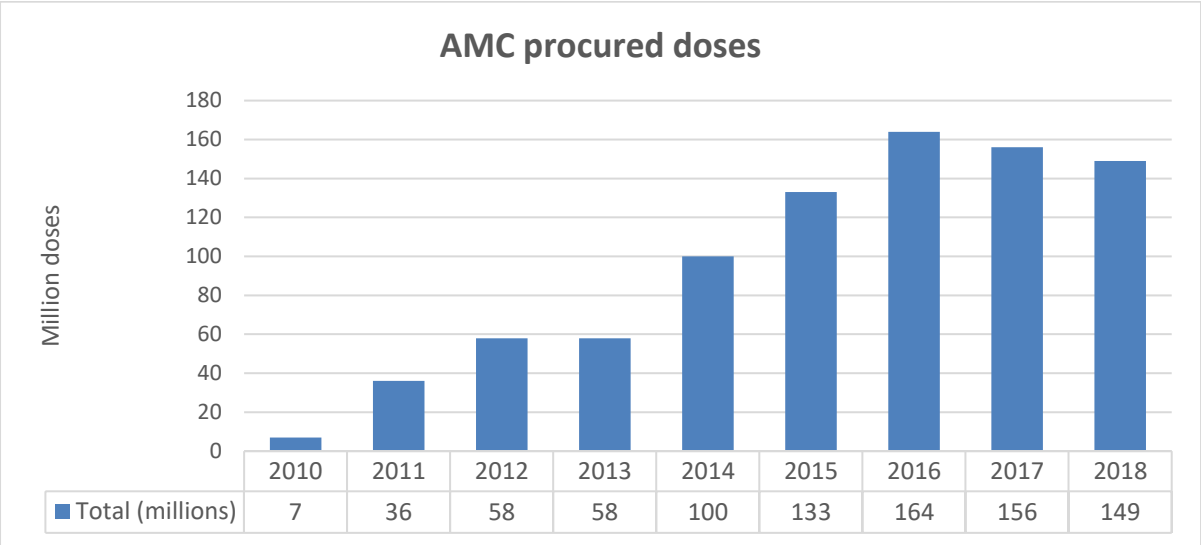
Source: UNICEF Supply Division
** Contracts are amended annually based on actual supply and demand to ensure that the total quantity on the supply agreements remain unchanged. Note: some numbers may appear not to add due to rounding.*

1.6 Doses procured between 2010 and 2018

A total of 149 million pneumococcal vaccine doses were procured in 2018. The total number of doses procured and delivered from 2010 to 31 December 2018 is summarised in Figure 2 below:

Figure 2. Pneumococcal vaccine: procured volumes 2010-2018 (in millions of doses)[ix]

[ix] *Source: UNICEF Supply Division. Please note that the figure above indicates the number of doses placed on purchase orders during the respective years, including for delivery in a subsequent year.*



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. Some supply constraints remained nonetheless. In 2016, 8.9 million additional doses were procured by pulling volumes from later years, which were initially carried over from previous years, to meet India's demand; 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.

1.7 Strategic demand forecasts

In early versions of the strategic demand forecasts, revisions to assumptions about eligibility for Gavi support and country interest in the vaccine were key drivers of changing projections. In the last several forecasts, however, the long-term view of demand has become relatively stable. Nevertheless, projections for the period through 2020 have been revised substantially. The relative variability during this period reflects the uncertainty of introduction and scale-up plans for a few large countries, particularly India and Indonesia.

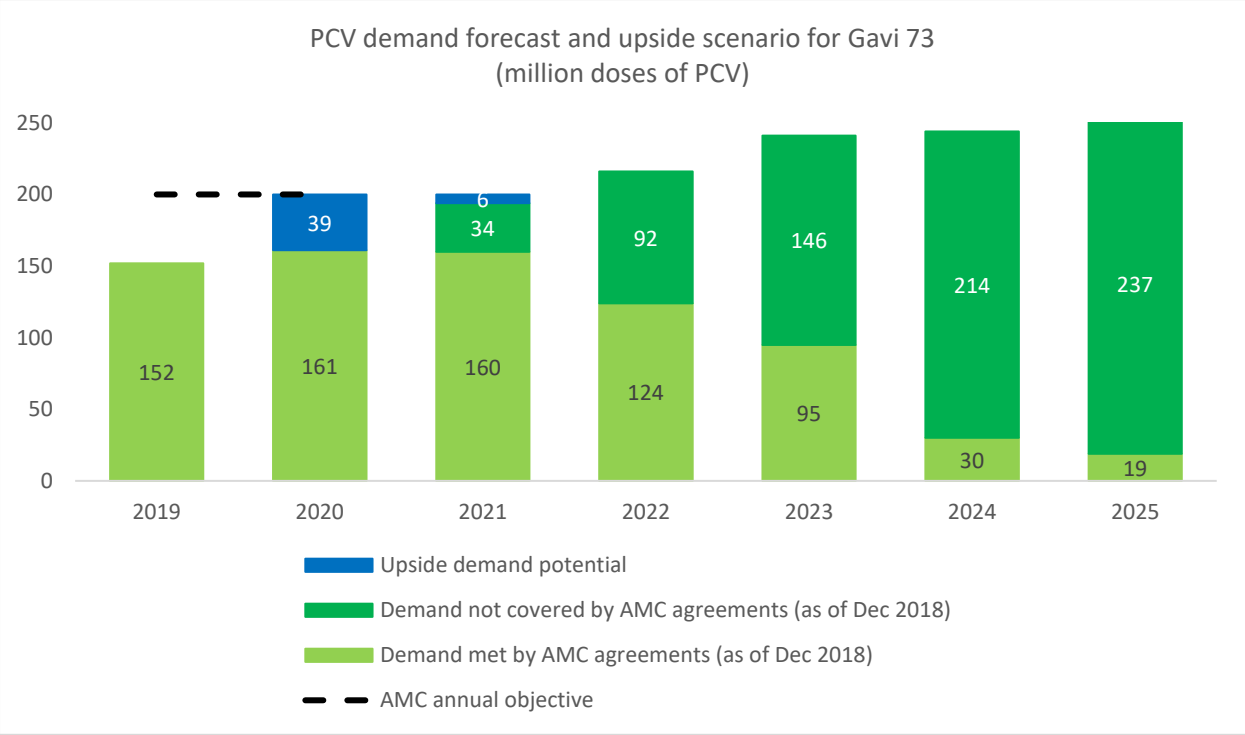
The following demand forecasts were developed, published and/or analysed in the reporting period:

- Demand forecasting for Gavi's v15.0 operational and financial forecast was completed in late 2017. This forecast represents the expected future demand through the AMC and UNICEF SD and is enhanced to represent AMC demand. This update includes several improvements to the forecasting approach. For example, the projection of needs for ongoing programmes was driven by individual country analysis and triangulation of multiple data sources. The volumes associated with the v15.0 financial forecast were published on Gavi's website in December 2017.

- Demand forecasting for Gavi's v16.0 operational and financial forecast was completed in late 2018. There is no significant change compared to v15.0, except regarding India, Indonesia and Nigeria. In 2019-20 the v16.0 demand is slightly lower than in the previous version primarily due to lower coverage estimates for Nigeria. The updated forecast also assumes a slightly faster initial sub-national roll-out in India versus v15.0 assumptions. Longer-term volume projections following India's and Indonesia's national roll-outs remain like previous versions of the forecast.

The latest demand forecast is shown in Figure 3 below. The upside demand potential represents potential demand factors that may result in the full allocation of 200 million annual doses before 2020.

Figure 3. Demand forecast[x]



1.8 Availability of pneumococcal vaccines

In the first quarter of 2017, Gavi finalised an updated supply and procurement roadmap for pneumococcal vaccines, which found that available supply of PCV is expected to exceed the demand of 73 Gavi-supported countries in the 2017–2026 period. However, there will still be limited buffer capacity in the 2017–19 period as India introduces Gavi-financed PCV in five states prior to pipeline manufacturers entering the market. After 2020, limited buffer capacity is expected to continue as current AMC supply contracts tail off and pipeline manufacturers ramp up supply.

[x] *Forecasted demand in Figure 3 is limited to the 73 AMC-eligible countries.*

Pfizer indicated at the end of 2018 that the price of the PCV13 4-dose vial available to Gavi-supported countries will be reduced from US$ 2.95 to US$ 2.90 per dose, effective 1 January 2019. PCV pricing will remain a primary focus of the Alliance's future efforts.

Several uncertainties have the potential to impact supply and demand over the next 10 years. These include:

- PCV introduction timelines and scale-up plans of large countries eligible to access pneumococcal vaccines at the price available through the AMC, such as Indonesia and India.
- The expansion of Gavi support to include support for catch-up vaccination at introduction for countries launching PCV routine immunisation programmes in 2019 or later (see also section 1.1), in line with the recently revised WHO recommendation for PCV vaccination.
- The market entry of pipeline manufacturers and their achievement of production capacity targets.
- The interest among countries to change their presentation preference, and the speed at which they wish to do so

An action plan was agreed by Gavi stakeholders and focuses on:

- mitigating potential supply risks;
- supporting pipeline manufacturers to bring vaccines to market to ensure competitive market dynamics and sufficient buffer capacity;
- maintaining market health by ensuring country presentation preferences are grounded in an evidence base and a consideration of supply availability and price; and
- driving continued price reductions.

Additional detail can be found in the public summary of the pneumococcal vaccine roadmap, available on the Gavi website.

1.9 AMC-registered manufacturers

Following the signature of AMC legal agreements on 12 June 2009, manufacturers can enter into an AMC registered manufacturers' agreement with Gavi, the Vaccine Alliance and the World Bank. As part of the registration agreement, manufacturers formally agree to the AMC terms and conditions; accept to provide an annual update on expected timing for application for AMC eligibility and for WHO prequalification; 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 an AMC-registered manufacturer application package to the AMC Secretariat. 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 who have made their registration public is as follows:[4]

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

- Serum Institute of India (India)

To date, only two of these manufacturers are producing WHO prequalified and AMC-eligible pneumococcal vaccines. The others are not expected to have WHO-prequalified vaccines until 2019/2020. 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

By 31 December 2018, 60 of the 73 AMC-eligible countries (82%) had applied and been approved for support for pneumococcal vaccines. One transitioned country, Bhutan, applied to access PCV at the AMC price in 2018 and plans to introduce the vaccine in January 2019. The remaining countries currently eligible to apply for PCV support are Comoros, Democratic People's Republic of Korea and Tajikistan. Chad, Guinea[xi], Somalia and South Sudan have not applied and are not eligible because of DTP3 coverage lower than 70%.

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 pneumococcal vaccines under the terms and conditions of the AMC – even after transitioning out of Gavi support. As a result of this decision, fully self-financing[xii] countries that have not yet been approved to receive Gavi support for pneumococcal vaccine are able to apply for and introduce it under the terms and conditions of the AMC. To do so, they need 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 yet applied and are eligible to do so are Cuba[xiii], India[xiv], Indonesia, Sri Lanka, Timor-Leste and Vietnam. Ukraine is not eligible to apply because of DTP3 coverage below 70%.

2.3 Pneumococcal vaccine introductions

As of 31 December 2018, 59 countries had introduced pneumococcal vaccines supported by the AMC. The introductions that have taken place to date are listed in Table 4 below.

Of the 59 countries with Gavi-supported pneumococcal vaccine programmes, 10 are using PCV10, while the remaining 49 are using PCV13. In 2017, Mozambique and Myanmar requested a switch from PCV10 to PCV13. Mozambique started shifting to the new presentation at the end of 2017. However, by the third quarter of 2018 5 of the 11 provinces had not completed the switch as there were still large amounts of PCV10 left in stock.

Myanmar started to prepare for its switch in late 2018. Two other countries (Armenia and Azerbaijan) successfully switched products in the second half of 2016.

Table 4. Pneumococcal vaccine introductions to date

Year	Country	Product	Status	Cumulative No.
2009	Gambia	PCV7 (donation)	Switched to PCV13 in 2011	1

[xi] Guinea, which does not currently meet the requirement of 70% DTP3 coverage, is nevertheless planning to introduce PCV in 2018 through the country engagement framework process. The country will need to meet the 70% DTP3 coverage requirement ahead of the introduction.

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

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

[xiv] India is in accelerated transition but can apply for the AMC tail price for the non-Gavi supported portion of its PCV vaccines.

	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
	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	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.)	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	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	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

** Ceremonial launch; National introduction in the following month*

In 2015, an updated analysis to identify the common hurdles faced by countries at the time of introduction was carried out, in order to continue to gather lessons learned on PCV programme implementation. The analysis covered 56 out of the 58 countries[xv] that had been approved for support at the time. Given the low number of introductions in 2016 and 2017, this analysis has not been updated. It will, however, be revised once considered relevant. As highlighted previously, the global supply constraints in the earlier years of the programme created uncertainty for countries and impaired adequate planning, which led to further delays. The key hurdles for countries yet to introduce are competing priorities at country level or DTP3 levels below the Gavi threshold of 70%. Gavi continues to strengthen its resource allocation and coordination mechanisms to ensure that these key cross-cutting bottlenecks are addressed.

[xv] *The two countries that originally introduced with donations were excluded from the analysis.*

2.4 Future pneumococcal vaccine introductions

One formerly Gavi-supported country, Bhutan, which has already been approved for pneumococcal vaccine support through the AMC, plans to introduce the vaccine in January 2019.

Table 5. Planned pneumococcal vaccine introductions

Year	Country	Product	Status	Cumulative No.
2019	Bhutan (self-financed)	PCV13	January 2019	60

2.5 Future pneumococcal vaccine applications

Out of the 73 AMC-eligible countries, only 13 (18%) have yet to be approved for pneumococcal vaccine support through the AMC. A subset of these countries have expressed strong interest in introducing the vaccine in the near future. However, only three (Comoros, the Democratic People's Republic of Korea and Tajikistan) are eligible to apply for Gavi support in 2019 based on eligibility and DTP3 coverage levels, which must be above than 70% (based on the latest WHO/UNICEF estimates of national immunisation coverage) as stated in Gavi's application guidelines.

Five countries that have already transitioned from Gavi support are still eligible to access pneumococcal vaccines through the AMC based on their DTP3 coverage levels. However, four of these countries – Cuba, Indonesia, Sri Lanka and Vietnam – will need to fully self-fund their introductions. Timor-Leste will receive Gavi support for its first year of introduction, expected in 2021, provided that a NITAG recommendation is made and accepted by the Ministry of Health before the end of 2019. The remaining countries – Chad, Guinea, Somalia, Ukraine and South Sudan – are currently ineligible due to their DTP3 coverage being below 70%. 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.

There will be three vaccine support application rounds in 2019 during which countries can apply for PCV support.

In addition to the application rounds, countries can access Gavi support through a new process: the country engagement framework (CEF). This tailored approach is aligned with a country's strategic multi-year plan and brings together all types of Gavi support into a single portfolio view for the upcoming 3-5-year period. Countries are moving towards the CEF process in stages. Guinea and Comoros have initiated the CEF process and have indicated their interest in introducing PCV.

2.6 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 continues to strengthen its coordination mechanisms with partners to ensure more effective and efficient technical support to countries. The new PEF structure, split between foundational support, targeted country assistance and strategic focus areas, ensures that Alliance resources, including technical assistance, are better targeted to address key bottlenecks at the country level.

At the global level, the Pneumococcal and Rotavirus Operational Working Group (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) 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;
- in close collaboration with countries and regional offices, determining technical assistance needs and mobilising relevant resources to ensure successful application, programme planning and implementation;
- gathering lessons learned and analysing experiences to optimise and improve future introductions.

A list of current PROWG members is provided in 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[xvi] have conducted PIEs for PCV. The PIEs carried out have concluded that PCV introduction is generally successful and high coverage is reached within a short period, due to high demand. Some of the issues identified include cold chain and vaccine management, training and reporting and monitoring. PEF aims to resolve these issues through targeted country assistance, in particular. The Gavi full country evaluations (see page 28) have also provided relevant lessons learnt regarding routine introductions of PCV[xvii].

2.7 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)[5]. 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.

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

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

Gavi has supported the advancement of GAPPD. As pneumococcal vaccines are introduced, and their coverage approaches that of DTP3 immunisation, there is a unique opportunity to strengthen the integration of service deliveries and help improve the coverage of other important interventions. Since 2014, Gavi also requires 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 serves a number of key functions. Most importantly, it has 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[xviii]. In addition, the IAC establishes when and if an adjustment of the preset 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 is subject to reappointment and may only be renewed once. The membership of three IAC members has been pending a 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 potentially replace all members whose terms have recently expired. The candidates will be assessed in early 2019 by the IAC Selection and Oversight Panel.
A list of IAC members can be found in Annex 4.

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

4. Monitoring and evaluation

In 2007 the United Kingdom's Department for International Development and the Canadian International Development Agency commissioned a monitoring and evaluability assessment study on behalf of the AMC for Pneumococcal Vaccines Donor Committee. The study proposed a monitoring and evaluation 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 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 AMC website each year since 2010. The baseline study was completed in 2010 and is available on the AMC website. The AMC process and design evaluation was carried out in 2012. Upon recommendation of the Gavi Evaluation Advisory Committee and following consultations with AMC stakeholders in 2013, the first impact evaluation of the AMC was completed in 2015 instead of in 2014 (see 4.2 below).

4.1 Programme performance reporting

A comprehensive PCV results framework is currently being used for regular monitoring of the Gavi pneumococcal vaccine programme and the AMC. At the end of 2015, additional indicators were added to reflect Gavi's new 2016-2020 strategy.

Pneumococcal vaccine coverage in Gavi-supported countries continues to be closely monitored. In 2017, weighted PCV3 coverage in the original 73 Gavi-supported countries was 43%, based on WUENIC data published in July 2018[6] – a 2 percentage point increase in relation to 2016. In the subset of Gavi-supported countries that introduced the vaccine prior to 2016 (54), average PCV3 coverage has reached 74%. Among countries that introduced prior to 2015 (46), average coverage has reached 72 %. Gavi's 2016-2020 strategy does not define targets for PCV coverage, but instead includes a composite indicator tracking overall coverage of all vaccines in Gavi's portfolio. Actual 2018 data will become available in July 2019 and reported in the next AMC Annual Report.

Figure 4 shows PCV3 coverage in 2017 (WUENIC July 2018 data). For the same group of countries, DTP3 coverage was 77%, demonstrating that most countries continue to successfully introduce PCV into their routine systems. In 47 countries, PCV3 coverage amounted to more than 90% of the coverage levels for DTP3[xix]. One country (Mongolia) reported less than 50% PCV3 coverage as a percentage of

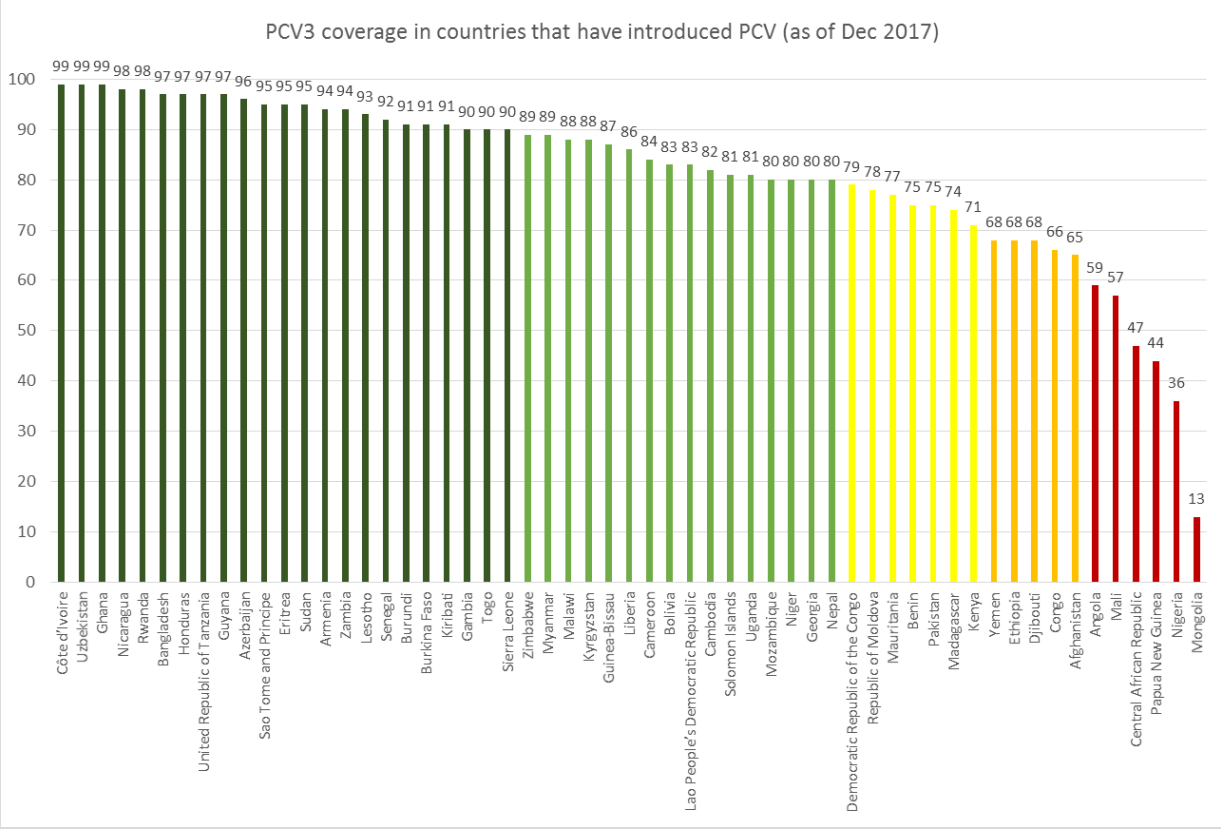
[xix] *This analysis excludes mid-2017 introductions and phased introductions.*

DTP3 coverage. This is mainly because the country only introduced the pneumococcal vaccine in 2016 and is still in the process of scaling up coverage.

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[xx] (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, where coverage for PCV3 reached the same level as DTP3 by the end of 2016, 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 IPV and is not in line with WHO recommendations, which recommend 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[xxi]. In complement, there is an ongoing study comparing invasive pneumococcal disease (IPD) pre- and post-introduction in the same population.

Figure 4. 2017 PCV3 coverage across Gavi-supported countries

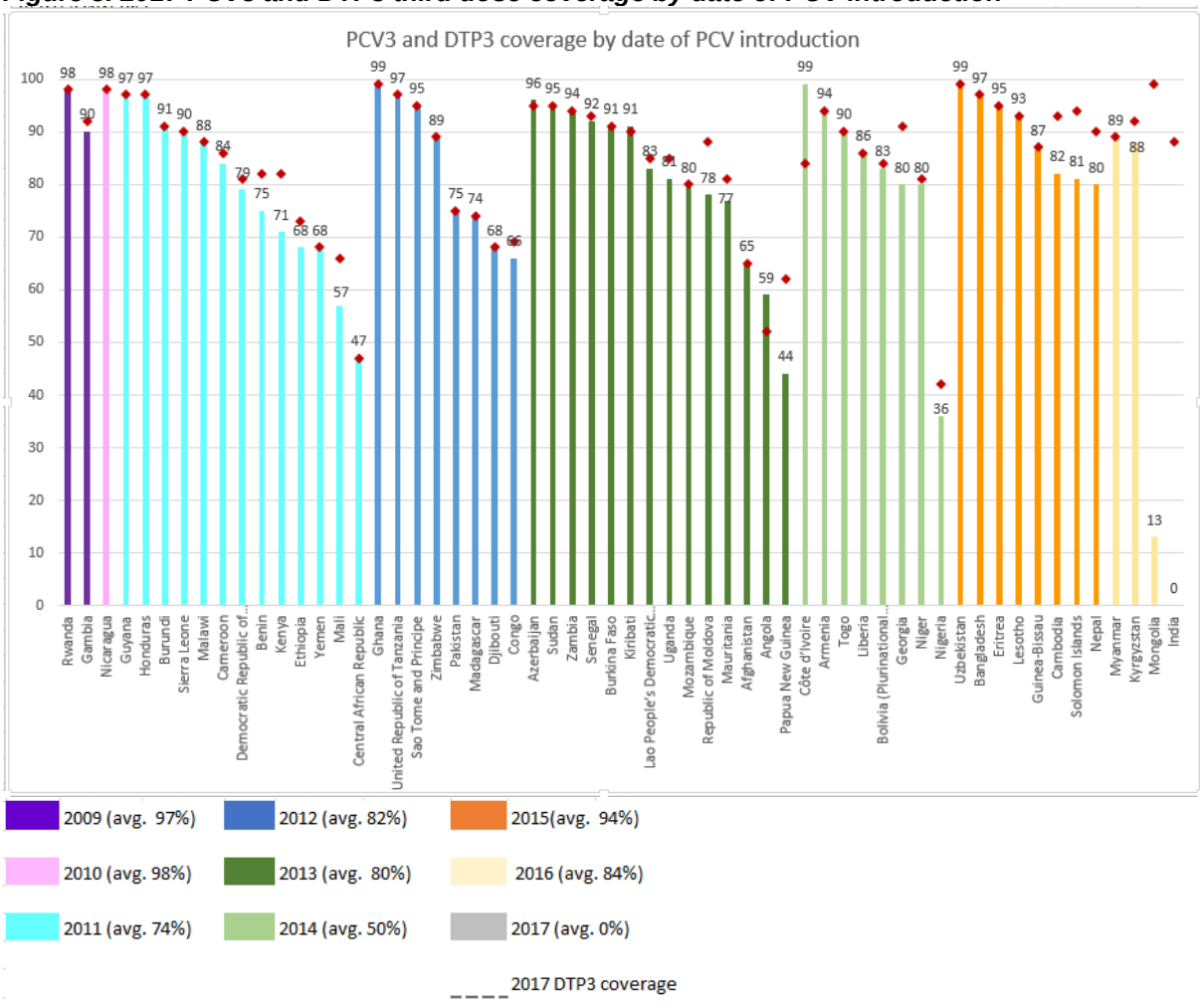


[xx] *Nepal has currently a 2+1 schedule (6 weeks, 10 weeks and a booster at 9 months).*

[xxi] 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 shows PCV3 coverage in 2017 (WUENIC July 2018 data) according to the date of PCV introduction into routine immunisation, versus the 2017 DTP3 coverage (WUENIC July 2018 data). Countries that introduced in 2016 and 2017 may not have had sufficient time to ensure routinisation of the third dose of PCV prior to data collection.

Figure 5. 2017 PCV3 and DTP3 third dose coverage by date of PCV introduction



Note: averages represent weighted means

4.2 AMC Outcomes and Impact Evaluation

In 2015, as stipulated in the AMC monitoring and evaluation 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[7]. 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 Evaluation Advisory Committee (EAC) also submitted an independent assessment of the quality and usefulness of the report.

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 full country evaluations (FCE) project: Bangladesh, Mozambique, Uganda and Zambia. Local research institutions in all four countries are partnering with the Institute of Health Metrics and Evaluation 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 level, 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 8). The 2016 report continued to monitor the routinisation of PCV in all four countries and presented findings of the impact of PCV ion pneumococcal disease burden, based on studies in Mozambique and Bangladesh.

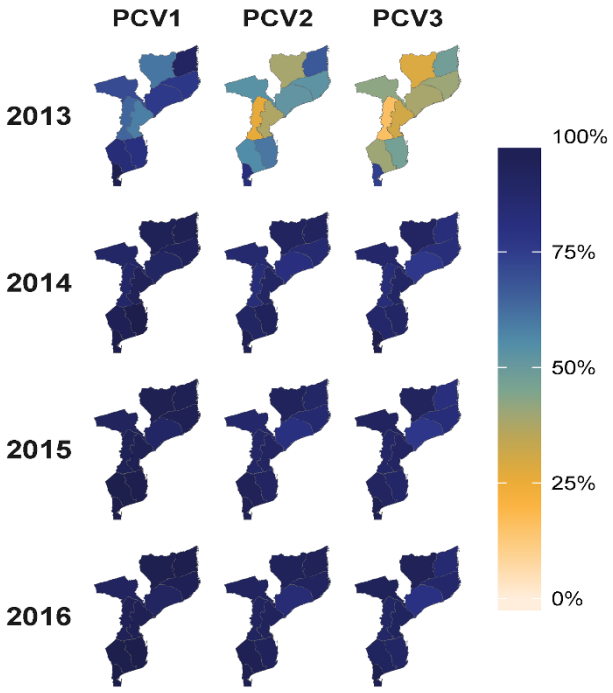
Table 6: Timeline of PCV vaccine introductions in Gavi FCE countries (2013-2016)

	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 rollout 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)

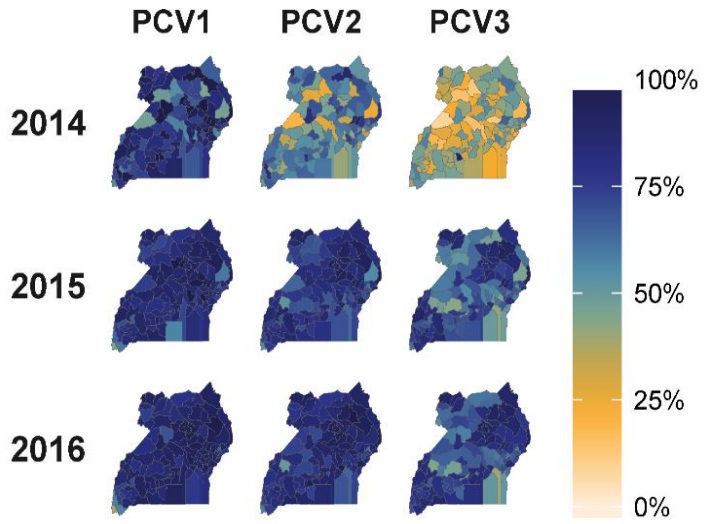
data in Bangladesh, where PCV was was introduced in March 2015, showed that PCV third-dose coverage amounted to 93% – just four percentage points below coverage with the third dose of pentavalent vaccine.

Figure 6. PCV coverage in Mozambique



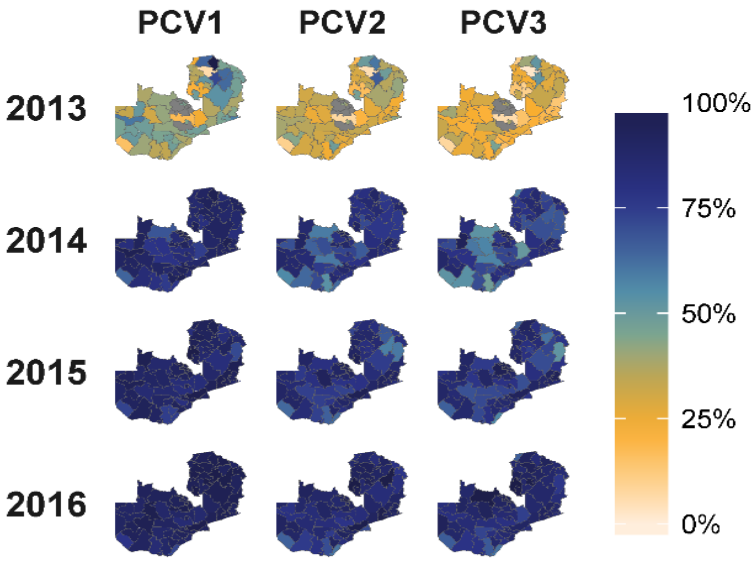
In Mozambique, PCV was introduced in April 2013 and was quickly integrated into the routine EPI system, as demonstrated by the coverage maps in Figure 6.

Figure 7. Map of 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 Uganda's National EPI 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 account for the reported undercoverage of PCV: supply-side challenges causing stock-outs and data quality issues. Although procurement and distribution of vaccines appear to be the main challenges around routinisation, there is a need for further research in this area and the FCE team is continuing to assess this.

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 invasive pneumococcal disease (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 invasive pneumococcal disease (IPD) and pneumonia[xxii].

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 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 1901 specimens were collected and processed among different age groups. In the post vaccine period, a total of 2060 specimens were collected. There were observed reductions in vaccine-type pneumococcal carriage among children who were age-eligible for PCV of approximately 25% but no change among age-ineligible children. There were increases in non-vaccine serotypes of 17%–20% among age-eligible children.

[xxii] 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.

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 a significant reduction in vaccine-type IPD of 94% (95% UI: 65.8, 99; Figure 9). 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

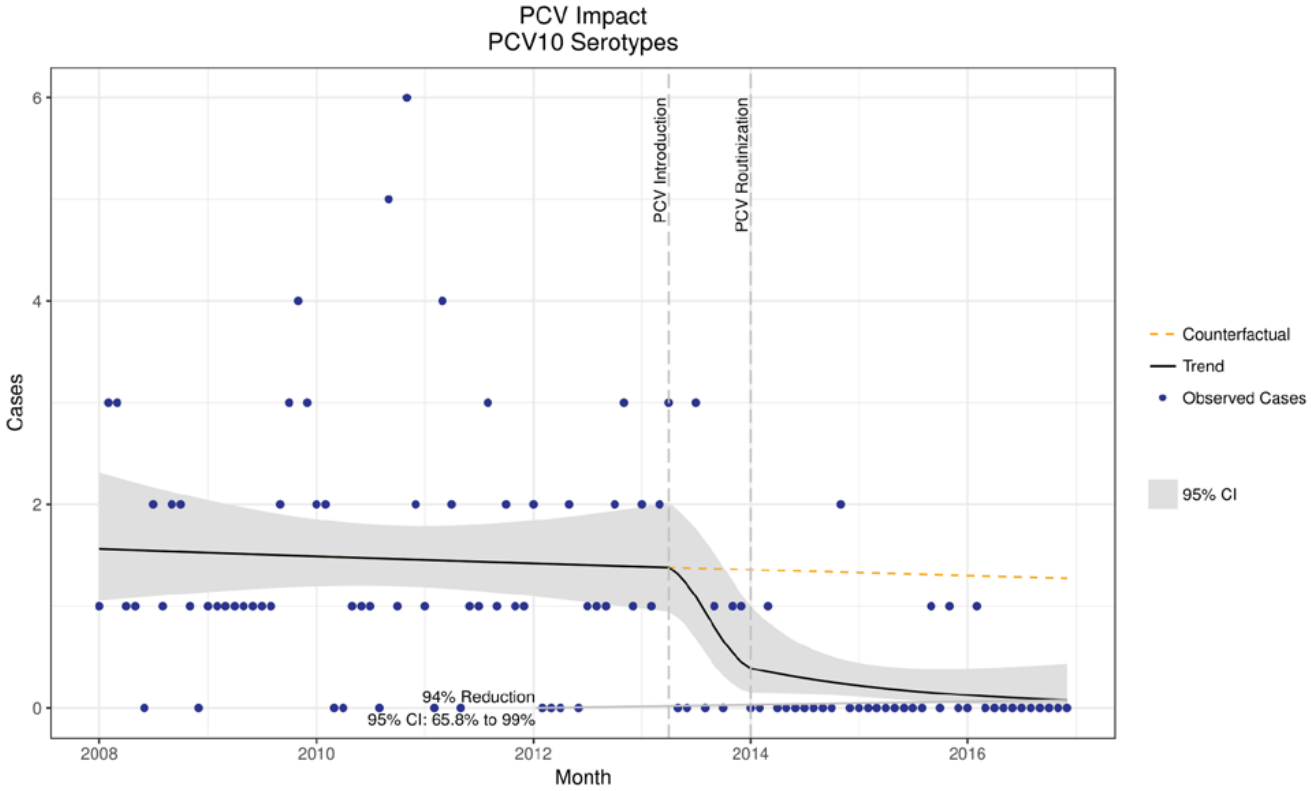


Figure 10: Reduction in X-ray confirmed pneumonia over time in Manhiça DSS

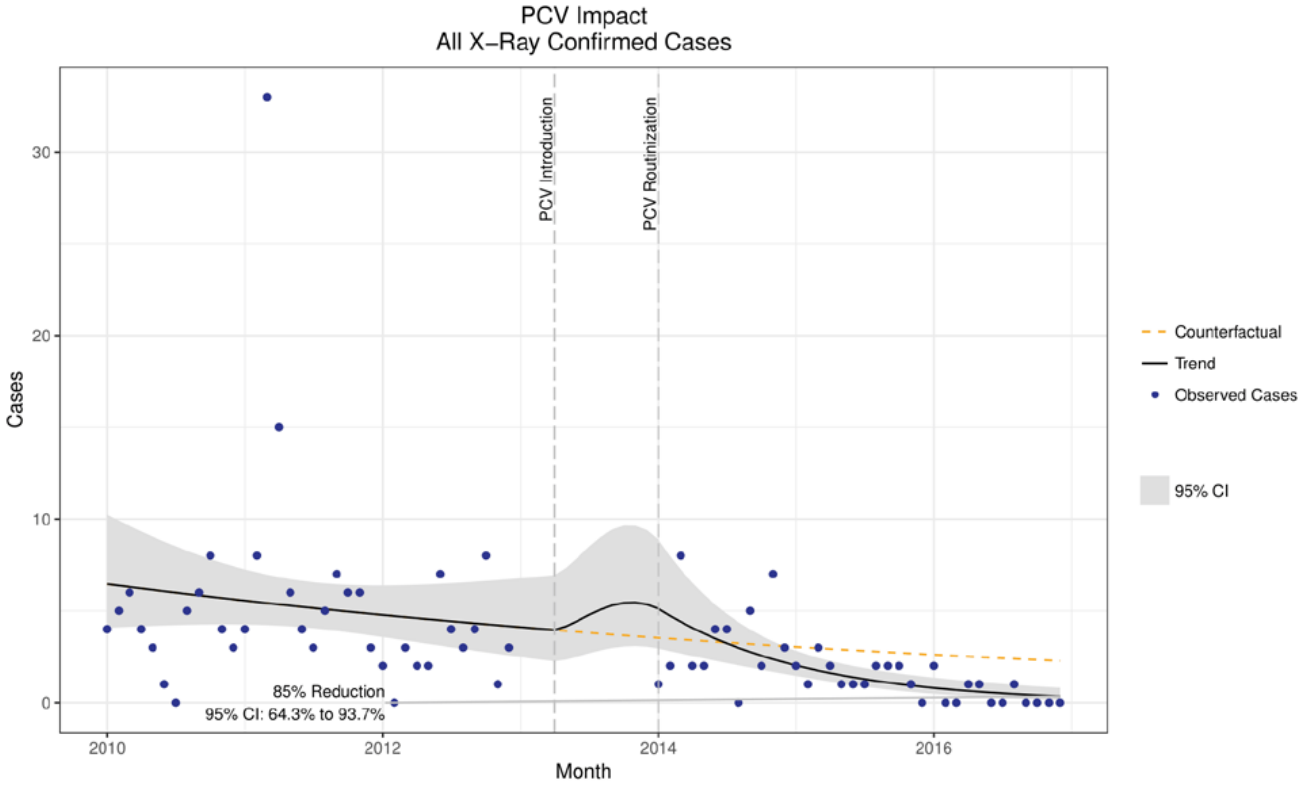
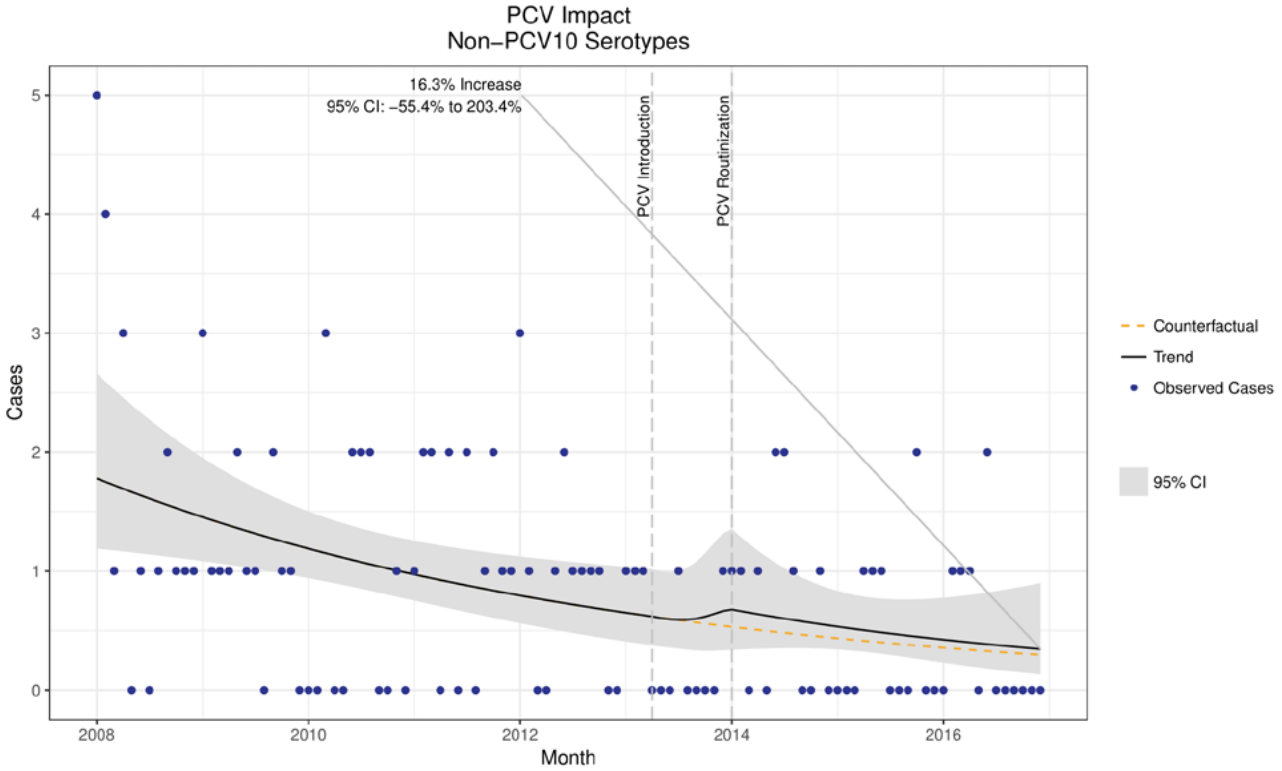


Figure 11: Change in non-vaccine-type IPD over time in Manhiça DSS



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 (see Finding 1 in the 2016 FCE cross-country report for further details). 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 (Figure 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 annual reports[8].

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 2016 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 current projections (Operational forecast version 16 (OPv16) and WUENIC 2018) completed in late 2018, PCV use is expected to avert over 700,000 future deaths among children in Gavi-supported countries by 2020.

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 developing countries. Studies will assess the impact of PCV on health and economic outcomes and monitor potential changes in pneumococcal serotype epidemiology. The status of the historical and ongoing studies and key findings are provided in 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

2020 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[xxiii]) 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 PD 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 magnitude similar to that measured in randomised controlled trials. Results from The Gambia indicated that cases of childhood invasive forms of pneumococcal disease are reduced by more than half with the introduction of PCV.

In June 2013, Gavi issued a 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 Oxford University) to conduct PCV impact studies in Pakistan, Nepal and Lao People's Democratic Republic. These studies are assessing a range of outcomes, including disease effects (e.g. IPD, hospitalised pneumonia and 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 and final results are expected in 2019 for Pakistan and Lao. The Nepal study site has been extended through 2020 to allow for additional long-term monitoring of serotype epidemiology and impact. 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 been extended until 2020 to provide robust post-vaccination data.

Gavi contracted the US Centers for Disease Control and Prevention (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 the end of 2019 to continue monitoring of serotype 1 up to five years after vaccine introduction.

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-

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

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, remains an important goal for Gavi's communications team.

5.1 Communications overview 2018

On World Pneumonia Day 2018, Gavi highlighted the AMC and its impact through its social media channels as well as through AMC-related content provided by IVACC to the Vaccines Work blog. IVACC also curated Gavi's @Vaccines Twitter platform.

Gavi's Board Chair, Ngozi Okonjo-Iweala, published an op-ed in Devex - *'Innovative finance doesn't mean reinventing the wheel'* - which used the AMC as a central argument that there are successful innovative finance models within development that deserve to be emulated.

The AMC was also highlighted in both the printed and online versions of Gavi's Annual Progress Report, as well as Gavi's Mid-Term Review Report. At the Mid-Term Review itself, the AMC was featured prominently in a special session on innovative solutions and was celebrated both for its past success and as a foundation for designing the next generation of effective financial tools for development.

In October 2018 the Gavi media team issued a press release announcing the introduction of PCV into Haiti's routine immunisation programme, securing positive coverage in the Miami Herald, amongst other international news outlets.

Gavi continued to highlight and explain the AMC in relevant communications materials throughout 2018. In addition to sharing updated material, Gavi ensured that appropriate speaking points were incorporated into the speeches of Alliance spokespeople at vaccine launch ceremonies and other events.

5.2 Communications outlook for 2019

2019 will see Gavi's Communications team begin planning for Gavi's replenishment, for which Gavi's innovative financing mechanisms such as the AMC will be a key messaging point. The AMC's success and impact will continue to be built into press releases, speeches, op-eds, features and reports to ensure visibility.

5.3 Donor and stakeholder communication

In 2018, additional efforts were made to provide regular updates to AMC stakeholders, through AMC stakeholder calls and an annual AMC stakeholder meeting. These provided opportunities to exchange information and obtain input from stakeholders on key issues. Topics included consultation on AMC scenarios, strategic demand forecasts and implications, changes in the AMC supply landscape, progress on AMC targets and supply and implementation of vaccines.

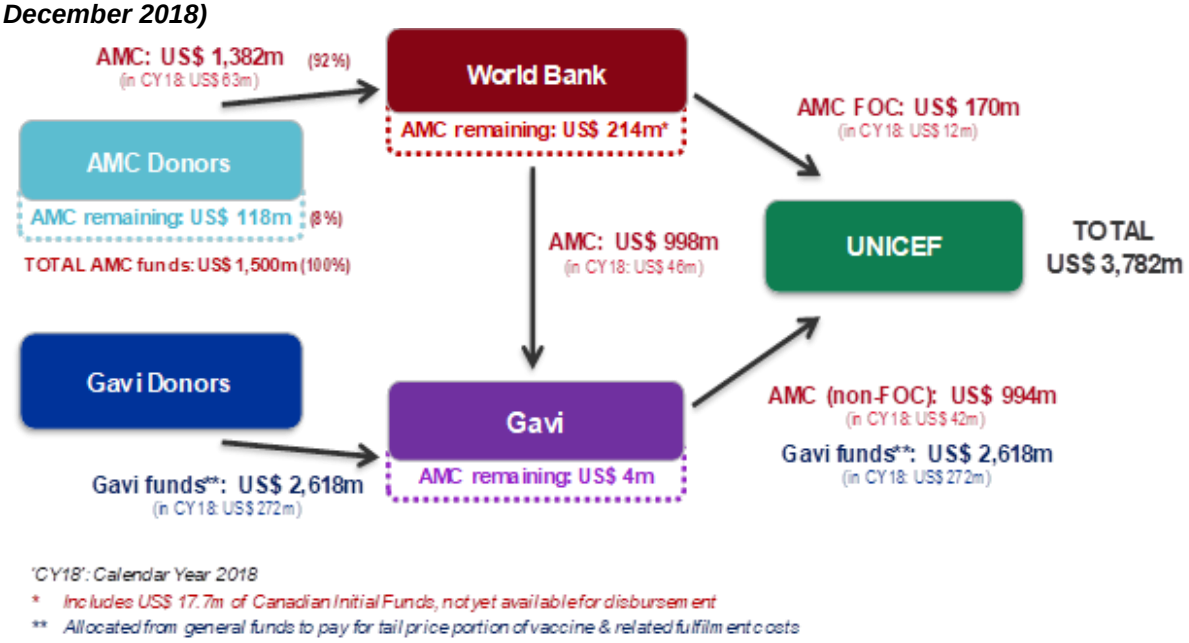
6. Financial activities

The financial structure of the AMC remains unchanged from previous years. It is composed of the six AMC donors (the Bill & Melinda Gates Foundation, Canada, Italy, Norway, Russia and the United Kingdom), the World Bank, Gavi, UNICEF, Gavi-supported countries and eligible vaccine manufacturers.[xxiv]

In summary, the process works as follows: the AMC donors, who have entered into grant agreements totalling US$ 1.5 billion with the World Bank, 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 2018)



'CY18': Calendar Year 2018

* *Includes US$ 17.7m of Canadian Initial Funds, not yet available for disbursement*

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

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

[xxiv] *Refer to AMC Annual Report 12 June 2009-31 March 2010 page 28-29 for the detailed description of the financial structure.*

Details are provided in sections 6.1 - 6.3 below.

6.1 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 together pledged a total of US$ 765 million to the AMC. The three on-demand donors have pledged US$ 735 million (see Table 7). These pledges combined bring the total available AMC funds to US$ 1,500 million, funds that are dedicated solely to the procurement of the pneumococcal vaccine.

6.2 Donor contribution receipts

As of 31 December 2018, the World Bank had received a total of US$ 1,382 million from AMC donors (see Table 7 below). The Bill & Melinda Gates Foundation, the Government of Canada and the Norwegian Ministry of Foreign Affairs have all paid the total amounts that they had committed to pay under their respective grant agreements.

Table 7. Grant receipts from AMC donors, as of 31 December 2018 (in US$ millions)

	Contribution Amount	Paid-in Amount	Remaining Balance
Fixed Schedule Donors			
Bill & Melinda Gates Foundation	50	50	-
Italy	635	588	47
Russia	80	72	8
sub-total:	**765**	**710**	**55**
On Demand Donors			
Canada	200	200	-
Norway	50	50	-
UK	485	422	63
sub-total:	**735**	**672**	**63**
Total	**1,500**	**1,382**	**118**

Source: The World Bank

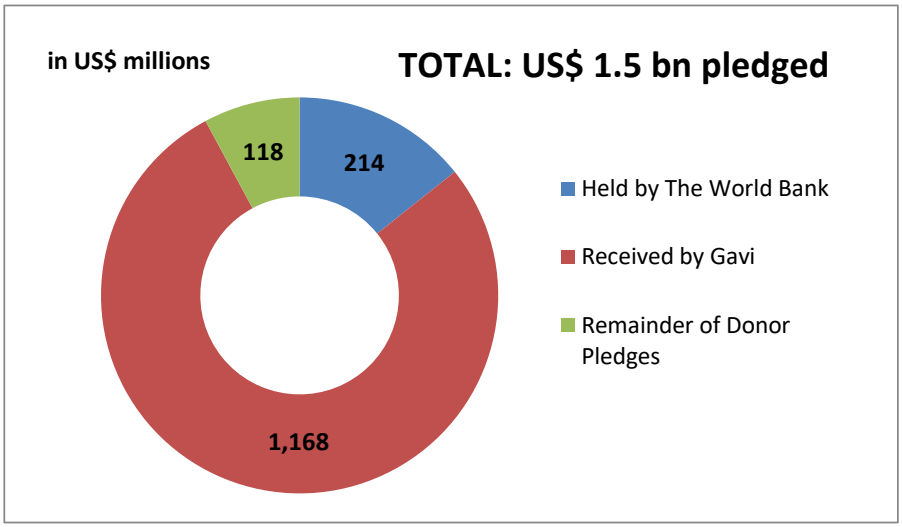
The World Bank has recorded the AMC donor funds in its financial statements as designated assets, with a corresponding liability to provide the funds to Gavi for the purchase of pneumococcal vaccines subject to the terms and conditions of the AMC. To enhance the predictability of AMC funding, the World 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[xxv].

6.3 AMC donor funds: inflow to Gavi

As of 31 December 2018, the World Bank had disbursed US$ 1,168 million (US$ 998 million to Gavi and US$ 170 million to the UNICEF procurement account relating to the Firm Order Commitments). Of the US$ 1,168 million, US$ 58 million[xxvi] was disbursed during 2018 (US$ 46 million to Gavi and US$ 12 million directly to the UNICEF procurement account relating to the Firm Order Commitments). This leaves a balance of US$ 214 million held by the World Bank, of which US$ 196 million is available for immediate disbursement to Gavi (see Figures 12 and 13).

Figure 13. Status of AMC donor funds, as of 31 December 2018 (in US$ millions)



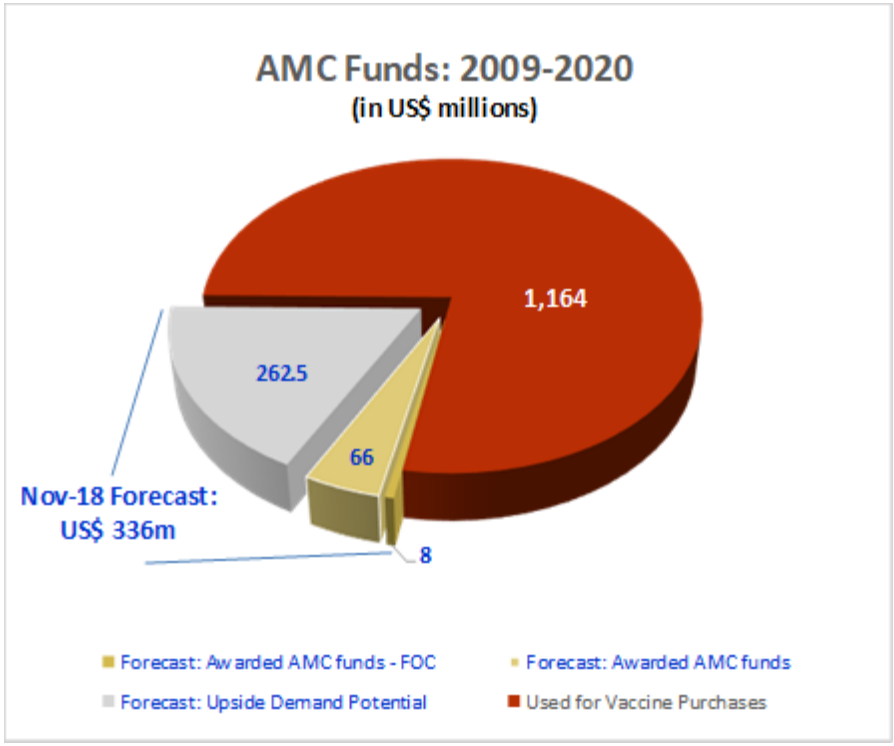
Source: Gavi Secretariat

As part of the reporting process, Gavi regularly submits a Semi-Annual Estimate (SAE) to the World Bank, which provides forecasted demand for pneumococcal vaccine doses and corresponding AMC funding on a rolling three-year basis. Gavi submitted one SAE in March 2018 with forecasted cost for the 2018-2020 time period.

At the November 2018 Gavi Board meeting, the financial forecast presented included approximately US$ 336 million of AMC funds required for the period of 2019-20. This equates to approximately 82 million doses of the pneumococcal vaccine.

Figure 14. Latest forecast of AMC funds needed, as presented at the November 2018 Gavi Board (in US$ millions)

[xxv] 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.



Source: Gavi Secretariat Nov-18 Board Forecast. Note: cash flow basis; some numbers may appear not to add due to rounding.

The AMC Secretariat has highlighted the dependencies underpinning key forecast assumptions regarding PCV demand and supply with the AMC donors throughout 2018. Utilisation of the US$ 262.5 million AMC funds yet to be awarded (shown in the graph above as "Upside Demand Potential") depends upon key demand drivers, particularly assumptions about national roll-outs in India and Indonesia, as noted in Section 1.7 above. Discussions are ongoing with AMC donors and the World Bank as the situation evolves during 2019.

6.4 UNICEF procurement: outflow of AMC donor funds

During 2018, US$ 326 million was disbursed to UNICEF for the purchase of pneumococcal vaccines. Of this amount, US$ 53 million pertains to the AMC-funded portion of the vaccine purchase. The remaining US$ 273 million was allocated from general Gavi funds to pay for the tail price portion of the vaccine purchase and related fulfilment costs[xxvii]. Total funds include the transfers relating to the AMC-funded portion of the minimum purchase obligation, also known as the Firm Order Commitment (FOC), on the seventh supply agreement amounting to US$ 12 million (see Figures 12 and 15).

Seven supply agreements have been signed under the AMC programme, to date. As of 31 December 2018, AMC funding allocated under six of these agreements was fully disbursed, and US$ 69 million for the seventh was also disbursed. The remainder of AMC funding allocated under this seventh agreement is expected to be disbursed during 2019 – 2020.

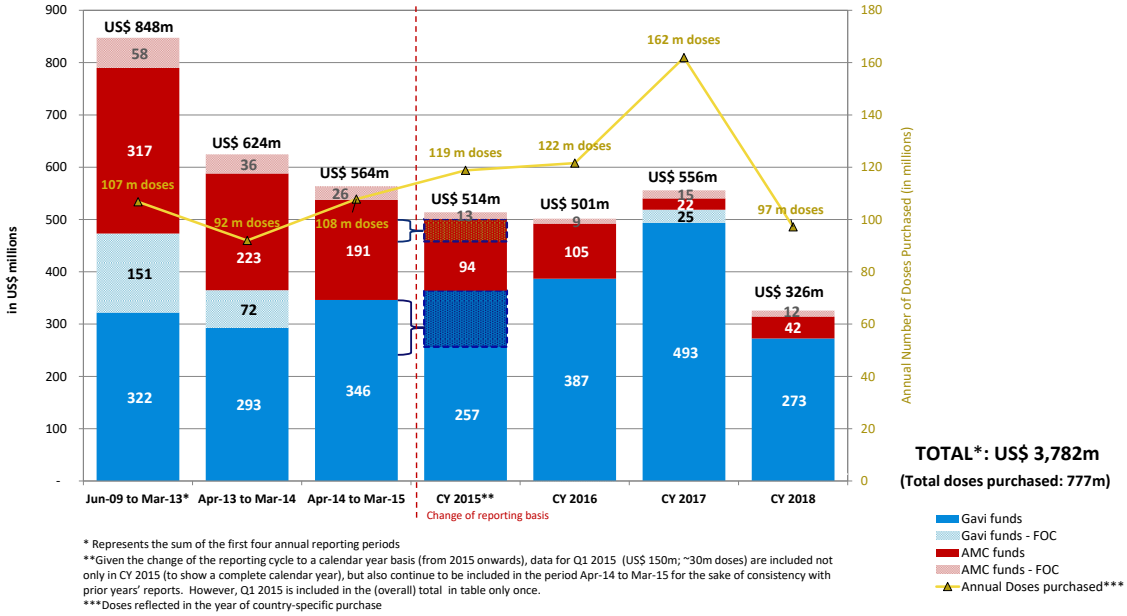
[xxvii] *Fulfilment costs are the extra costs incurred in supplying vaccines (estimated at US$ 0.08 per dose during the 2016-2020 period), in addition to the cost of the vaccine itself. These costs typically include the cost of syringes, safety boxes and freight.*

In total, as of 31 December 2018 US$ 417 million had been transferred to Gavi's 'UNICEF procurement account' regarding the FOCs for the seven existing signed supply agreements. Of this amount, US$ 248 million represents the Gavi-funded portion of the FOCs and US$ 170 million represents the AMC-funded portion of the FOCs. Of the US$ 417 million transferred, US$ 412 million (approximately 99%) has been utilised and this represents the draw-down of already transferred FOC funds relating to all supply agreements.

Figure 15. Total cash disbursements to Gavi's 'UNICEF procurement account' (inception to 31 December 2018, in US$ millions)

in US$ millions

Funding Source	Jun-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	TOTAL	of which: AMC / Gavi	of which: FOC	of which: Non-FOC
AMC Funds - FOC	58	36	26		13	13	9	15	12	170	1,164	170	
AMC Funds	317	223	191	43	94	137	105	22	42	994			994
Gavi Funds - FOC	151	72	-	-	-	-	-	25		248	2,618	248	
Gavi Funds	322	293	346	107	257	364	387	493	273	2,370			2,370
TOTAL:	848	624	564	150	364	514	501	556	326	3,782		417	3,364



* Represents the sum of the first four annual reporting periods
**Given the change of the reporting cycle to a calendar year basis (from 2015 onwards), data for Q1 2015 (US$ 150m; ~30m doses) are included not only in CY 2015 (to show a complete calendar year), but also continue to be included in the period Apr-14 to Mar-15 for the sake of consistency with prior years' reports. However, Q1 2015 is included in the (overall) total in table only once.
***Doses reflected in the year of country-specific purchase

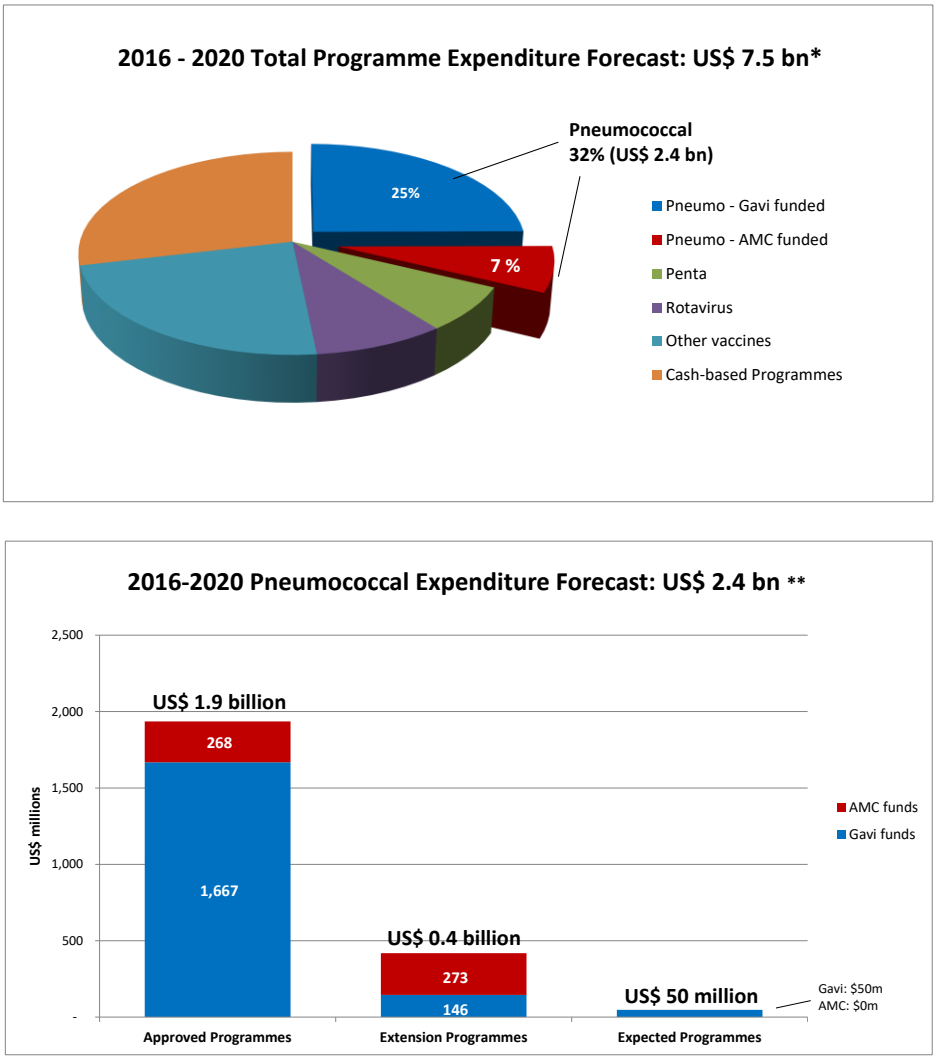
Source: Gavi Secretariat. Notes: 1) For each successive reporting period, the total number of doses purchased has increased relative to the amount of funds disbursed, due to an increasingly higher proportion of doses being procured under the Gavi-funded tail price only; 2) The spike in purchases at the end of 2017 is primarily attributed to an increase in volume in Q4 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.

6.5 The AMC and Gavi's long term financial forecast

At the November 2018 Gavi Board meeting, an update was presented of Gavi's Long Term Financial Forecast[xxviii]. Total programme expenditures are projected to be US$ 7.5 billion for the 2016-2020 period, of which pneumococcal vaccine expenditures are anticipated to amount to US$ 2.4 billion, representing approximately 32% of total programmatic expenditures (see Figure 16).

For the 2019 and 2020 programmatic years, 48 countries had been approved to receive financial support for the procurement of the pneumococcal vaccine. The 2019 commitments amount to US$ 449 million and 2020 commitments amount to US$ 190 million. The commitments are included as part of the total 2016-2020 expenditure forecast, presented in Figure 16 below.

Figure 16. AMC within total Gavi forecasted expenditure 2016-2020



Source: Gavi Secretariat

** Total amount shown does not include US$ 89 million of additional programmatic funding decisions taken at Nov-18 Gavi Board*
** Approved Programmes are those approved by the Gavi Board. Extension Programmes are forecasted continuations of those*

[xxviii] *November 2018 Board Paper entitled "Board-2018-Mtg-2-Doc 05 Financial update including forecast"*

programmes, subject to future approval. Expected Programmes are defined as those which are forecasted based on Operational Forecast v16.0 and the latest supplier assumptions.

7. Challenges and future priorities

The implementation of the pilot pneumococcal AMC has been very successful to date, with high demand and uptake at country level. Some challenges remain nonetheless: there has been a decrease in new country demand in the past 24 months; despite high vaccination coverage overall. A small subset of countries is facing PCV coverage challenges; and countries are starting to transition out of Gavi support and will start to fully self-finance the PCV programme. Moving forward, key priorities include managing the uncertainty of demand, strengthening decision-making processes in countries that have not yet applied to introduce PCV with Gavi support, and continue to sustain PCV implementation and improve coverage in countries that have already introduced the vaccine. As countries start to transition out of Gavi support, measuring impact continues to be key, as is reducing the price of pneumococcal vaccines. Ensuring proper balance of supply and demand also remains a key priority.

7.1 Supporting country introductions and product switches

The Alliance is focusing its efforts on ensuring that the remaining approved countries are ready to introduce pneumococcal vaccines in the 2018-19 period, and that technical assistance is provided where appropriate to ensure high quality of implementation. Alliance partners continue to closely monitor country introduction status and coordinate technical assistance activities, with 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

Supporting the application, introduction and implementation of pneumococcal vaccines in the AMC-eligible countries that have not yet applied also remains a key priority, particularly with regard to the seven countries that remain Gavi eligible. Four of the seven countries are not eligible to apply due to the >70% DTP3 coverage eligibility criterion. In these countries, the current focus of the Alliance is on strengthening the routine immunisation system in the short term. This will help ensure that the vaccine can be introduced as soon as possible to address the high pneumococcal disease burden.

7.3 Sustaining implementation and ensuring high coverage

The Gavi-wide efforts on strengthening of health systems and routine immunisation are also key to addressing the challenges that some of the AMC-eligible countries are facing with PCV implementation. In addition, PCV implementation will continue to be closely monitored to identify issues in coverage performance in specific countries and/or settings. Efforts will also be made to better leverage PCV implementation towards improving coverage and equity of other vaccines, given the high demand for this vaccine at country level.

7.4 Ensuring sustainability for transitioning and transitioned countries

So far, the AMC procurement mechanism has achieved a “tail-price” reduction of, at most, 17% compared with the initial “tail-price” cap of US$ 3.50/dose. The current vaccine price may still be challenging for sustainable

pneumococcal vaccination, especially as countries start to transition out of Gavi support. As outlined in the pneumococcal vaccine supply and procurement roadmap, a key priority objective is to significantly reduce the weighted average price of the “tail price” by 2020. Sustainability is also being addressed through Gavi’s 2016-2020 strategy and PEF, particularly through the strategic focus areas for sustainability and political will.

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 going forward through Gavi-supported special studies. An AMC outcomes and impact evaluation to assess the achievements of the AMC pilot took place in 2015 and was published in early 2016.

7.5 Managing supply and demand

Thanks to the AMC, manufacturers have entered into 10+ 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. While the scaling up of supply has so far been managed with limited interruptions by suppliers and flexibility to supply quantities across years, the coming years will require scaling up of production capacity in order to meet additional country demand. This will demonstrate the ability of the limited supplier base to continue to meet the requirements. As current demand exceeds 160 million doses annually, the limited supply base remains a risk to implementation. The Gavi Secretariat will continue to work closely with UNICEF’s Supply Division to monitor the supply situation and manage the balance between supply and demand.

Conclusion

Country demand for pneumococcal vaccines has been unprecedented, with close to 82% of the 73 AMC-eligible countries already approved for support and 59 country introductions completed as of 31 December 2018. Third-dose PCV coverage increased by 2 percentage points from 2016 to 2017, reaching 43% in 2017. Based on current projections through 2020, PCV-use will avert over 700,000 future deaths among children vaccinated in Gavi countries.

Despite this unparalleled success, as countries enter the pathway to transition out of Gavi support, programme sustainability becomes an area 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 2018

Team	Staff member
Vaccine Implementation	**Veronica Denti** Senior Programme Manager
Resource Mobilisation	**Sebastian Meaney** Head, UK Strategy, Resource Mobilisation
Finance	**Minzi Lam Meier** Head, Financial Forecasting & AMC **Eric Godfrey** Senior Manager, Financial Forecasting & AMC
Monitoring & Evaluation	**Hope Johnson** Director, Monitoring & Evaluation
Public Policy Engagement	**Susan Brown** Director
Communications	**Frédérique Tissandier** Head, Global and Country Media
Market Shaping	**Edward Baker** Senior Specialist, Strategy Development & Tenders **Anna Osborne** Senior Manager, Strategy Development & Tenders
Legal	**Helene Gaudin de Villaine** Associate Legal Counsel

Source: Gavi Secretariat, as of 31 December 2018

Annex 2 – Summary of previous call for offers

7.6 First AMC supply agreements

The first procurement cycle for the supply of pneumococcal vaccines 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 (PSA) with two manufacturers – GlaxoSmithKline Biologicals (GSK) and Pfizer Inc. – the only companies whose Product Summary File (PSF) 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, as part of the AMC Capacity Development Period3F[xxix] Both suppliers have subsequently communicated the ability to increase such early supplies, should there be demand and based on demand, quantities on contracts have been 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 and Pfizer's products received WHO prequalification in 2010 and were deemed AMC Eligible by the AMC Independent Assessment Committee (IAC) respectively on 16 April 2010 and 23 August 2010. 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.

7.7 Second AMC supply agreements

Following the publication of SDF v3.0 in March 2011, Gavi, in consultation with UNICEF, decided to issue a new Call for Supply Offers for the procurement of pneumococcal vaccines that 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 starting 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. will start 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 amounts to 48 million annually.

[xxix]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.

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

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, to contribute to the creation of a healthy market with multiple suppliers, and to enhance the possibility to access lower tail prices through future offers, quantities have been 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 have been 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 Offers and will be available for successive rounds of calls for offers.

7.8 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 pneumococcal conjugate vaccines under the Advance Market Commitment (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 will start 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 amounts 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 amounts to 740 million.

In addition, Pfizer has 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 has provided a financial guarantee for the Tail Price component, equivalent to 80% of the total contracted quantities in the period between 2013 and 2015. The standard AMC commitments of 20%, 15% and 10% in the first three years of each supply agreement will be counted towards the financial guarantee. It has also been agreed to accelerate the procurement of doses at US$ 7.00 under the new supply agreement to ensure that all doses at that price will have been procured before 2016.

As part of these supply agreements, GSK and Pfizer Inc. have agreed to provide a total of 42 million doses during the AMC capacity development period.

UNICEF has opted not to award the full quantities of the Gavi Strategic Demand Forecast for 2017 in response to this third 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, to contribute to the creation of a healthy market with multiple suppliers, and to enhance the possibility of accessing lower tail prices through future offers.

27% of the AMC funds corresponding to US$ 405 million remain unallocated and will be available for later calls for offers.

7.9 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 pneumococcal conjugate vaccines under the AMC. This new supply agreement includes 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 5th 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 are 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 amounts 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, to contribute to the creation of a healthy market with multiple suppliers, and to enhance the possibility of accessing lower tail prices through future offers.

17.5% of the AMC funds corresponding to US$262.5 million remain unallocated and will be available for later calls for offers. Gavi and UNICEF will determine if there is a need to issue a new call for supply offers based on demand presented through applications to Gavi.

Annex 3 – Membership of the PROWG in 2018

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

Organisation	Members
Gavi Secretariat	**Veronica Denti** (August 2016 – present) Senior Programme Manager, Vaccine Implementation, Country Programmes **Karuna Luthra** (April – August 2018) Temporary replacement for maternity leave of Veronica Denti **Melissa Ko** (March 2015 – July 2016) Senior Programme Manager, Vaccine Implementation, Country Programmes **Cassandra Quintanilla** (November 2016 – July 2017) Vaccine Programme Manager, Vaccine Implementation, Country Programmes **Sara Sá Silva** (January – November 2016) Vaccine Programme Manager, Vaccine Implementation, Country Programmes **Mugen Ujiie** (November 2016 – April 2017) Senior Programme Manager, Vaccine Implementation, Country Programmes
PATH	**Allison Clifford** Senior Communications Officer, Center for vaccine Innovation and Access **Laura Kallen** Scientific Communications Officer, Center for Vaccine Innovation and Access
JHU	**Julie Buss Younkin** Scientific Communications Manager, International Vaccine Access Center **Molly Sauer** Deputy Director, Policy, Advocacy & Communications, International Vaccine Access Center
UNICEF Programme Division	**Richard Duncan** Senior Immunisation Specialist, Health Section **Ben Hickler** Communication for Development (C4D) Specialist, Routine Immunisation and New Vaccines, Health Section

UNICEF Supply Division	**David K. Mutuerandu** Contracts Manager, Vaccine Introductions Unit, Vaccine Centre **Abraham Kofi Ntow** Contract Specialist, Vaccine Introductions Unit, Vaccine Centre **Gideon Chelule** Contracts Manager, Vaccine Introductions Unit, Vaccine Centre
WHO	**Adam Cohen** Immunization, Vaccines and Biologicals, IVB/EPI **Alejandro Ramirez Gonzales** Immunization, Vaccines and Biologicals, IVB/EPI **Ikechukwu Udo Ogbuanu** Medical Officer, New Vaccines, EPI
CHAI	**Yann LeTallec** Director, Global Vaccine Delivery **Julia Roper** Senior Associate, New Vaccine Introductions

Source: PROWG Terms of Reference, as of 31 December 2017

Annex 4 – Membership of the Independent Assessment Committee in 2018

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

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

Arthur Elliott
Senior Program Manager, Vaccines and Anti-Viral Agents, US Department of Health and Human Services, USA

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

Shahnaaz Kassam Sharif
Chief Medical Specialist, Senior Deputy Director Medical Services, Head of Preventive and Promotive Health Services, Ministry of Health, Kenya

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

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

Vitaly Zverev
Director, I.I. Mechnikov Institute of Vaccine Sera under the RAMS, Russia

Source: Gavi Secretariat, as of 31 December 2018

Annex 5 – Summary of Gavi investments in targeted assessments

Gavi annually invests approximately US $12 million in targeted assessments (note: excludes Malaria Vaccine Pilots, 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 (2012-2020)	
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 92% in children under 5 years of age. 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, ≥15 years, respectively. There was no significant change in the incidence of non-PCV10 type IPD suggesting no replacement disease. • Hospitalizations for clinical pneumonia had been declining progressively prior to PCV introduction, but fell an additional 27% with the introduction of PCV10; PCV reduced radiologically-confirmed pneumonias 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 $153 which falls well below the WHO cost-effectiveness threshold of 1 GDP per capita, or $1,445.
5.1.2 Impact of PCV on disease, nasopharyngeal carriage, and health economics in Nepal Oxford University (2013-2020)	
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 hospitalized 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 $160 for pneumonia to $370 for meningitis, which translates to 25-50% of the median per capita annual income of $670 in Nepal. • The cost of hospitalized pneumococcal disease per 100,000 children 1-59m ranged from $73,000 to $156,000. About a third of costs were incurred prior to hospitalization. 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 hospitalized 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 (2013-2020)	
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 hospitalized 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 12-23 month old children. 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 Centers for Disease Control and Prevention (2013-2018)	
Objective(s)	• Measure the health impact of PCV use in Burkina Faso
Finding(s)	• In the 3rd year since PCV introduction, the incidence of PCV13-type meningitis significantly decreased among vaccine-age-eligible children, by 87% in children under one year of age, and by 59% in one- to four-year-olds. • Vaccine-type meningitis also declined in older children and adults by 31% and 34%, respectively, suggesting indirect benefits of PCV in unvaccinated individuals. • The impact on serotype 1 is still in question since the incidence was stable over the period from 1 year pre-PCV through the 3 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. • Incidence of non-PCV13 type meningitis among children <5 years was stable for the first 2 years post-PCV but increased 26% in the 3rd 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 12-23 months old by 23% in the first 3 years since PCV introduction; there was no significant decrease in unimmunized infants (5-8 week olds), 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 $340 per patient per episode was much higher than that for pneumonia at $160; however, with a GNI per capita of less than $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 rollout of PCV, coverage increased only marginally (e.g., Penta3 increased from 22% to 39%) and remained low (<40% fully immunized) through the duration of the study • Vaccine-type colonization 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: colonization decreased from pre-PCV to year 3 post-PCV by only 25% and in year 2 of the PCV program the vaccine-type colonization 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 PCV-10 immunization resulted in rapid decline of pneumococcal meningitis children less than 5 years old 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 to 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 BMGF: 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 maximizing 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 invasive pneumococcal disease (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 under 5 years of age, PCV13 reduced all cause pneumonia by up to 39% each year following introduction; this translated to 7-9 prevented hospitalization 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 2–23 months of age 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 $1,616,943 or $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$15-144 per case (up to 29 times the average daily household expenditure in the country)
5.2.11 Cost-effectiveness of PCV10 catch-up in Kenya PneumoADIP Special Studies (2004 – 2013)	
Objective(s)	• Model the impact and cost-effectiveness of PCV catch-up campaigns among under-one year olds, under-two year olds (current WHO recommendations), and under 5 year olds, in Gavi-eligible countries
Finding(s)	• Preliminary results suggest that catch-up campaigns not only lead to more rapid reduction in the IPD burden but also increase efficiency of the vaccine schedule in the first years after vaccination through rapid establishment of herd protection • Any catch-up campaign in the first years after introduction, particularly among under two and five year olds, is likely to prevent a high number of IPD cases for comparatively fewer extra vaccine doses than routine immunization; more targeted campaigns aimed at under 1 year olds achieve additional direct benefits but fewer indirect benefits.
5.2.12 Economic value of vaccination in India PneumoADIP Special Studies (2004 – 2013)	
Objective(s)	• Evaluate the potential health impact and costs averted through immunisation with three vaccines—Hib, PCV, RV vaccines. • Generate new evidence on the health and economic benefits of these vaccines at the national level & in four states in India (Bihar, Delhi, Maharashtra, and Tamil Nadu), specifically in three categories: (i) death & cases averted; (ii) disease costs averted; and (iii) productivity loss averted
Finding(s)	• By introducing and scaling up coverage of Hib, PCV and RV, India could save over US$ 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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