ADVANCE MARKET COMMITMENT FOR PNEUMOCOCCAL VACCINES

Annual Report
1 January – 31 December 2016

Prepared by the AMC Secretariat of Gavi, The Vaccine Alliance

Gavi
The Vaccine Alliance

AMC ADVANCE MARKET COMMITMENTS for vaccines

Contents

Abbreviations

AMC	Advance Market Commitment
AMP	Agence de Médicine Préventive
CDC	US Centers for Disease Control and Prevention
DTP	Diphtheria, Pertussis, Tetanus vaccine
EPI	Expanded Programme on Immunisation
FCE	Full Country Evaluations
FOC	Firm Order Commitment
Gavi	Gavi, the Vaccine Alliance
Gavi Secretariat	Secretariat of Gavi, the Vaccine Alliance
IAC	Independent Assessment Committee
IPD	Invasive Pneumococcal Disease
IRC	Independent Review Committee
M&E	Monitoring and Evaluation
NVS	New Vaccines Support
PEF	Partners' Engagement Framework
PCV	Pneumococcal Conjugate Vaccine
PROWG	Pneumo & Rota Operational Working Group
PSA	Provisional Supply Agreement
PSF	Product Summary File
RFP	Request for Proposals
SD	Supply Division (UNICEF)
SDF	Strategic Demand Forecast
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 Immunisation 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 report is the eighth pneumococcal AMC Annual Report[i] and covers the period from **1 January to 31 December 2016**. This is the second AMC Annual Report where the reporting cycle is aligned with the calendar year; the aim of this change is to increase efficiencies and create alignment with other annual reporting requirements for the Gavi pneumococcal vaccine programme and the AMC Secretariat.

Supply and demand

The pilot AMC for pneumococcal vaccines is now in its eighth year of implementation and significant progress continues to be made.

A total of 164 million doses of pneumococcal conjugate vaccine (PCV) were procured through the AMC in 2016, a 23% increase from 2015 (133 million doses)[ii]. With the current six supply agreements, the total contracted supply amount through 2024 amounts to 1.46 billion doses. Out of the US$ 1.5 billion AMC funds, the two suppliers that have prequalified PCV have been allocated US$ 1.095 billion of the funds. Twenty-seven percent of the AMC funds remain available.

In terms of country demand, 81% of AMC-eligible countries (59 out of 73) have been approved to introduce the AMC-eligible pneumococcal vaccines to date. As of 31 December 2016, 57 countries have introduced these life-saving vaccines, including three during this reporting period (1 January to 31 December 2016)[iii]. The remaining two countries that have been approved for Gavi support are expected to introduce in the coming eighteen months. Despite the remarkable performance in terms of the number of introductions, there continued to be some challenges with introduction delays and vaccination coverage. Drawing from implementation lessons gathered to date, Gavi is strengthening the coordination mechanism among partners, identifying and addressing bottlenecks to assist countries in their pre- and post-introduction activities.

Based on Strategic Demand Forecast (SDF) v11.0 and v12.0, which were approved during the 2015 procurement cycle, the Gavi Secretariat, in consultation with UNICEF Supply Division (SD), decided to not issue a fourth Call for Supply Offers for the procurement of pneumococcal vaccines. The decision to conduct a tender in 2017 will be made by Alliance partners based on the AMC Terms and Conditions, Gavi's 2017 strategic demand scenarios and the outcomes of the latest rounds of applications in 2017 for New Vaccines Support (NVS) to the Gavi Secretariat.

Monitoring and evaluation

AMC progress continues against selected indicators as shown in Table 1. From programme start to 2015 (latest data available), it is estimated that more than 76 million children have been vaccinated with AMC-supported pneumococcal vaccines, with a projection of more than 114 million children vaccinated by 2016

[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.

[iii] Kyrgyzstan, Mongolia and Myanmar introduced in 2016

(actual 2016 data to become available in July/August 2017). The continued scale up of PCV is forecasted to result in the prevention of approximately 740,000[iv] deaths by 2020.

Table 1. Selected non-confidential indicators for AMC progress tracking (calendar year view)

	2009	2010	2011	2012	2013	2014	2015	2016
Objective 1: To accelerate the development of pneumococcal vaccines that meet developing country needs.								
Cumulative number of AMC eligible TPP vaccines	0	2	2	2	2	2	2	2
Cumulative number of AMC registered manufacturers who have made their registration public	0	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
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
Cumulative number of AMC-eligible/Gavi-supported countries that have been approved	3	17	37	46	51	55	58	59
Cumulative number of AMC-eligible/Gavi-supported countries introducing TPP vaccines	0[v]	1[vi]	16	24	38	46	54	57
Coverage of PCV in AMC-eligible/Gavi-supported countries*	0%	1%	5%	9%	19%	28%	35%	n/a**
Cumulative number of children vaccinated with Gavi support (in millions)	-	0.5	4	10	26	48	76	n/a**

Source: Gavi Secretariat

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

*** WUENIC coverage data and WHO-reported number of immunised for 2016 will be available in July 2017*

PCV coverage performance at the country level continues to be tracked, using WHO/UNICEF Estimates of National Immunisation Coverage (WUENIC) data, which are published annually in July for the previous year. Information to date shows that countries continue to successfully introduce PCV into their routine systems, with PCV third dose (PCV3) coverage tracking well against the third dose coverage of

[iv] *While programmatically there was little change in the number of children vaccinated remaining on target and the effectiveness of the vaccine, the impact of the vaccine is revised downward predominantly due to new information on the vaccine preventable burden of disease and slower roll out of the vaccine among high burden populations. These modelled forecasts use the WHO established Child Health Epidemiology Reference Group (CHERG) estimates of causes of child mortality as an input to the models. In the latest version of these estimates pneumococcal related mortality was revised down. Hence the burden preventable by the vaccines was also revised down and this is reflected in the lower impact estimates.*

[v] *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.*

[vi] *Same as above.*

Diphtheria-Pertussis-Tetanus vaccine (DTP3) by the second year of implementation, apart from a small subset of countries.

As part of the AMC monitoring and evaluation framework, and as recommended by the Gavi Evaluation Advisory Committee and agreed by the AMC stakeholders, the first AMC Outcomes and Impact Evaluation took place in 2015 and the final report was published in early 2016[vii].

The Gavi Full Country Evaluations project, which ran from 2013 to 2016, continued to track PCV implementation in Bangladesh, Mozambique, Uganda and Zambia. This Gavi-funded project, which is separate from the AMC monitoring and evaluation framework, has provided important findings and recommendations for programme design and implementation[viii].

Gavi also continues to fund a number of special studies demonstrating the effectiveness and impact of PCV 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 57 countries have now introduced pneumococcal vaccines in their national immunisation schedule.

Financial activities

From 1 January to 31 December 2016, US$ 501 million was disbursed to UNICEF for the purchase of pneumococcal vaccines[ix]. Of this amount, US$ 114 million was from the AMC funds to pay for the AMC-funded portion of the vaccine purchase. The remaining US$ 387 million was allocated from general Gavi funds to pay for the tail price portion of the vaccine purchase and related fulfilment costs[x].

Challenges and priorities ahead

With 59 AMC-eligible countries approved for PCV and 57 having already introduced since the first introduction in 2010, the priorities moving forward will be focused on supporting the two remaining future introductions of countries that have been approved, as well as supporting countries that have not yet applied to access pneumococcal vaccines through the AMC. For countries that have introduced, the priorities remain to sustain PCV implementation and improve coverage, support product switches, as well as measuring impact of PCV, especially as countries start to transition from Gavi support. Reducing the price of pneumococcal vaccines and ensuring proper balance of supply and demand remain key priorities, in addition to continuing strategic discussions on optimal PCV schedules and catch up vaccination.

[vii] *See Section 4.2 for further details or access the full report at http://www.gavi.org/results/evaluations/pneumococcal-amc-outcomes-and-impact-evaluation/*

[viii] *See Section 4.3 for further details*

[ix] *See Section 6.2 for further details*

[x] *Fulfilment costs are the extra costs incurred in supplying vaccines (estimated at US$ 0.14 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.*

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 and 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 diseases, preventing an estimated seven million childhood deaths by 2030. The objectives of the pneumococcal AMC are:

1. **to 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. **to 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. **to 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. **to 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 81% of 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 report is the eighth pneumococcal AMC Annual Report[xi] and covers the period from **1 January to 31 December 2016**. This is the second AMC Annual Report where the reporting cycle is aligned with the calendar year; the aim of this change is to increase efficiencies and create alignment with other annual reporting requirements for the Gavi pneumococcal vaccine programme and the AMC Secretariat.

The report was developed by the AMC Secretariat at Gavi, in collaboration with the World Bank and UNICEF Supply Division (SD), and was approved by the AMC Independent Assessment Committee (IAC) on 10 April 2017.[xii] For more information about the AMC Secretariat, please refer to Annex 1.

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

[xii] Note that as a public document, this report does not include any confidential information.

1. Supply and procurement update

1.1. WHO recommendation and AMC-eligible pneumococcal vaccines

WHO recommends the inclusion of pneumococcal vaccines be given priority in childhood immunisation programmes worldwide, especially in countries with under-five mortality of greater than 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 6 weeks of age. Gavi currently supports PCV for administration in infant routine immunisation programmes.

WHO also states that catch-up vaccination can be conducted as part of pneumococcal vaccine introduction to accelerate herd protection and therefore the PCV impact on disease and carriage[2]. Following discussions in 2012, Gavi deemed it was not able to provide support for catch-up vaccination due to the PCV supply situation at the time. The SAGE Working Group on PCV was established to review the effectiveness of different schedules and strategies for PCV, including the effect of the catch-up vaccination and the preference for a 2+1 or 3+0 schedule, and to provide the appropriate recommendations to SAGE in October 2017; a possible change in schedule will have programmatic implications that would require country support, while a proven impact of catch-up vaccination might prompt Gavi support for those countries that have yet to introduce.

As of 31 December 2016, there are currently two pneumococcal conjugate vaccines (PCV) available for procurement under the AMC. These two vaccines meet the criteria for TPP, which describes the minimum characteristics required for a pneumococcal vaccine to be eligible for AMC financing. No additional manufacturers are expected to have WHO-prequalified vaccines before 2019/2020.

1.2. Pneumococcal conjugate vaccine, 10-valent

The 10-valent PCV (PCV10) is a liquid vaccine 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 IAC. Both doses in the vial are required to be used within six hours of the vial being opened, otherwise, any remaining dose will need to be discarded.

Due to the presentation lacking preservative, WHO requires that countries ensure programmatic readiness to introduce PCV10, with a pre-condition of special training requirements (i.e. specific training on the use of this presentation must have taken place at all levels before shipment and distribution of the vaccine), and the placement of stickers that state ‘do not return an opened vial of PCV10 to the fridge’ on refrigerators at all levels. After countries send a written confirmation to UNICEF, WHO is responsible for assessing that these conditions are met, after which UNICEF and the supplier are authorised to ship the first doses of the vaccine to countries. WHO will also assist the countries in performing post introduction evaluations six to 12 months after the introduction, with a specific focus on assessing health care worker knowledge and behaviour related to the safe use and handling of this vaccine presentation.

GSK is currently developing a 4 dose vial presentation of PCV10[3], which includes preservative and is expected to be prequalified by WHO in late 2017. 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. PCV10 2-dose will continue to be available for countries until PCV10 4 dose vial has acquired local registration.

1.3. Pneumococcal conjugate vaccine, 13-valent

The 13-valent PCV (PCV13) is a liquid vaccine in a one 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 recently developed a 4 dose vial presentation of PCV13, which also includes preservative and with a Phase 3 safety, tolerability and immunogenicity study completed in 2015[4]. The multidose vial presentation obtained WHO prequalification on 14 July 2016 and it was deemed AMC eligible on 9th August 2016. The PCV13 single dose vial presentation remains available after the PCV13 4-dose vial presentation has been prequalified by WHO.

1.4. Supply offers and agreements

There have been three Calls for Supply Offers for supply of PCVs under the AMC to date. The third and last Call for Supply Offers was published in July 2012, followed by the signatures of two new supply agreements in July 2013. A summary of the First, Second and Third AMC Supply Agreements can be found in Annex 2. A summary of the current supply commitments is shown in Table 2 below.

Table 2. Status of overall supply commitments

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 and US$ 3.05 from 2017**	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 and US$ 3.05 from 2017**	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**	2016	US$ 195 million

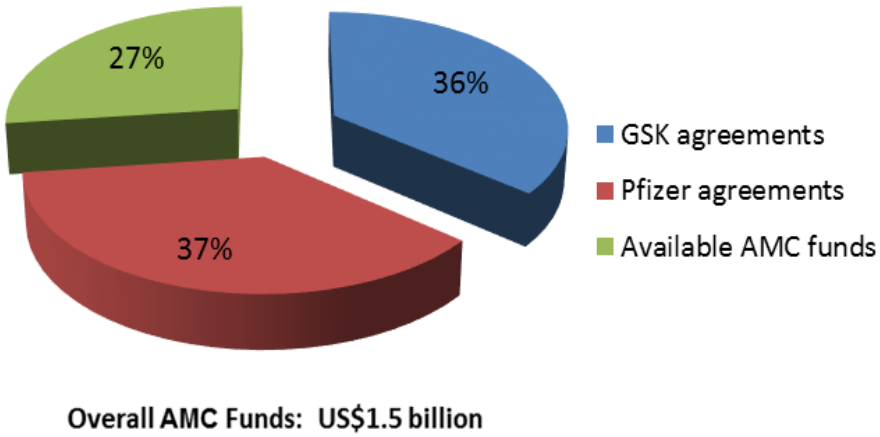
**Reduced tail price as announced on March 2016*

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

The first price reduction achieved under the third Supply Agreements and the second tail price reduction from 2017 will likely contribute to a total savings of US$ 185 million and US$ 285 million respectively over the lifetime of the agreements.

The allocation of AMC funds is summarised in Figure 1.

Figure 1. Allocation of AMC funds



Based on the Strategic Demand Forecast (SDF) v11.0 and v12.0 (see Section 1.7 below), which were approved during the 2015 procurement cycle, the Gavi Secretariat, in consultation with UNICEF SD, decided to not issue a fourth Call for Supply Offers for the procurement of pneumococcal vaccines. The decision to conduct a tender in 2017 will be made by Alliance partners based on the AMC Terms and Conditions, Gavi's 2017 strategic demand scenarios and the outcomes of the latest rounds of applications in 2017 for New Vaccines Support (NVS) to the Gavi Secretariat.

1.5. Doses contracted to date

The number of doses on contract has increased since the 2013 supply agreements have been 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 July 2013.

Table 3. Total annual contracted supply as of July 2013, in millions*

Year	2010	2011	2012	2013	2014	2015	2016 - 2020 [xiii]	2021	2022	2023	2024	TOTAL
Doses procured/ contracted in 2010	5.5	28.9	54	60	60	39.2	300	47.4	5			**600**
Doses procured/ contracted in 2011			13	17	36	36	180	36	36	6		**360**
Doses contracted in 2013				3	19	64.8	250	50	50	49.2	14	**500**
TOTAL	**5.5**	**28.9**	**67**	**80**	**115**	**140**	**730**	**133.4**	**91**	**55.2**	**14**	**1460**

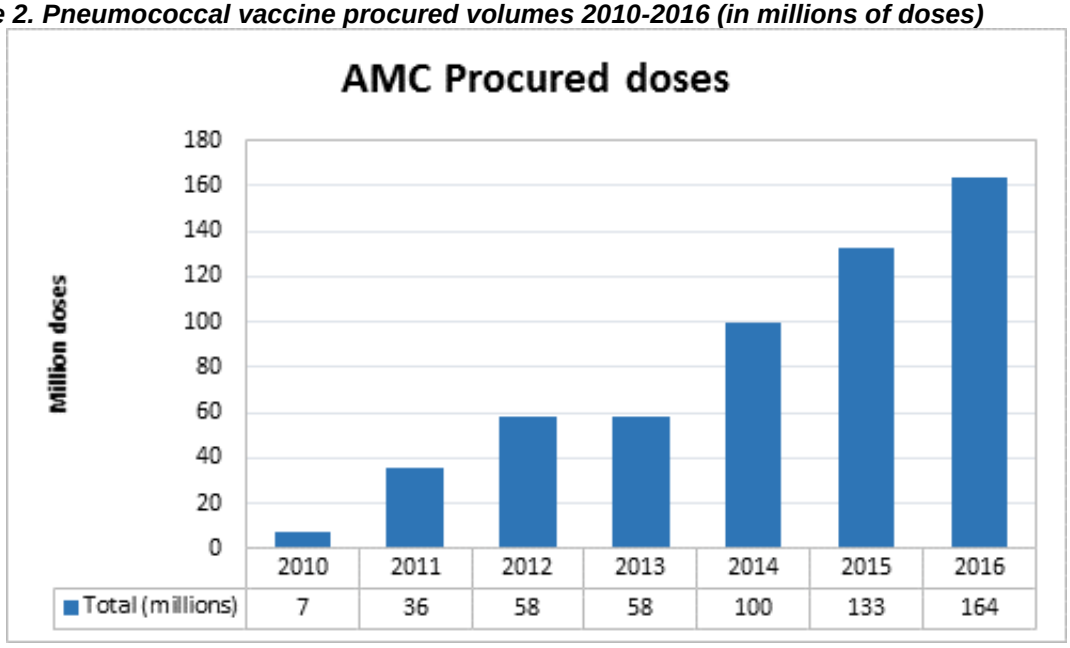
Source: UNICEF Supply Division

** 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 2016

A total of 164 million doses were procured in 2016. The total number of doses procured and delivered from 2010 to 31 December 2016 is summarised in Figure 2 below:

Figure 2. Pneumococcal vaccine procured volumes 2010-2016 (in millions of doses)



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.

[xiii] *In the period 2016-2020, annually contracted doses are 60 (first row, "Doses procured/ contracted in 2010"), 36 (second row, "Doses procured/ contracted in 2011") and 50 (third row, "Doses contracted in 2013").*

It should be noted that special measures were undertaken with both suppliers in 2012 to ensure production at maximum capacity level to ensure 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 (reflected in Figure 3 under 2012 doses). These doses were delivered during 1st 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 (included in Figure 3 under 2016 doses); these doses were delivered in 2017.

1.7. Strategic demand forecasts

Strategic demand forecasts for pneumococcal vaccine have evolved over time, with important changes in the forecasted demand. In early versions of the forecasts, revisions to assumptions about eligibility for Gavi support and country interest in the vaccine were key drivers of changing projections. However, for the last several forecasts the long-term view of demand has become relatively stable between forecasts. On the other hand, projections for the period through 2020 have been revised substantially. The relative instability during this period reflects the uncertainty on the introduction plans for a few large countries, in particular India and Indonesia. Across the forecast versions, the expectation on when these countries will introduce has generally been pushed back; however, the most recent forecasts change this trend with an earlier introduction in India than previously anticipated.

Demand forecasts developed, published and/or analysed in the reporting period are as follows:

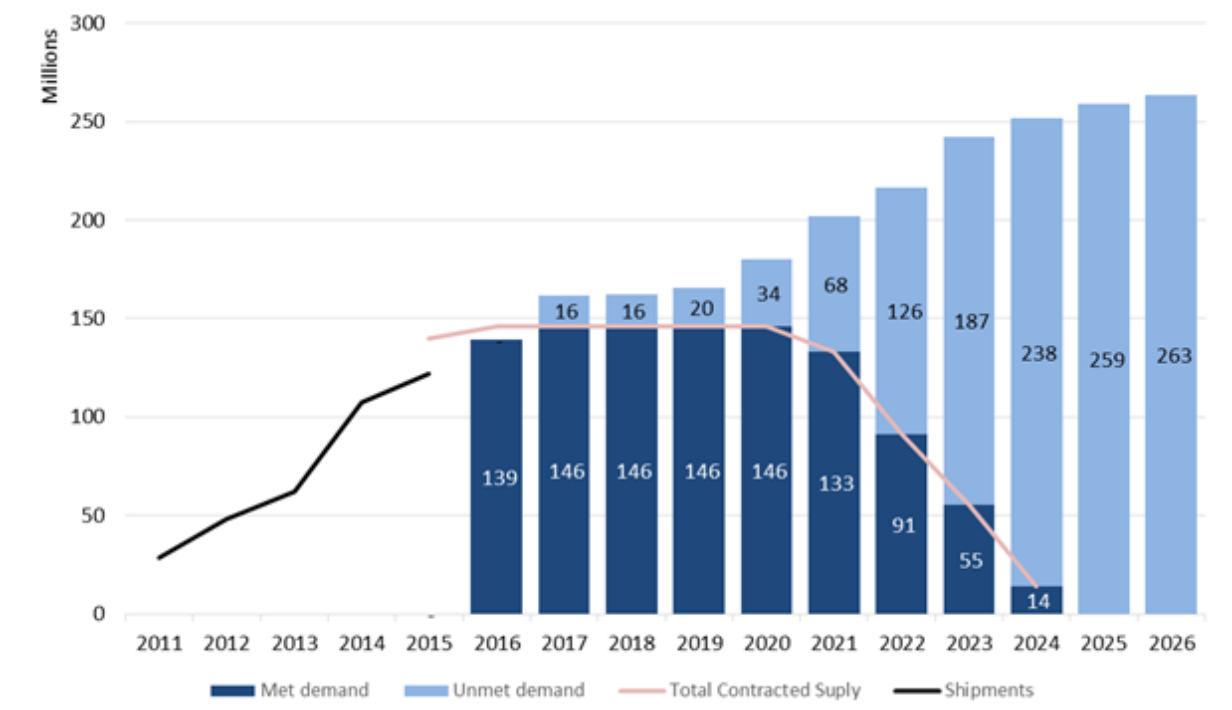
- SDF v12.0 was completed in October 2015 and included in the previous AMC Annual report. It was published on the Gavi website in early 2016[5]. Updates in the forecast include refreshing key inputs to include the latest population and coverage estimates. The forecast also integrates new Gavi eligibility and co-financing policies, as well as some revisions to the projections for new introductions. The Gavi Secretariat and UNICEF completed an assessment of the need for the issuance of the next tender based on SDF v11.0 and v12.0 and concluded that a Call for Supply Offers was not needed[6].
- Demand forecasting for Gavi's v14 [xiv]operational and financial forecast was completed in late 2016. This update includes several improvements to the forecasting approach. For example, the projection of needs for on-going programmes was driven by individual country analysis and triangulation of multiple data sources. The volumes associated with the v14 financial forecast will be published in early 2017. Gavi's strategic demand forecasting is in the process of being improved to be more tailored to addressing specific strategic decision-making needs. The first strategic demand forecasts with this new approach will be published in the first half of 2017. Pneumococcal vaccine will be included in the first set of vaccines that will utilize this new approach.

The latest demand forecast is shown in Figure 3 below. Nearer-term demand aggregated over 2016-2020 is nearly the same as the SDF v12.0 projection included in the last AMC Annual Report, when excluding India. The major change in the forecast is India, with the introduction timing changing from an

[xiv] *The v.13 numbering was skipped from the demand forecasting sequence in order to align with the financial forecast version numbers.*

assumption of 2021 in SDF v12.0 to a Gavi supported and approved introduction in 2017. With the earlier India introduction, total volumes increase by approximately 15% over SDFv12 for the 2016-2026 period. The projection of longer-term demand starting from 2025 remains similar to SDFv12 levels.

Figure 3. Demand Forecasts[xv]



1.8. Availability of pneumococcal vaccines

In 2016, demand for PCV continued to increase. In 2016 UNICEF and Gavi decided not to issue another call for offers. Instead, they agreed to manage the timing of supply of contracted doses by managing carry over doses and 'pulling forward doses' from the end of already signed 10 year AMC supply agreements until additional supply agreements could be executed.

In Q1 2017, Gavi finalised an updated Pneumococcal Vaccine Supply and Procurement Roadmap. It found that the global supply of pneumococcal vaccines is expected to exceed demand of the Gavi 73 during 2017 to 2026. However, in the short term there will be limited buffer capacity as India introduces Gavi-financed PCV in 5 states between 2017-2019 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.

In 2016, GlaxoSmithKline (GSK) announced a subsequent 10% price reduction (to US$ 3.05 per dose) for the PCV10 2-dose vial, while in January 2017, Pfizer announced a new reduced price of US$ 3.05 per dose for its PCV13 4-dose presentation; both changes take effect from January 1st 2017. Price of PCV vaccines will remain a focus of Gavi Alliance efforts in the future.

[xv] *Forecasted demand in Figure 3 is limited to the 73 AMC-eligible countries. There are a few countries (Indonesia, Cuba, Ukraine) that are not included in Gavi's operational and financial forecasting as no direct Gavi financial liability is expected from these countries. To make this graph comparable to prior reports, these countries have been added using the SDF v12.0 forecasted volumes.*

In addition, there are several uncertainties that have the potential to have additional impact on supply and demand over the next 10 years. These include:

- PCV introduction timelines and scale up plans of large countries such as Indonesia and India.
- The market entry of pipeline manufacturers and their achievement of production capacity targets.
- The potential for countries to change their presentation preference
- Potential changes in vaccine schedules (movement to 2+1 and 1+1 schedules and catch ups) which will be discussed at SAGE in coming years could have an impact on long term demand.

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
- Driving continued price reductions.

Additional detail can be found in the Pneumococcal Roadmap public summary, published 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 the Gavi 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 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 to take 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[7]:

- GlaxoSmithKline (GSK) Biologicals (Belgium)
- Panacea Biotec Ltd. (India)
- Pfizer Inc. (U.S.)
- Serum Institute of India (India)

To date, only two of these manufacturers are producing WHO prequalified and AMC-eligible pneumococcal vaccine, while the rest are not expected to have WHO prequalified vaccines before 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

As of 31 December 2016, 59 of the 73 AMC-eligible countries (81 %) have applied and been approved for support for pneumococcal vaccines.

Gavi opened three NVS application rounds in 2016, with a deadline for countries to submit applications by January, May and September 2016 for review by the Independent Review Committee in March, June and November 2016, respectively. However, no new countries applied for PCV support through the AMC during these three applications rounds. In December 2015, the Gavi Board approved a new Gavi-India partnership strategy to provide support for the introduction of new vaccines, it was under this tailored approach that India submitted their application for PCV support in May 2016, and was approved in September 2016. Further information on non-supported countries is provided in Section 2.5 below.

2.2. Introduction of PCV in countries in accelerated transition or transitioned from Gavi support

In June 2010, the Gavi Board approved that all Gavi-eligible countries as per the 2003 definition continue to have access to pneumococcal vaccines through Gavi under the terms and conditions of the AMC. As a result of this Board decision, countries in accelerated transition or fully self-financing[xvi] that have not yet been approved for pneumococcal vaccine are able to apply and introduce this vaccine under the terms and conditions of the AMC, provided that they procure through UNICEF. However, these countries will need to self-finance the tail price component of the AMC price from the outset. Also, all countries must have achieved DTP3 coverage at or above 70% according to WHO/UNICEF estimates. Accelerated transition or fully self-financing countries that have not yet applied and are eligible to do so are as follows:

	Eligible to apply according to DTP3 coverage (>70%)	Not eligible to apply according to DTP3 coverage (<70%)
Eligible to apply according to transition phase	Comoros, Korea DPR and Tajikistan	Chad, Guinea[xvii], Somalia and South Sudan
Accelerated transition or fully self-financing (can access AMC prices)	Bhutan, Cuba[xviii], Indonesia, Sri Lanka, Timor-Leste and Vietnam	Ukraine

2.3. Pneumococcal vaccine introductions

As of 31 December 2016, 57 countries have introduced pneumococcal vaccines supported by the AMC. Three of these introductions took place in the period between 1 January and 31 December 2016 (versus eight in 2015). All the introductions that have taken place to date are outlined in Table 4 below.

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

[xvii] Guinea, although it does not currently meet the requirement of 70% DTP3 coverage, is planning to introduce PCV in 2018 through the Country Engagement Framework process. The country would need to meet the 70% DTP3 coverage requirement ahead of the introduction.

[xviii] Cuba is planning to introduce PCV7, hence it would not access AMC products/prices.

The Gavi Strategic Goal target of 45 PCV introductions in Gavi countries by the end of 2015 was successfully reached, with the 45th introduction taking place in Georgia more than one year ahead of schedule. This represents a rate of introduction in Gavi countries more than three times faster than Pentavalent (DTwP-HepB-*Hib*) vaccine introduction over an equivalent period[xix]. Gavi's 2016-2020 Strategy does not include targets for pneumococcal vaccine introductions or coverage, using instead a composite indicator tracking overall coverage of all vaccines in Gavi's portfolio.

Of the 57 countries with Gavi-supported pneumococcal vaccine programmes, 11 countries were using PCV10, whereas the remaining 46 countries were using PCV13. In 2016, only Mozambique requested a switch in PCV product (from PCV10 to PCV13) and will be switching in 2017; while 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
	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, DR	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 Rep	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

[xix] *More than 54 PCV introductions in Gavi countries in the first five years of the programme (Dec 2010- Nov 2015), in comparison to 14 Pentavalent vaccine introductions in the equivalent period (2001-2005).*

	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 North	PCV13	Introduced in August	30
	Moldova	PCV13	Introduced in October	31
	Lao PDR	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 IPV)	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

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

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 approved countries[xx] at the time. Given the low number of introductions in 2016, this analysis was not updated this year, but it will 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. Training and cold chain readiness remain the key bottlenecks, as well as the availability of funds (either due to delays in disbursement from Gavi to countries and/or to funding flow issues within the country as a result of decentralisation, for example) and competing priorities at country level, such as multiple concurrent vaccine introductions and campaigns. As highlighted in Section 2.6 below, Gavi continues to strengthen its resource allocation and coordination mechanisms to ensure that these key cross-cutting bottlenecks are addressed in future introductions.

2.4. Future pneumococcal vaccine introductions

Two Gavi countries already approved for pneumococcal vaccine support through the AMC are expected to introduce the vaccine in 2017. These future pneumococcal vaccine introductions are outlined in Table 5 below.

Table 5. Future planned pneumococcal vaccine introductions

Year	Country	Product	Status	Cumulative No.
2017	India	PCV13	Planned for Q1[xxi]	58
	Haiti	PCV13	Planned for Q4	59

2.5. Future pneumococcal vaccine applications

From the 73 AMC-eligible countries, only 14 (19 %) have not yet been approved to access pneumococcal vaccine through the AMC. Although a subset of these countries has expressed strong interest in introducing the vaccine in the near future, only three are eligible to apply to access Gavi support in 2017 based on Gavi eligibility and on DTP 3rd dose (DTP3) coverage, which must be higher than 70% (based on WHO/UNICEF Estimates of National Immunisation Coverage) as per Gavi application guidelines – Comoros, Korea DPR, and Tajikistan.

There are also six countries in accelerated transition or transitioned from Gavi support that are eligible based on DTP3 coverage and can access PCV through the AMC, but these will need to fully fund the vaccine from the programme outset – Bhutan, Cuba, Indonesia, Sri Lanka, Timor-Leste, and Vietnam. The remaining five countries are currently ineligible due to <70% DTP3 coverage – Chad, Guinea, Somalia, Ukraine[xxii] and South Sudan. Gavi will continue to support strengthening of health systems and routine immunisation in these countries to ensure adequate readiness to introduce PCV and other vaccines in the future.

There will be three rounds for NVS applications in 2017 during which countries can apply for PCV support. Table 6 shows the timeline for new application submission, review and decision. The existence of three

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

[xxi] *India's introduction was initially planned for March 2017, but the latest information indicates introduction in Q2*

[xxii] *Ukraine is a fully self-financing country but is still eligible to procure from UNICEF Supply Division under the AMC.*

separate rounds provides more flexibility and better alignment with countries' timelines and planning cycles.

Table 6. 2017 Gavi NVS application timelines

	Round 1	Round 2	Round 3
Deadline for application submission	18 January 2017	3 May 2017	8 September 2017
Application review dates	13-24 March 2017	14-23 June 2017	3-17 November 2017
Gavi Board decision	By June 2017	By November 2017	By March 2018

In addition to the NVS application rounds, there is a new process to access Gavi support – the Country Engagement Framework (CEF). This is a tailored approach, aligned with a country's strategic multi-year plan which 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 has already started their CEF process and have indicated their interest in introducing PCV (although currently not eligible due to low DTP3 coverage), while Comoros will also present their request through CEF in 2017.

An update on the outcome of the 2017 applications rounds and status of PCV requests through CEF will be provided in the next AMC Annual Report.

2.6. Coordination and support for pneumococcal vaccine introductions and implementation

With the transition from the Business Plan to the Partners' Engagement Framework (PEF) for the 2016-2020 strategic period, Gavi continues to strengthen its coordination mechanisms with partners to ensure that technical assistance to countries can be delivered more efficiently and effectively. The new PEF structure, split between Foundational Support, Targeted Country Assistance and Strategic Focus Areas, ensures that Alliance resources, including technical assistance, are delivered more efficiently and effectively to address key bottlenecks at country-level.

At the global level, the Pneumo and Rota Operational Working Group (PROWG) was established in 2011 with the aim of facilitating effective partner coordination, including country communication and operational decision-making, in order to create favourable conditions for Gavi-supported countries to succeed with the application, introduction, and sustained use of pneumococcal and rotavirus vaccines as per Gavi's mission and AMC goals and objectives.

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

- Monitor and support country application development, including development of introduction plans.
- Monitor preparedness issues and implementation milestones for successful launch and sustained use of the vaccines.
- 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, determine technical assistance needs and mobilise relevant resources to ensure successful application, programme planning and implementation.
- Gather lessons learned and analyse experiences to optimise and improve future introductions.

In the context of the new Gavi strategic cycle 2016-2020 and the evolving pneumococcal vaccine programme lifecycle, the PROWG objectives and terms of reference will be revisited. A list of current PROWG members is provided in Annex 3.

At the country level, programmatic challenges post-introduction are being gathered through Post Introduction Evaluations (PIEs), which are evaluations of the overall impact of the introduction of a new vaccine(s) on a country's national immunisation programme. PIEs are conducted as standalone assessments or as part of comprehensive Expanded Programme on Immunisation (EPI) reviews. During 2016, five countries[xxiii] have conducted a PIE for PCV. 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 to the vaccine. 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. The PIEs carried out to date have identified 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 as well as reporting and monitoring. Resolution of these aims to be addressed through PEF, and in particular through the Targeted Country Assistance. The Gavi Full Country Evaluations also provided relevant lessons learnt regarding routinisation of PCV[xxiv].

2.7. Global Action Plan for the prevention and control of Pneumonia and Diarrhoea (GAPPD)

In 2013, WHO/UNICEF published the integrated Global Action Plan for the Prevention and Control of Pneumonia and Diarrhoea (GAPPD)[8]. GAPPD proposes a cohesive approach to ending preventable pneumonia and diarrhoea deaths and provides a roadmap for national governments and their partners to plan and implement integrated approaches for the prevention and control of pneumonia and diarrhoea. It 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.

Gavi works within this broader context, supporting the advancement of GAPPD and funding pilot projects until 2015 with this objective. As pneumococcal vaccines are introduced, and their coverage approaches that of DTP3 immunisation, this presents 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 to describe in their PCV applications the status of implementation of other complementary interventions for disease prevention and control, and how they could leverage the opportunity of new vaccine introduction to strengthen an integrated approach. This was not designed to raise the

[xxiii] *Burkina Faso, Cote d'Ivoire, Eritrea, Kyrgyzstan and Nigeria*

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

requirements for proposal approval, but rather, as an opportunity to prompt countries' consideration and planning on comprehensive disease prevention and control at the time of proposal development.

On World Pneumonia Day 2016, the WHO department of Maternal Child and Adolescent Health (MCA) launched a Monitoring and Visualization Tool for GAPPD[xxv]. This tool allows users to review progress against the SDG 3 and GAPPD target towards ending preventable under-five deaths from pneumonia and diarrhoea by 2030. The data is classified on 24 key indicators related to the protection, prevention and treatment of diarrhoea and pneumonia in children under five years of age and two indicators on mortality due to the two diseases. The tool allows you to access country-specific profiles for 136 countries, and thus review specific coverage and health impact indicators that will be useful to avert childhood diarrhoea and pneumonia deaths.

[xxv] http://www.who.int/maternal_child_adolescent/epidemiology/gappd-monitoring/en/

3. AMC Independent Assessment Committee

The Independent Assessment Committee (IAC) serves a number of key functions. Most importantly, it has the mandate to review and approve the Target Product Profile (TPP) and thereby the minimum technical requirements that candidate products must meet to be eligible for AMC funding[xxvi]. In addition, the IAC establishes when and if an adjustment of the pre-set long-term price of vaccines is necessary. During the current reporting period, IAC members met twice (in June and August 2016) to review Pfizer's application for AMC eligibility of the PCV13 4 dose vial presentation, in addition to being called upon to approve the AMC Annual Report.

The IAC currently comprises nine members representing expertise in: public health, health economics, vaccine business development, vaccine industry economics, contract law, public-private finance and clinical performance and delivery systems. A list of IAC members can be found in Annex 4.

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, hence the membership of three IAC members will be revised in 2017 and the IAC Selection and Oversight Panel will appoint a successor.

[xxvi] *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 in conjunction with 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;
- Impact Evaluations every four years from the entry into the first AMC supply agreement to assess the achievements of the AMC and 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

Gavi has a comprehensive PCV results framework currently being used for regular monitoring of the Gavi pneumococcal vaccine programme and the AMC. At the end of 2015, some additional indicators were added to reflect the new Gavi strategy 2016-2020. Table 7 below highlights some of the key indicators being tracked, for which information can be made publicly available.

Table 7. Selected non-confidential indicators for AMC progress tracking (calendar year view)

	2009	2010	2011	2012	2013	2014	2015	2016
Objective 1: To accelerate the development of pneumococcal vaccines that meet developing country needs.								
Cumulative number of AMC eligible TPP vaccines	0	2	2	2	2	2	2	2
Cumulative number of AMC registered manufacturers who have made their registration public	0	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
Objective 3: To accelerate vaccine uptake by ensuring predictable vaccine pricing for countries and manufacturers.								

	2009	2010	2011	2012	2013	2014	2015	2016
Cumulative number of countries that have applied for Gavi support for PCV	21	21	49	52	59	59	59	60
Cumulative number of AMC-eligible/Gavi-supported countries that have been approved	3	17	37	46	51	55	58	59
Cumulative number of AMC-eligible/Gavi-supported countries introducing TPP vaccines	0[xxvii]	1[xxviii]	16	24	38	46	54	57
Coverage of PCV in AMC-eligible/Gavi-supported countries*	0%	1%	5%	9%	19%	28%	35%	n/a**
Cumulative number of children vaccinated with Gavi support (in millions)	-	0.5	4	10	26	48	76	n/a**

Source: Gavi Secretariat

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

*** WUENIC coverage data and WHO-reported number of immunised for 2016 will be available in July 2017*

Pneumococcal vaccine coverage performance in Gavi countries continues to be closely monitored. In 2015, 3rd dose coverage amongst 73 Gavi-eligible countries was 35%, based on the WUENIC data published in July 2016[9], a 7% point increase in relation to 2014. For the subset of Gavi countries that introduced the vaccine prior to 2015 (n=54), 3rd dose coverage has reached 76% (omitting countries that introduced in 2014) or 72% as unweighted average. The current projection for 3rd dose coverage in 2016 is 46%; Gavi's 2016-2020 strategy does not define targets for PCV coverage, rather utilising a composite indicator tracking overall coverage of all vaccines in Gavi's portfolio. Actual 2016 data will become available in July 2017 and reported in the next AMC Annual Report.

Figure 4 shows the PCV3 coverage in 2015 (WUENIC July 2016 data). For the same group of countries, DTP3 coverage was 85%, demonstrating that most countries continue to successfully introduce PCV into their routine systems. Eleven countries have more than 90% relative PCV3 coverage as a percentage of DTP3, while there is a similar number of countries that are below 87%[xxix]. Three countries (Georgia, Papua New Guinea and Armenia[xxx]) have less than 50% of PCV3 coverage as a percentage of DTP3 coverage; the situation in these countries is being closely monitored and bottlenecks are being addressed through Alliance support.

A few countries had chosen to move the PCV 3rd dose administration to a later visit (e.g. Nepal, 9 months[xxxi], with measles first dose; Bangladesh, 18 weeks, visit for PCV only; Moldova, 12 months). Information from the PIE in Bangladesh indicated that the PCV coverage was not optimal; however, further review during a Full Country Evaluation indicated that the coverage had increased towards a 1:1

[xxvii] *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.*

[xxviii] *Same as above.*

[xxix] *This analysis excludes mid-2015 introductions and phased introductions.*

[xxx] *Armenia introduced PCV in September 2014, and so only 45 % of children were included in the denominator (up to 11 months and 29 days) in 2015. Coverage figures are expected to reach regular levels in 2016 and beyond.*

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

ratio between PCV and DTP by the second half of 2016[xxxii], and a decision from the National Committee for Immunization Practices (NCIP) in January 2017 moved the PCV 3rd dose administration to 14 weeks. In the case of Nepal, the change is not in line with WHO recommendation, which recommends at least 8 weeks between 1st and 2nd dose in the 2p+1 schedule. Immunogenicity studies are currently being carried out in Nepal to ensure that the change to a novel schedule does not affect the immunogenicity of PCV.

Figure 4. 2015 PCV3 coverage across Gavi countries

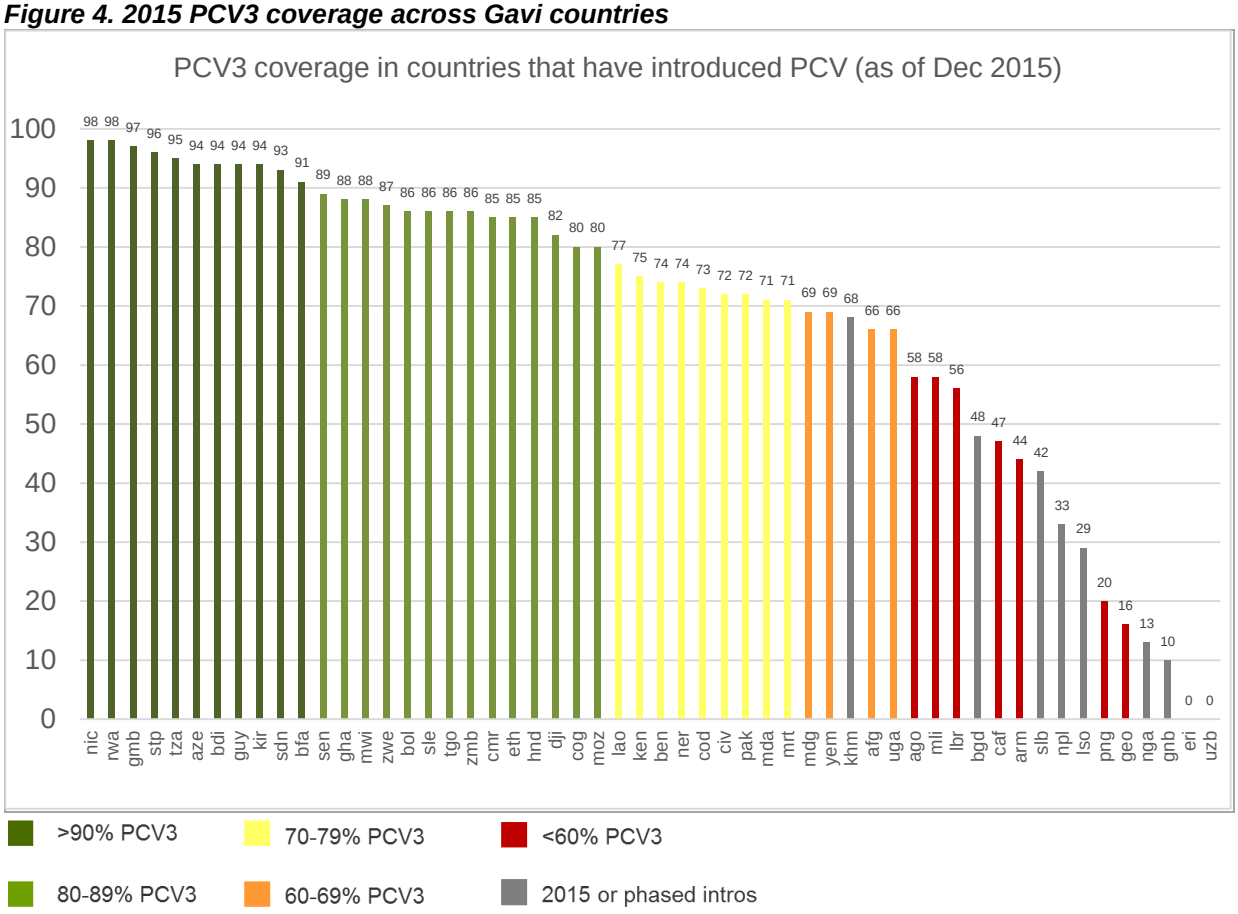
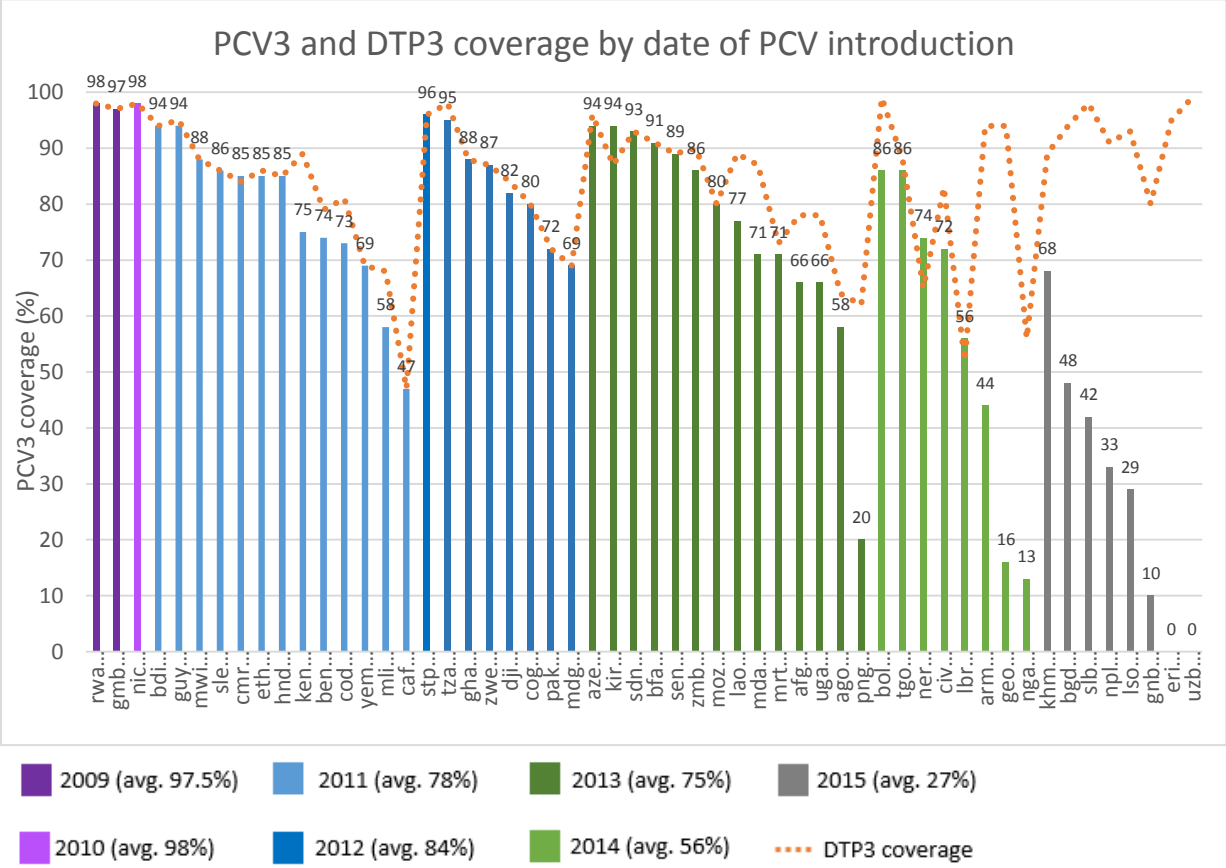


Figure 5 shows the PCV3 coverage in 2015 (WUENIC July 2016 data) according to the date of PCV introduction in routine immunisation, versus the DTP3 coverage in 2015 (WUENIC July 2016 data). Countries that introduced in 2014 and 2015 might not have had sufficient time to ensure routinisation of the third dose of PCV prior to the data collection (e.g. Armenia introducing in September 2014). From countries that introduced in 2013 and prior, Papua New Guinea stands out with 42 percentage points gap between PCV3 and DTP3; this difference is due to a phased rollout that concluded in 2016 as well as vaccine management issues.

[xxxii] *See Section 4.3 for further information on Full Country Evaluations.*

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



4.2. AMC Outcomes and Impact Evaluation

In 2015, and as per the AMC monitoring and evaluation framework, the Gavi Secretariat commissioned The Boston Consulting Group (BCG) for an Outcomes and Impact evaluation, in order to assess the extent to which the pilot AMC has achieved its stated objectives and the overarching goal of reducing morbidity and mortality from pneumococcal disease. The evaluation also captures lessons learned in the pilot and recommendations for future impact evaluations of the AMC.

The Request for Proposals (RFP) for the evaluation was published in March 2015. AMC stakeholders and partners were widely consulted on the evaluation questions, design options and other methodological matters. The RFP was also reviewed and approved by Gavi's EAC. Proposals were submitted through an open and competitive bidding process and then judged by an independent selection committee. The committee recommended the selection of BCG. After the review of the draft report by the AMC stakeholders, the final report was published on the Gavi website in early 2016[10]. The Gavi Secretariat has prepared a management response to the findings and recommendations, which is publicly available with the report on the Gavi website. The EAC also submitted an independent assessment of the quality and usefulness of the report.

The evaluation validated that the pilot pneumococcal AMC contributed towards reducing morbidity and mortality from pneumococcal disease, accelerating vaccine supply availability (as per the second objective of the AMC) and uptake (as per the third objective of the AMC) in Gavi countries, as well as supporting reduction in morbidity and mortality from pneumococcal disease, with 3 million under-five

deaths estimated to be averted by 2030[xxxiii]. Although the AMC has not succeeded in accelerating the development timelines for additional manufacturers, as per the first objective of the AMC, it did have two positive R&D effects: first, it proved that there would be a large low-income country market after the conclusion of the AMC, which likely encouraged many manufacturers to continue to pursue development. Second, the creation of this market stimulated presentation innovation specifically for Gavi markets by existing suppliers.

4.3. Full Country Evaluations

In 2013, Gavi launched a set of evaluations with the aim of understanding and quantifying the barriers to and drivers of immunization program improvement, with emphasis on the contribution of Gavi, in four countries. There are four countries taking part in the Full Country Evaluations (FCE) project: Bangladesh, Mozambique, Uganda and Zambia. Local research institutions in all FCE countries are partnering with the Institute of Health Metrics and Evaluation (IHME) and PATH to collect information, data, and evidence to help improve immunisation programmes. The introduction and implementation of PCV in the routine immunisation programme (routinisation) in these four countries were evaluated as part of this project. The original FCE project contract ended in December 2016, prior to that, the EAC agreed on a two-year continuation with a targeted approach by country for Mozambique, Zambia and Uganda (three of the four FCE first phase countries).

In previous Gavi FCE reports (2013, 2014 and 2015) the introduction process and routinization of PCV in Mozambique, Uganda and Zambia and the joint introduction of PCV with IPV in Bangladesh were evaluated (Table 8).The 2016 report (draft) presents the continued monitoring of the routinization of PCV in all 4 countries, and presents findings of the impact of the PCV introduction on pneumococcal disease burden, based on studies in Mozambique and Bangladesh.

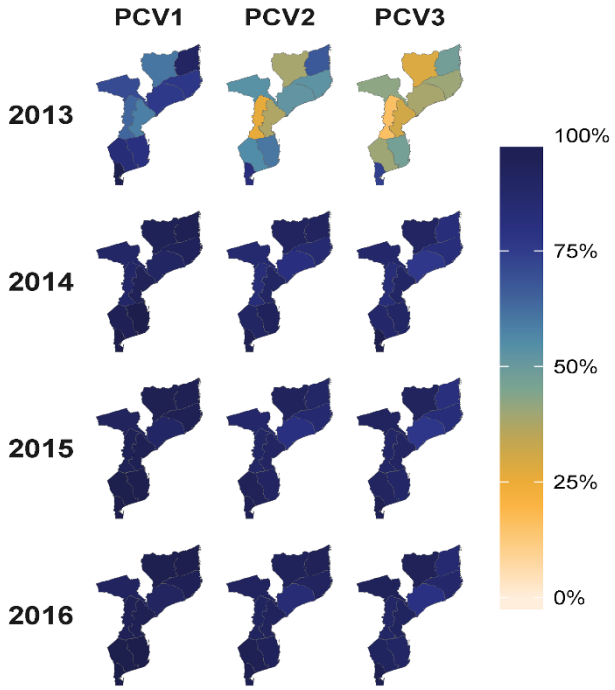
Table 8: Timeline of PCV vaccine introductions in Gavi FCE countries (2013-2016)

	Bangladesh	Mozambique	Uganda	Zambia
2013		PCV introduction (April 2013)	PCV introduction in April 2013 (one district)	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 Gavi FCE countries in 2016 have experienced variable success in routinising PCV as shown in coverage maps below. PCV was introduced in Bangladesh in March 2015 and based on a review of EPI HMIS data, is well routinised; EPI HMIS data of January-October 2016 showed that PCV third-dose coverage is 93%, compared to 97% pentavalent third dose.

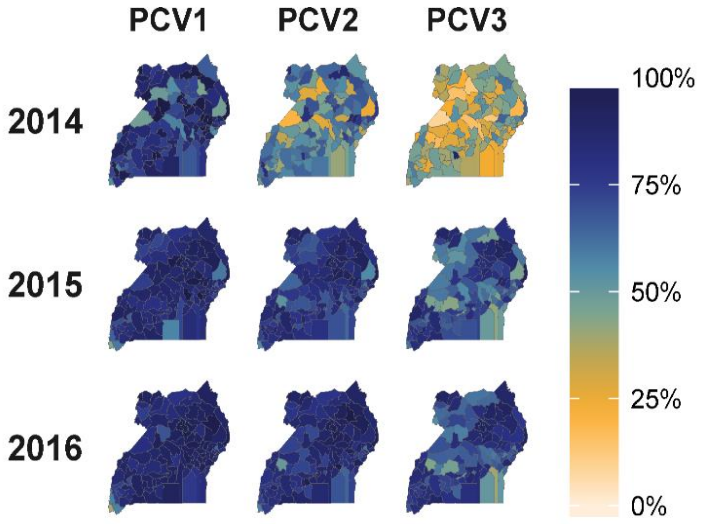
[xxxiii] *These estimates are a result of an external evaluation and not Gavi targets.*

Figure 6. Map of PCV coverage in Mozambique



In Mozambique, PCV was introduced in April 2013 and was quickly integrated into the routine Expanded Program on Immunization (EPI), as demonstrated by the coverage maps in Figure 6.

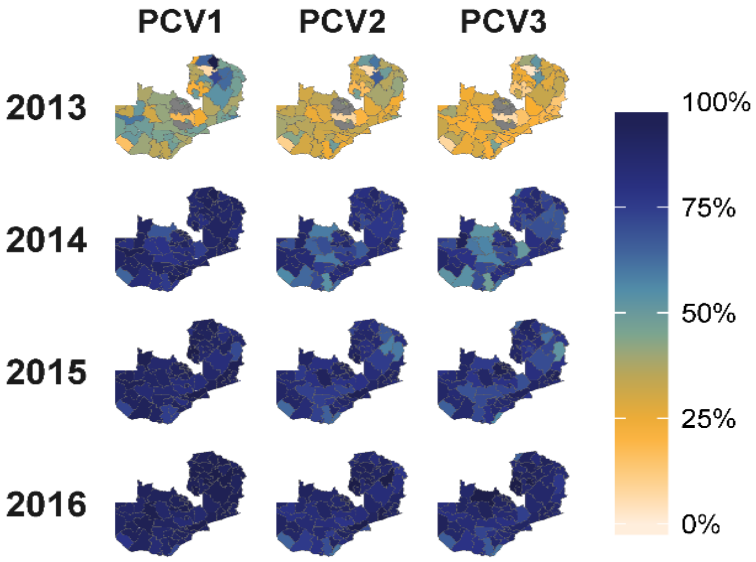
Figure 7. Map of PCV coverage in Uganda



In Uganda, PCV was nationally rolled out in 2014 and challenges in routinisation in 2014 and 2015 were driven by vaccine stock-outs and were covered in detail in the 2015 report. The PCV/pentavalent ratio improved tremendously in 2015 and 2016, and the improvement coincided with strategic interventions by Uganda National Expanded Program on Immunization (UNEPI) and partners including scale-up of the Reach Every District micro-planning strategy and training of health workers on data quality improvement by Data Improvement Teams throughout the country. In 2016, the evaluation findings suggest that the discrepancy in delivery between PCV and pentavalent vaccines may be due to reporting issues at the

facility level with pentavalent vaccine being better recorded as it is a performance indicator for facilities in Uganda. This potential root cause highlights data quality issues in administrative and Health Management Information Systems (HMIS) data and suggests that a population-based coverage survey or data quality audit would be necessary to confirm the discrepancy between PCV and pentavalent vaccine delivery in Uganda. Based on subnational data collection, no stock-outs of PCV were observed in facilities visited in 2016.

Figure 8. Map of PCV coverage in Zambia



In Zambia, where PCV was introduced in 2013, two factors may account for the reported under coverage 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 will continue assessing it.

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

In Mozambique, evidence from vaccines effectiveness studies suggest that the introduction of PCV in 2013 has reduced nasopharyngeal carriage of vaccine-type pneumococcus and reduced the incidence of vaccine-type IPD and pneumonia.

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) after PCV introduction.

- A 41% (95% CI 6–69) reduction in VT pneumococcal carriage was observed in HIV-uninfected children receiving three doses.
- A 61% (95% CI 9–82) reduction in VT pneumococcal carriage was observed in HIV-infected children receiving three doses.
- As expected, there was also an increase in pneumococcal carriage of non-PCV10 VT, including serotypes in PCV13 (i.e., 19A).

The reduction in carriage has been accompanied by a reduction in vaccine-type invasive pneumococcal disease (IPD). Based on surveillance data from the Manhiça demographic surveillance system (DSS), it has been estimated a statistically significant reduction in vaccine-type IPD of 87.7% (95% CI 44.1–97.3). There was also a trend towards reduction in X-ray-confirmed pneumonia (64.9%, 95% CI -4.4–88.2).

Findings from the pneumococcal impact study in Bangladesh also suggest some reductions in both the overall transmission of pneumococci and serotypes included in the vaccine (VT) 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. Results from the impact study in Bangladesh will be showcased in the final report.

The 2016 draft report also includes a number of key recommendations for the Alliance and for the four FCE countries. As per the previous years, the four countries and the 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 will become available on the Gavi website in the second quarter of 2017, 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), as it has been done for the previous annual reports[11].

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 and Melinda Gates Foundation to estimate the impact of vaccination in the 73 Gavi countries. In January 2016 this was formalised into a modelling consortium, named the 'Vaccine Impact Modelling Consortium' and 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 the estimates. The consortium continues to base their approach on the methodologies adopted previously by Gavi and Gates.

Based on current projections (OPv14 and WUENIC 2016) completed in late 2016, PCV use is estimated to avert approximately 740,000 future deaths among children vaccinated in Gavi 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 PneumoADIP and VI-TAC grant, including pneumococcal vaccine effectiveness and impact studies in Kenya and South Africa, economic impact evaluations of pneumococcal vaccines in Ghana and The Gambia, concluded in 2015. PCV impact in Kenya will continue through 2017 to monitor potential changes in the epidemiology of 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 Nepal, mentioned in Section 4.1) to determine the most effective schedules to reduce pneumococcal disease. In addition to a comprehensive dosing landscape analysis (published in 2014 and currently being updated[xxxiv]) and Gambia economic peer-reviewed publications, in 2014 the Kenya and South Africa effectiveness studies produced several key publications highlighting their results including herd protection with reductions in transmission of the disease by reducing nasopharyngeal colonisation of vaccine-serotype strains in both vaccinated and unvaccinated individuals; reductions in antibiotic resistant strains of the disease in the very young post-vaccine introduction; and overall substantial effectiveness of PCV against vaccine serotype and all serotype invasive pneumococcal disease (IPD) among children, as well as the broader scope of PCV impact on severe disease. 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. More recently, results from The Gambia indicate that cases of childhood invasive forms of pneumococcal disease are reduced by more than one-half with introduction of PCV.

In June 2013, Gavi issued a RFP for the 'Evaluation of PCV Effectiveness in Asia' to assess the impact of PCV in early adopting Gavi countries in Asia, and upon 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 PDR. These studies are assessing a range of outcomes, including disease effects (e.g. invasive pneumococcal disease, 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 anticipated in 2016-2018. A fourth study, to assess the impact of phased PCV introduction on the incidence of radiological pneumonia in Mongolia has been commissioned and began collecting pre-introduction data in 2015 with results anticipated in 2018 due to delayed timeline for vaccine use in the study setting.

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 with anticipated results in 2017.

As mentioned previously, pneumococcal vaccine effectiveness and impact studies were conducted in Bangladesh and Mozambique as a component of the FCE work which ended in 2016, including population-based assessment of changes in agent transmission and impact of PCV on invasive

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

pneumococcal disease and x-ray confirmed pneumonia in Mozambique. We are in discussions with researchers in Mozambique to continue existing work to evaluate the upcoming transition from PCV10 to PCV13. These assessments of pneumococcal vaccines in selected epidemiologic settings will help to further assess the impact of vaccination on the burden of disease and serotype epidemiology.

5. Media and Communications

Increasing AMC visibility through traditional, online and social media remains an important goal for Gavi's communications team.

5.1. Communications overview 2016

Gavi continued to highlight and explain the AMC in relevant communications materials throughout 2016. In addition to sharing updated materials, Gavi also ensured that appropriate speaking points were incorporated into the speeches of Alliance spokespeople at launch ceremonies and other events.

In February 2016 Gavi's media team issued a press release to media outlets worldwide announcing the findings of the AMC Outcomes and Impact Evaluation. In March 2016 Gavi also publicly welcomed GSK's decision to lower the price of PCV10 to $3.05. Both of these media activities were supported on Gavi's social media channels.

Gavi's communications team heavily promoted World Pneumonia Day 2016 on Twitter, Facebook and www.vaccineswork.org, producing blogposts and infographics to highlight progress made in expanding access to PCV. The Secretariat also supported the International Symposium on Pneumococci and Pneumococcal Diseases (ISPPD 2016) on Gavi's social media channels.

5.2. Communications outlook for 2017

Gavi will continue to integrate AMC messaging into all relevant materials and seek to profile the AMC mechanism during pneumococcal vaccine launches. Gavi will continue to brief journalists who demonstrate an interest in the AMC, the Gavi model and in innovative finance mechanisms more generally, to ensure fair and accurate representations of the AMC.

5.3. Donor and stakeholder communication

Continuing in 2016, additional efforts were made to provide updates to AMC stakeholders, through regular AMC stakeholder calls and an annual AMC stakeholder meeting. These provided opportunities to exchange information and obtain input on key issues. Topics included the strategic demand forecasts and implications, PCV roadmap development, revised disease burden and impact estimates progress on implementation, the progress on AMC targets and supply and implementation of vaccines. With regards to vaccine introductions, AMC donors were kept informed of progress and invited to participate in the vaccine launch events.

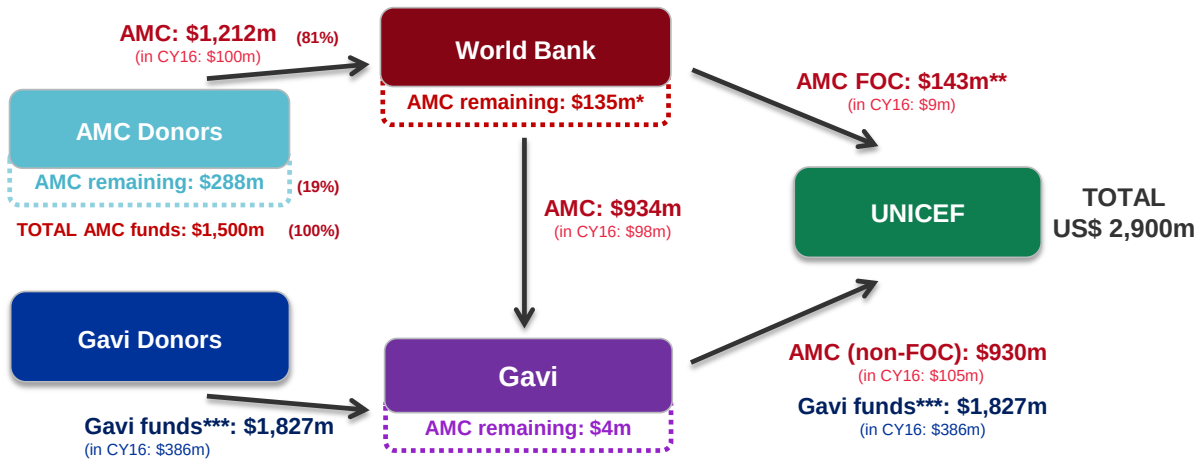
6. Financial activities

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

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 9. Summary of AMC Financial Process Flow and funds disbursed (inception to 31 December 2016)



'CY16': Calendar Year 2016

* *Includes $51.7m of Canadian Initial Funds, not yet available for disbursement*

** *Includes US$ 840,000 conversion from Gavi-funded FOC to AMC-funded FOC and US$ 10.5m conversion from FOC to 'regular' / non-FOC funds; both of which were effected after receipt of funds from the World Bank (see footnote ii in text)*

*** *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.

Details are provided in sections 6.1 - 6.3 below.

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

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 and 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 8). 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 2016, the World Bank had received a total of US$ 1,212 million from AMC donors (see Table 9 below). The Bill and 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 9. Grant receipts from AMC donors, as of 31 December 2016 (in US$ millions)

(in US$ millions)

	Grant Amount	Paid-in Amount	Remaining Balance
Fixed Schedule Donors			
Bill & Melinda Gates Foundation	50	50	-
Italy	635	479	156
Russia	80	56	24
sub-total:	**765**	**585**	**180**
On Demand Donors			
Canada	200	200	-
Norway	50	50	-
UK	485	377	108
sub-total:	**735**	**627**	**108**
Total	**1,500**	**1,212**	**288**

Source: The World Bank

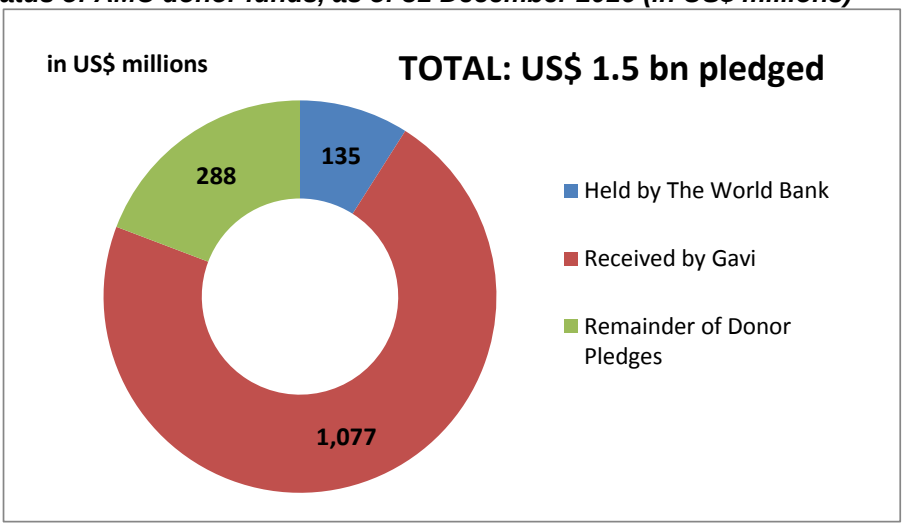
The World Bank has recorded the AMC donor funds in its financial statements as designated assets, with a corresponding liability to provide the funds to Gavi for the purchase of pneumococcal vaccines subject to the terms and conditions of the AMC. To enhance the predictability of AMC funding, the World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

AMC donor funds: inflow to Gavi

As of 31 December 2016, the World Bank had disbursed US$ 1,077 million (US$ 934 million to Gavi and US$ 143 million directly to the UNICEF procurement account relating to the Firm Order Commitments[xxxvii]). Of the US$ 1,077 million, US$ 107 million was disbursed during 2016 (US$ 98 million to Gavi and US$ 9 million directly to the UNICEF procurement account relating to the Firm Order Commitments). This leaves a balance of US$ 135 million held by the World Bank, of which US$ 83 million is available for immediate disbursement to Gavi (see Figures 10 and 11).

Figure 10. Status of AMC donor funds, as of 31 December 2016 (in US$ millions)



Source: Gavi Secretariat

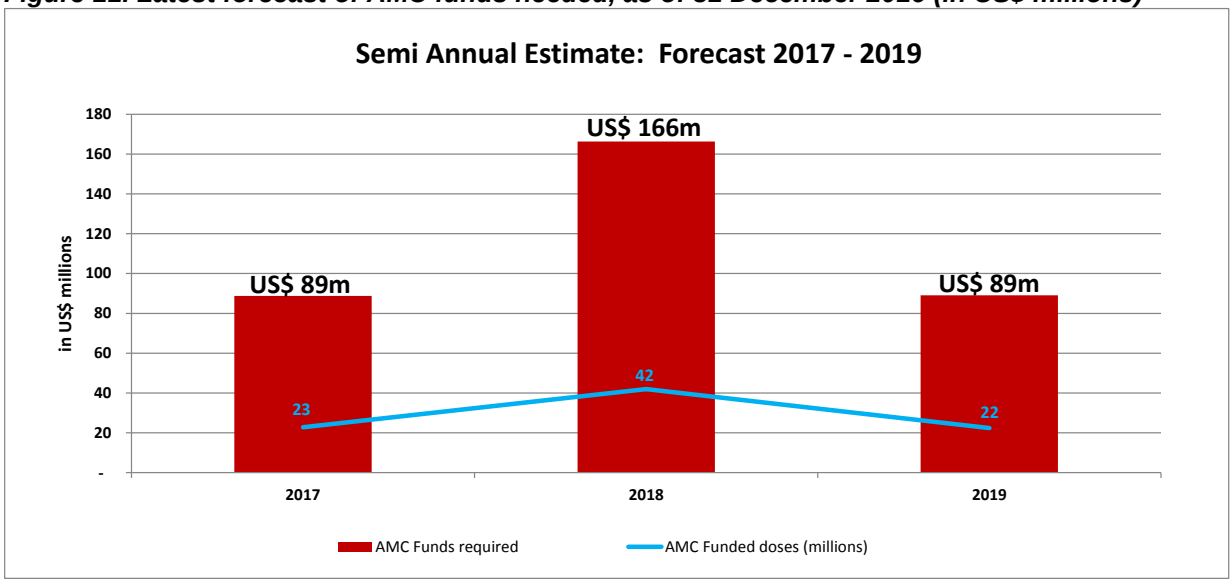
As part of the reporting process, Gavi regularly submits a Semi-Annual Estimate (SAE) to the World Bank, which provides forecasted demand for pneumococcal vaccine doses and corresponding AMC funding on a rolling three-year basis. Gavi submitted two SAEs during 2016 (in May and in November), the latest of which forecasted a need for US$ 344 million of AMC funds to procure 87 million doses of the pneumococcal vaccine between 1 January 2017 and 31 December 2019[xxxviii].

[xxxvi] *A provision was made in the AMC Stakeholders Agreement to finance the IBRD's financial management and administrative service fees primarily via investment income (with any shortfall thereafter paid by the United Kingdom, up to a certain limit). Given the market conditions over the past several years, the realised investment income has been far less than originally forecasted and, therefore, insufficient to cover these fees (in addition, the amount provided by the United Kingdom has also not been enough to cover the fees). As a result, it was subsequently agreed among the stakeholders that Gavi and the IBRD would fund the remainder.*

[xxxvii] *A reduction in the tail price for supply agreement GSK #3 (FOC #5) in 2016 accelerated payment of AMC funds, including AMC FOC funds. As the overall total FOC amount is fixed for each supply agreement, the difference of US$ 840,000 was transferred from the Gavi-funded portion to the AMC-funded portion of the FOC. Thus, the overall AMC FOC transferred to UNICEF at 31 December 2016 increased from US$ 142 million to US$ 142.8 million. In addition, the FOC and non-FOC totals were previously adjusted for the conversion of US$ 10.5m from FOC funds to non-FOC funds during 2015 (ref. footnote xxi in the 1 April 2014 – 31 March 2015 Annual Report).*

[xxxviii] *The US$ 344 million forecasted need is covered by the funds held by the World Bank and Gavi, as well as the remainder of pledges funds still held by the AMC donors, as shown in Figure 10.*

Figure 11. Latest forecast of AMC funds needed, as of 31 December 2016 (in US$ millions)



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

6.3. UNICEF procurement: outflow of AMC donor funds

During 2016, US$ 501 million was disbursed to UNICEF for the purchase of pneumococcal vaccines. Of this amount, US$ 114 million pertains to the AMC-funded portion of the vaccine purchase. The remaining US$ 387 million was allocated from general Gavi funds to pay for the tail price portion of the vaccine purchase and related fulfilment costs[xxxix]. 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 GSK supply agreement amounting to US$ 9 million (see Figures 10 and 13).

Six supply agreements have been signed under the AMC programme, to date.[xl] As of 31 December 2016, AMC funding allocated under five of the six agreements has been fully disbursed. The remainder of AMC funding allocated under the third GSK agreement will be disbursed during 2017.

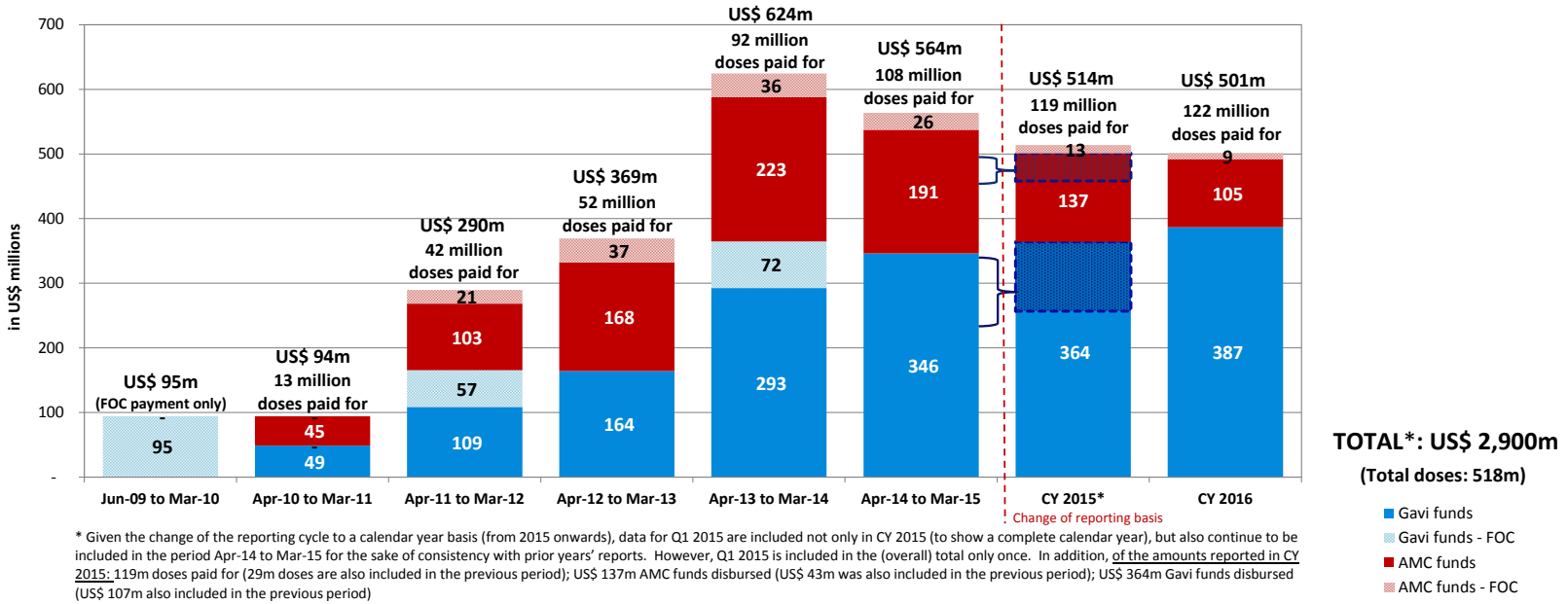
In total, as at 31 December 2016 US$ 365 million has been transferred to Gavi's 'UNICEF procurement account' regarding the FOCs for the six existing signed supply agreements. Of this amount, US$ 223 million represents the Gavi-funded portion of the FOCs and US$ 143 million represents the AMC-funded portion of the FOCs. Of the US$ 365 million transferred, US$ 357 million (approximately 98%) has been utilised and this represents the draw-down of already transferred FOC funds relating to all six supply agreements.

[xxxix] *Fulfilment costs are the extra costs incurred in supplying vaccines (estimated at US$ 0.14 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.*
[xl] *For details refer to Section 1.2 and Annex 1*

Figure 12. Total cash disbursements to Gavi's 'UNICEF procurement account' (inception to 31 December 2016, in US$ millions)

in US$ millions

Funding Source	Jun-09 to Mar-10	Apr-10 to Mar-11	Apr-11 to Mar-12	Apr-12 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	TOTAL	of which: AMC / Gavi	of which: FOC	of which: Non-FOC
AMC Funds - FOC	-	-	21	37	36	26		13	13	9	143	1,073	143	
AMC Funds	-	45	103	168	223	191	43	94	137	105	930			930
Gavi Funds - FOC	95	-	57	-	72	-	-	-	-	-	223	1,827	223	
Gavi Funds	-	49	109	164	293	346	107	257	364	387	1,604			1,604
TOTAL:	95	94	290	369	624	564	150	364	514	501	2,900		365	2,535



* Given the change of the reporting cycle to a calendar year basis (from 2015 onwards), data for Q1 2015 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 only once. In addition, of the amounts reported in CY 2015: 119m doses paid for (29m doses are also included in the previous period); US$ 137m AMC funds disbursed (US$ 43m was also included in the previous period); US$ 364m Gavi funds disbursed (US$ 107m also included in the previous period)

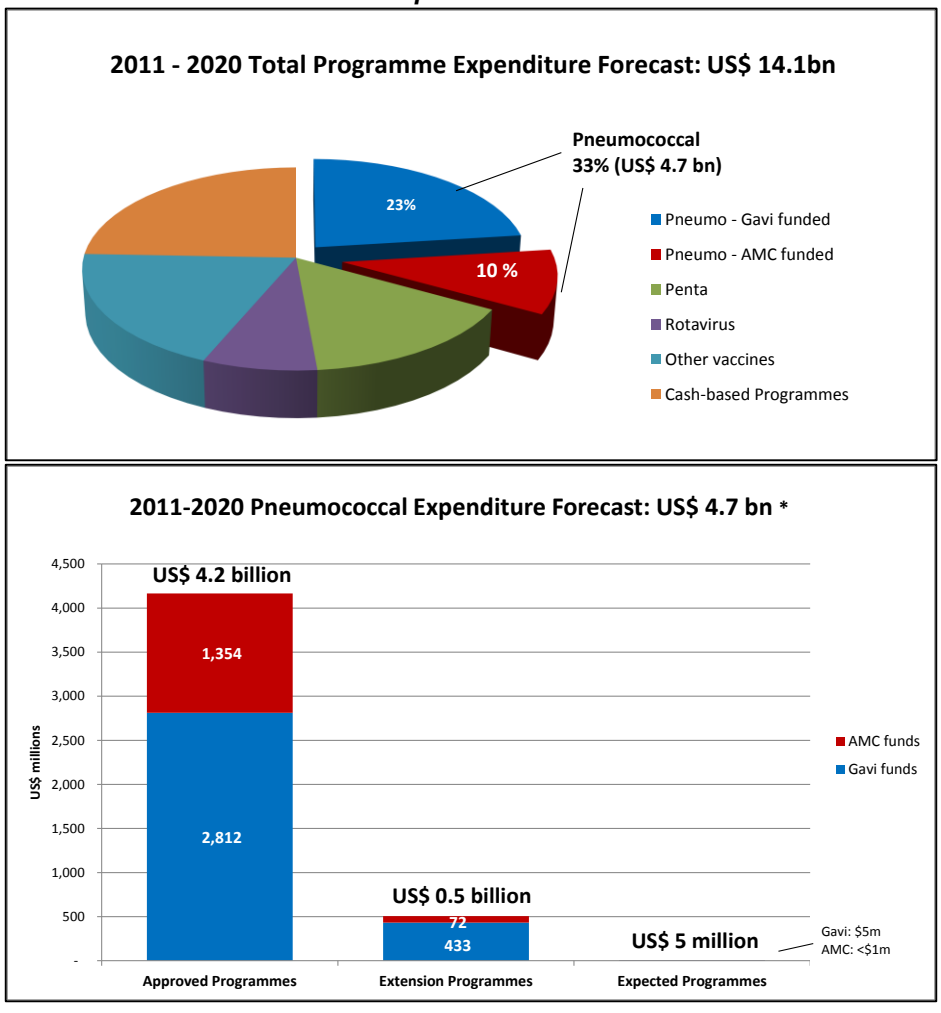
Source: Gavi Secretariat. Note: For the latest three reporting periods (April 14 – March 15, CY 2015 and CY 2016) the total numbers of doses have increased from the previous reporting periods while the overall amounts paid have decreased. This is due to a higher proportion of doses being procured under the Gavi-funded tail price only. Some numbers may appear not to add due to rounding.

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

At the December 2016 Gavi Board meeting, an update was presented of Gavi's Long Term Financial Forecast.[xli] Total programme expenditures are projected to be US$ 14.1 billion for the 2011-2020 period, of which pneumococcal vaccine expenditures are anticipated to amount to US$ 4.7 billion, representing approximately 33% of total programmatic expenditures (see Figure 13).

For the 2017 and 2018 programmatic years, 52 countries had been approved to receive financial support for the procurement of the pneumococcal vaccine. The 2017 commitments amount to US$ 490 million and 2018 commitments amount to US$ 532 million. The commitments are included as part of the total 2011-2020 expenditure forecast, presented in Figure 13 below.

Figure 13. AMC within total Gavi forecasted expenditure 2011-2020



Source: Gavi Secretariat

** Approved Programmes are those approved by the Gavi Board. Extension Programmes are forecasted continuations of those programmes, subject to future approval. Expected Programmes are defined as those which have received conditional IRC recommendation or are forecasted based on Adjusted Demand Forecast v14.0 and the latest supplier assumptions.*

[xli] *December 2016 Board Paper entitled "Board-2016-Mtg-2-7-8 December 2016 Doc 05 Financial Forecast and Programme Funding Envelopes "*

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 are 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 supporting the remaining two countries that have not yet introduced pneumococcal vaccine and strengthening health systems and decision-making processes in those that have not yet applied to access PCV through the AMC. For countries that have introduced, the priorities remain to sustain PCV implementation and improve coverage. 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

Efforts are focused to ensure that the remaining two approved countries are ready to introduce pneumococcal vaccines in the 2017-2018 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 the partners working 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 product, Gavi and partners will continue to monitor and support the operational and strategic aspects of the switches, paying particular attention to the programmatic challenges and encouraging 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 for pneumococcal support also remains a key priority, particularly the seven that remain Gavi eligible. Four of the eight countries are not eligible to apply due to the >70% DTP3 coverage eligibility criterion, so the current focus of the Alliance is on strengthening the routine immunisation system in the short term to ensure that the pneumococcal vaccine can be introduced as soon as possible to address the high pneumococcal disease burden in these settings.

7.3. Sustaining implementation and ensuring high coverage

The Gavi-wide efforts on strengthening of health systems and routine immunisation are also key to address 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.

An optimum dosing schedule for PCV will be discussed at the SAGE meeting in October 2017, in addition to further discussion on catch-up vaccination; possible changes arising from these recommendations will be closely monitored since they may have programmatic implications for countries as well as implications in Gavi's support.

7.4. Ensuring sustainability for transitioning and transitioned countries

So far, AMC procurement mechanisms achieved a 'tail-price' reduction of at most 13% from the initial 'tail-price' cap of US$ 3.50/dose. This price of the vaccine may be challenging for sustainable pneumococcal vaccination as Gavi countries start to transition out of support. As outlined in the Pneumococcal Vaccine Supply and Procurement Roadmap, a key priority objective is also to significantly reduce the 'tail-price' WAP short- to mid-term (2015–2020). Sustainability is also being addressed through the new Gavi 2016-2020 strategy and Partners' Engagement Framework, particularly through the SFAs for Sustainability and Political Will.

Demonstrating the impact of PCV is also key to ensure sustainability of the programme after transition. A focus on gathering evidence on vaccine effectiveness and impact will continue moving forward, through Gavi-supported special studies. The 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 and will demonstrate the ability of the limited supplier base to continue to meet the requirements. As the demand increases to more than 150 million doses annually, the limited supply base remains a risk to implementation. The decision to conduct a tender in 2017 will be made by Alliance partners based on the AMC Terms and Conditions and taking into account the strategic demand scenarios and the latest rounds of applications in 2017. The Gavi Secretariat will continue to work closely with UNICEF SD to monitor the supply situation and manage the supply and demand balance.

8. Conclusion

Country demand for pneumococcal vaccines has been unprecedented, with close to 81% of the 73 AMC-eligible countries already approved for support and 57 introductions as of 31 December 2016. Third dose PCV coverage also increased 7 percentage points from 2014 to 2015, reaching 35% in 2015, and is projected to reach 46% by the end of 2016. Based on current projections through year 2020, PCV use will avert an estimated 740,000 future deaths among children vaccinated in Gavi countries.

Despite this unparalleled success, as countries enter the pathway to transition from 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

Team	Staff member
Vaccine Implementation	**Devi Aung** Senior Programme Manager **Mugen Ujiie** Senior Programme Manager **Cassandra Quintanilla** Vaccine Programme Manager
Resource Mobilisation	**Katja Rouru** Senior Manager
Finance	**Minzi Lam Meier** Head, Financial Forecasting & AMC **Eric Godfrey** Senior Manager, Financial Forecasting & AMC
Monitoring & Evaluation	**Hope Johnson** Head, Outcomes & Impact **Alba Vilajeliu** Senior Programme Officer, Evaluations **Olivia Bullock** Program Officer, Monitoring
Public Policy Engagement	**Susan Brown** Director
Communications	**Frédérique Tissandier** Senior Manager
Market Shaping	**Edward Baker** Senior Manager, Market Dynamics
Legal	**Alison Jensen** Associate Legal Counsel **Helene Gaudin de Villaine** Associate Legal Counsel

Source: Gavi Secretariat, as of 31 December 2016

Annex 2 – Summary of previous call for offers

8.1. 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[xlii] 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.

8.2. 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.

[xlii]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.

8.3. 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. The total doses awarded to GSK under its three supply agreements amounts to 720 million.

Pfizer will start 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 and US$ 3.30 from 2014 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.

Annex 3 – Membership of the PROWG

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

Organisation	Members
Gavi Secretariat	**Melissa Ko** (March 2015 – present) Senior Programme Manager, Vaccine Implementation, Country Programmes **Devi Khin Aung** (November 2016 – present) Senior Programme Manager, Vaccine Implementation, Country Programmes **Mugen Ujiie** (November 2016 – present) Senior Programme Manager, Vaccine Implementation, Country Programmes **Cassandra Quintanilla** (November 2016 – present) Vaccine Programme Manager, Vaccine Implementation, Country Programmes **Sara Sá Silva** (January – November 2016) Vaccine Programme Manager, Vaccine Implementation, Country Programmes
PATH	**Allison Clifford** Communications Officer, Vaccine Development
JHU	**Julie Buss Younkin** Manager Scientific Communications (International Vaccine Access Center) **Molly Sauer** Scientific Communications & Policy Officer (International Vaccine Access Center)
UNICEF Programme Division	**Ben Hickler** Communication for Development (C4D) Specialist, Routine Immunisation and New Vaccines, Health Section **Benjamin Schreiber** Senior Immunisation Specialist, Health Section (alternate member) **Richard Duncan** Senior Immunisation Specialist, Health Section
UNICEF Supply Division	**Jesus Barral-Guerin** Senior Contracts Manager **David K. Mutuerandu**

	Contracts Manager - PCV **Gideon Chelule** Contracts Manager – Rotavirus vaccine **Sonia Freitas** Contracts Specialist – PCV
WHO	**Carsten Mantel** (January – November 2016) Leader – Priority Area New Vaccines and Innovation **Hemanthi Dassanayake-Nicolas** Technical Officer – Strategic Information Group, EPI **Ikechukwu Udo Ogbuanu** Medical Officer – New Vaccines, EPI

Source: PROWG Terms of Reference, as of 31 December 2016

Annex 4 – Membership of the Independent Assessment Committee

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

Soonman Kwon (Vice Chairperson)
Director, Brain Korea Centre for Aging and Health Policy, South Korea

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 2015

Annex 5 – Summary of Gavi investments in surveillance PCV special studies

Gavi invests annually approximately US$ 15-22 million in surveillance and targeted assessments across the vaccine portfolio to inform evidence-based decision making, document programme outcomes and impact and generate learning to inform programme improvements from a subset of settings predominantly through primary data collection. The table below summarises recent Gavi commissioned investments in surveillance and targeted assessments for PCV.

Study	Status of Activities	Key findings
A. Surveillance		
WHO Coordinated global surveillance networks for Invasive Bacterial Vaccine Preventable Diseases (IB-VPD) **Hib Initiative supported IB-VPD surveillance in India and Pakistan**	Ongoing Completed	With guidance from an informal Technical Advisory Group (ITAG) and external partners, WHO continues to support countries in improved surveillance data quality, analysis and interpretation and enhanced country ownership and transition of surveillance to support country monitoring of burden of disease, short- and long-term impact of new vaccine introductions (e.g., Hib, PCV, Meningococcal A), and leveraging the surveillance platform to monitor other vaccine-preventable diseases (e.g., typhoid).
B. VI-TAC Special Studies		
1. Grant A-4: January 2009 - September 2013		
Landscape analysis of PCV dosing (analysis updated in 2016-2017 with funding by the BMGF: PCV Review of Impact Evidence (PRIME)	Analysis of dosing studies published through 2014 is complete. Nine-paper supplement published in the January 2014 issue of *Pediatric Infectious Diseases Journal*. Presentations given at ISPPD 2012. Leveraged for updated systematic review on PCV impact to inform PCV Product Assessment and review of evidence by SAGE to be presented at October 2017 for revisions of position paper as appropriate.	The available literature shows that each of three schedules (3+1, 3+0 and 2+1) all showed significant reductions in pneumococcal disease (IPD and/or pneumonia), and many programs also used catch-up campaigns. Choice of schedule should balance practical considerations and epidemiology, but achieving high coverage should be a primary goal to ensure herd protection. Varying study designs and epidemiologic settings made direct comparison of impact between schedules difficult. The landscape analysis of PCV dosing was leveraged and updated through support from the BMGF and from Gavi to inform the PCV Product Assessment. The report is a summary document to inform Gavi decisions on product switch requests and initiate country-level guidance on PCV product choice.
Effectiveness of PCV7 against IPD (South Africa)	Evaluation of impact of PCV7 is complete.	Even in a setting of routine use and with high pneumococcal transmission, PCV delivered on a novel 2+1 schedule is highly effective for HIV-

Study	Status of Activities	Key findings
	Publication in Vaccine in 2012 discussed effects of study on changes to PCV dosing schedule made by South African NAGI. Presentations given at ISPPD 2012 and 2014. Publication in PIDJ on risk factors for IPD among children in South Africa. Publication in CID in 2014 on effectiveness of PCV in this case-control study. Publication in PIDJ in 2015 on risk factors for IPD.	uninfected children (VE 74%), but insufficient among HIV-infected children (VE -12%). This may indicate the benefit of a booster dose for HIV+ children on this schedule. In addition, the study identified risk factors for IPD in HIV-uninfected children include underlying medical conditions, upper respiratory infections, day-care attendance, HIV exposure and siblings under 5 years of age.
Effectiveness of PCV7 against presumed bacterial pneumonia (PBP) (South Africa)	This case-control study measuring PCV effectiveness in HIV-infected and HIV-uninfected children is complete and published. This was the first published study on the impact of PCV on pneumonia in conditions of routine use in Africa. Poster displayed at ISPPD 2014. Publication in Thorax in 2015 showed effectiveness of PCV at preventing PBP in HIV-uninfected children.	In the matched case-control study, PCV7 was 39.2% effective (95% CI: 8.46-59.6%) in preventing Probable Bacterial Pneumonia (defined as consolidation on chest X-ray) in children 3 months to 2 years of age (those who had received two primary doses plus a booster), under conditions of routine use and using a hospital control group for comparison. There was vaccine efficacy of 20.1% when including children beginning after the first dose of PCV. Importantly, these effectiveness estimates were similar to those found in the more controlled environment of randomized trials.
Pneumo/Rota time series (South Africa)	Data collection is complete; the initial work was continued in subsequent grant portfolios – see grant A-11 below. Time series analysis of PCV impact manuscript has been submitted for publication and is under consideration	The impact of simultaneous introduction of PCV and rotavirus vaccine can inform other countries with high burden of pneumonia and diarrhoea, who are looking to adhere to the recent GAPPD recommendations. Among HIV (-) children under 5 years of age, PCV13 use was associated with reductions in all cause pneumonia of 27%-39% by year following introduction. This translated to 7-9 prevented hospitalization for every 1,000 children vaccinated.
PCV/Hib conjugate vaccine impact manual	The PCV/Hib impact manual has been completed and published on the WHO website for download. A presentation on the manual was	The manual organises information on designing and conducting impact studies in one place for vaccine decision-makers and implementers in countries considering adoption or having recently adopted either Hib of PCVs. The manual includes

Study	Status of Activities	Key findings
	made at NUVI meeting in May 2012.	guidance for study design and tools to assist with study protocols.
Economic impact of PCV (The Gambia)	Assessment of the economic impact of The Gambia's introduction of PCV is complete. Poster displayed at ISPPD 2014. Manuscript describing the cost of pentavalent and pneumococcal conjugate vaccine delivery in the Gambia before and after introduction published in April 2014 in *Vaccine*. The results for this Gambian pneumococcal economic impact study have been published in 2016 in *Cost Effectiveness and Resource Allocation.*	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 vaccine. Savings from the switch from tetravalent to pentavalent vaccine slightly offset the large additional cost of introducing PCV. The Gambian gov't assumed 16% of the added systems costs of the two vaccine schedule changes, while donor agencies contributed the remainder – Gavi (52%), UNICEF (31%), WHO (1%, plus significant staff time contributed for training).
2. Grant A-11: September 2012 – December 2015		
PCV10 Impact (Kenya)	This is a continuation from the PneumoADIP PCV impact evaluation in Kenya. Results were presented at ISPPD-9 in March 2014 and at ISPPD-10 in June 2016. Manuscript on impact of PCV10 on NP-carriage of *S. pneumoniae* and non-typeable *H. influenzae* was published in *Lancet Global Health* in June 2014. Multiple additional publications are expected, including analyses on PCV impact on pneumonia and IPD and indirect effects. The pneumococcal disease surveillance system is also used to monitor Hib invasive disease. A publication in *Lancet Global Health* in 2016 shows results from 15 years of surveillance following Hib introduction.	Substantial reductions in the incidence of vaccine-type invasive pneumococcal diseases (IPD) among children less than five years of age have been shown since PCV10 was introduced in 2011. Between 2013-2016 there have cumulatively been only 4 cases of vaccine-type IPD in children under 5 years in the Kilifi Health and Demographic Surveillance System compared with annual cases counts of 15-40 cases per year prior to vaccine. The nasopharyngeal carriage study has shown that introduction of PCV10 in a developing country setting with a catch-up campaign has led to a two-thirds reduction in prevalence of vaccine-serotype pneumococci carried in both children targeted for vaccination and in older people who were not vaccinated. Vaccine effectiveness of Hib vaccine during 15 years of use was 93% in children younger than 13 years of age (using a 3-dose schedule without a booster)
PCV13 Effectiveness (South Africa)	This study is a continuation of the VI-TAC Special Study in South Africa PCV7 evaluation (Grant A-4).	Effectiveness of PCV13 against vaccine-type disease among HIV-uninfected children was 85% (95%CI: 37-96) and 91% (95% CI: -35, 100) in

Study	Status of Activities	Key findings
	The continuation extends the effectiveness analysis through the switch to PCV13, which has replaced PCV7. The data on PCV13 effectiveness against IPD are published in *Lancet Global Health* 2017; 5(3):e359-e369.	HIV-infected children. The effectiveness against the 6 serotypes not in PCV7 was 92% (95% CI: 40, 99) among HIV (-) children. The PCV13 vaccine effectiveness for PCV7 serotypes among malnourished children who were HIV (-) was 90% (53 to 98)
C. PneumoADIP Special Studies		
1. Grant: March 2004 - December 2013		
PCV Impact in Kenya	Rolled over to VI-TAC. (see above)	
PCV Impact in The Gambia	Rolled over to VI-TAC in part (for economic analyses); additional continuation funding provided by BMGF. This is a continuation of the Gambia PCV7 Impact study and is now evaluating the impact of PCV13. The results on the economic analysis are published in *Cost Eff Resour Alloc*. 2016 Feb 17; 14:4. doi: 10.1186/s12962-016-0053-4. The results on IPD are published in *Lancet Infect Dis*. 2016 Jun;16(6):703-11	The economic burden results show average provider costs per patient for treating pneumococcal disease (including outpatient pneumonia, inpatient pneumonia, pneumococcal sepsis and meningitis) ranged from $8-124, respectively, while the average out of pocket costs per patient were $6-34, respectively. The economic burden increased to $15-170 when family members' time loss from work was taken into account. Incidence of IPD decreased after vaccine introduction by 55% (95% CI 30%–71%) in the 2–23 month age group (253 vs 113 per 100 000 in 2013/14). This was due to an 82% (64%–91%) reduction of serotypes covered by PCV13.
Cost-effectiveness of PCV catch-up (Kenya)	Analysis of the impact and cost-effectiveness of PCV catch-up among under-one year olds, under-two year olds (current WHO recommendations), and under 5 year olds, in Gavi-eligible countries is complete but as yet unpublished. The disease transmission model is complete and preliminary cost-effectiveness results are available but have not been published.	Preliminary results from the disease transmission model found that catch-up campaigns not only lead to more rapid reduction in the IPD burden but also increases 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 immunisation. Under 1 year old catch up campaigns achieve additional direct benefits but fewer indirect benefits. Preliminary cost-effectiveness results suggest catch up campaigns in the target age group may result in cost savings from the societal perspective.

Study	Status of Activities	Key findings
Economic value of vaccination in India	The overarching goal of this analysis was to look at the potential health impact and costs averted through immunisation with three vaccines—Hib, PCV, RV *vaccines.* The project aimed to generate new evidence on the *health and economic benefits of these vaccines* at the national level and in four states in India (Bihar, Delhi, Maharashtra, and Tamil Nadu). The analysis generated new evidence in 3 categories: (i) death and cases averted; (ii) disease costs averted; and (iii) productivity loss averted. Presentation at ISPPD-9 in March 2014. All activities for this project have been completed and a publication being prepared.	Introduction or scale-up Hib, PCV, and RV in India can result in immediate benefits to the gov't and households in terms of saving deaths and averting cases. Cost savings varied by vaccine and coverage scenarios. Across the 3 vaccination programs and coverage scenarios, the majority of the cost savings was attributable to averted lost productivity due to premature death. At the state level, the greatest savings to the public sector were realised in Bihar, where the burden of disease was high. Bihar also maintained the highest economic benefit from improved vaccination rates. Overall, the expanded use of PCV in India could result in US$2 billion of costs averted in a single year. Most of the total costs averted were due to lost productivity due to premature pneumococcal death. Across the 3 vaccines, majority of deaths averted were attributed to PCV (37%), followed by Hib (34%) and RV (29%).
D. Other Gavi Targeted Assessments		
1. PCV Effectiveness in Asia		
Impact of PCV-10 on IPD in Lower Sindh, Pakistan (Aga Khan University)	Enrolment into a case-control study evaluating PCV impact on IPD, meningitis and pneumonia and using surveillance data began in 2013 and are ongoing aiming to achieve case count targets. A simultaneous cost-of-illness study using the same cases continues along a similar timeline. A nasopharyngeal carriage survey comparing pre-introduction (2013) to post-introduction carriage (2014-2016) completed data collection in 2016, along with the final round of a vaccine coverage survey. Data analysis is underway, with future publications *expected.*	Surveillance for IPD has detected 73 cases of IPD (25 cases of radiologically proven pneumonia and 48 of meningitis) within the study catchment area between 2013 and mid-2016. Only 16 of these are vaccine serotype cases that can contribute to the vaccine effectiveness analysis; however 28 cases are needed to complete this portion of the study, which is unlikely to occur by the study completion date of mid-2017. Study findings from the coverage estimates and NP carriage are anticipated in 2017. Case-control (if possible) and cost of illness study results are expected in 2018.
Impact of PCV on disease, nasopharyngeal carriage, and health	Enrolment continues in surveillance-based studies evaluating invasive bacterial disease and pneumonia, along with studies examining PCV	Preliminary analysis of pre-introduction data (i.e. pre-2015) indicate that pneumococcal carriage rates in hospitalized pneumonia cases were 42%; importantly75.7% of pre-vaccine pneumococcal

Study	Status of Activities	Key findings
economics in Nepal (Oxford University)	impact on nasopharyngeal carriage in hospitalized pneumonia cases and healthy children. A head to head immunogenicity study comparing two dose schedules (at 6+10 weeks and 6+14 weeks, respectively) opened recruitment in August 2015 and reached target enrolment in April 2016; analysis will commence when final samples have been collected (no later than Feb 2017) and lab testing is complete. An analysis of PCV10 impact on hospitalized pneumonia and meningitis using administrative data began in Q4 2015. The data are nearly complete and will be fully analysed by July 2017. A health economic impact study (cost of illness) study has completed data collection and analysis is expected to be complete by Q3/2017.	isolates identified would have been included in the PCV10 vaccine; PCV13 would have contributed just 4.2% additional coverage (79.9%) The community carriage study in children has shown a decrease in VT-carriage among healthy children under 2 years in the post-vaccine era; however effects in older children have not yet been observed, as was expected. Preliminary analysis of cost of illness data shows an average cost of $232.59 per pneumonia episode. On average, a child was sick for about a week before being admitted to the hospital, during which time substantial costs (both direct and indirect resulting from productivity loss) were incurred. Preliminary analysis of retrospective hospitalized pneumonia data shows that before vaccine introduction, pneumonia, meningitis and sepsis together accounted for a significant number of childhood hospital admissions at Patan hospital. A decrease in admissions for these syndromes in 2016 has been observed but formal data analysis is ongoing. Complete study results, including post-introduction findings, analyses of surveillance data, head-to-head immunogenicity results, and the review of administrative data on hospitalized pneumonia and meningitis are expected to begin rolling out in 2017.
Impact of PCV introduction on hospitalised pneumonia, IPD and nasopharyngeal carriage in Lao PDR (Murdoch Children's Institute)	Pre-PCV13 data collection was complete as of 2014. Post-introduction carriage survey began in 2015 and continued in 2016; lab testing and data analysis are ongoing. Surveillance for IPD continues. The retrospective pneumonia review has commenced and data collection and analysis are currently ongoing.	Preliminary pre-introduction results suggest approximately 35% of healthy children and infants carry pneumococci in the nasopharynx, while approximately 20% carry vaccine-type pneumococci. Over 80% of carriage samples with pneumococci contained antibiotic resistant genes as identified by microarray. Post-introduction findings, along with IPD surveillance and retrospective pneumonia review results are anticipated in 2017.
Impact of PCV on hospitalized pneumonia and nasopharyngeal carriage in Mongolia	Hospitalized pneumonia enrolment began in 2015, with chest x-ray capacity building activities ongoing	Preliminary estimated carriage of pneumococcus among healthy children and infants before vaccine introduction was 61% among healthy

Study	Status of Activities	Key findings
(Murdoch Children's Institute)	such that 78% of cases enrolled had an x-ray image recorded. The first (pre-introduction) community carriage survey was successfully completed between May and August 2015, and the first post-introduction survey will be performed in 2017	children aged 12-23 months; of these, 42.8% were vaccine-type. Preliminary analysis of pre-introduction hospitalized pneumonia data suggests approximately 19% of pneumonia cases with radiographs are positive for primary endpoint pneumonia. Although comparison of pre- and post-introduction data is not yet possible as PCV13 introduction occurred in summer 2016, enrolment and assessment of films continues and preliminary pre-post analysis may be possible by 2017.
2. Centers for Disease Control and Prevention (2013-2016)		
Evaluating the impact of PCV in Burkina Faso	Evaluation of the impact of PCV on meningitis using data from national surveillance continues data collection. Analysis of baseline (pre-introduction) meningitis surveillance was published in *PLoS ONE* in 2016. Post-introduction data collection continued through 2016, including for the proposed indirect cohort study. Results are expected in 2017.	Average annual adjusted incidence rates in the pre-vaccine period (2011-2013) were 26.9 (<1 year), 5.4 (1±4 years), 7.2 (5±14 years), and 3.0 (>15 years). Of 1,528 cases, 1,036 (68%) were serotyped: 71% were PCV13- associated serotypes, 14% were non-PCV13-associated serotypes, and 15% were non-typeable by PCR.
3. Full Country Evaluations (2013-2016)		
3.1 Evaluating the impact of PCV on nasopharyngeal carriage, IPD and x-ray confirmed pneumonia in Mozambique	Vaccine effectiveness studies will potentially continue in 2017.	Evidence from vaccine effectiveness studies suggests that the introduction of PCV in 2013, which was rapidly routinised in the country, has reduced nasopharyngeal carriage of vaccine-type pneumococcus and reduced the incidence of vaccine-type invasive pneumococcal disease (IPD) and pneumonia. The nasopharyngeal carriage study aimed to estimate the effects of PCV10 introduction on pneumococcal nasopharyngeal carriage (i.e. vaccine preventable disease transmission) 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

Study	Status of Activities	Key findings
		was observed at the first round (within 18 months) after PCV introduction. • A 41% (95% CI 6–69) reduction in VT pneumococcal carriage was observed in HIV-uninfected children receiving three doses. • A 61% (95% CI 9–82) reduction in VT pneumococcal carriage was observed in HIV-infected children receiving three doses. • As expected, there was also an increase in pneumococcal carriage of non-PCV10 VT, including serotypes in PCV13 (i.e., 19A). The reduction in carriage has been accompanied by a reduction in vaccine-type invasive pneumococcal disease (IPD). Based on surveillance data from the Manhiça demographic surveillance system (DSS), it has been estimated a statistically significant reduction in vaccine-type IPD of 87.7% (95% CI 44.1–97.3). There was also a marginally significant reduction in X-ray-confirmed pneumonia (64.9%, 95% CI -4.4–88.2).
3.2 Impact of PCV on nasopharyngeal carriage in Bangladesh	Manuscript for the impact of PCV on nasopharyngeal carriage was completed in Dec 2016,	Findings from the pneumococcal impact study in Bangladesh also suggest some reductions in both the overall transmission of pneumococci and serotypes included in the vaccine (VT) 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. • Among 4-11 months age group, pneumococcal colonization decreased from 65% to 61% and VT coverage reduced by 8% (32% to 24%). • Among 12-23 months age, pneumococcal colonization decreased from 63% to 52% and VT coverage reduced by 10% (39% to 29%). • In 24-35 months age group (age group eligible for the vaccine Yr3 of the study), pneumococcal colonization decreased from 52% to 48%, whereas VT coverage remained same (44% and 43%).

Sources

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