Dalberg

Gavi PCV AMC pilot: 2nd Outcomes and Impact Evaluation

Final Evaluation Report

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I. EXECUTIVE SUMMARY

Context

The Pneumococcal Conjugate Vaccine Advance Market Commitment (PCV AMC) pilot was established as an innovative financing mechanism with the overarching goal of reducing morbidity and mortality from pneumococcal disease and preventing hundreds of thousands of childhood deaths in developing countries by accelerating development, availability and uptake of PCV. The PCV AMC pilot was designed between 2006 and 2008, and launched in 2010, with the purpose of incentivizing vaccine makers to develop and build manufacturing capacity, thereby improving PCV access in developing countries.

The formal objectives of the PCV AMC pilot were 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);
- **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 incentivizes manufacturers to invest in scaling up production capacity to meet developing country vaccine demand;
- **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
- **Test the effectiveness of the AMC mechanism** as an incentive for needed vaccines and to learn lessons for possible future AMCs."[1]

Objectives of this evaluation

This is the third evaluation commissioned on the PCV AMC pilot, following the 2012 process and design evaluation and the 2015 midterm evaluation. The PCV AMC pilot finished in 2020, though the contracts with manufacturers extend until 2029[2]. This final evaluation aims to look back at the whole of the PCV AMC pilot, bringing together the findings, conclusions and lessons learned to generate recommendations. The primary objective of this evaluation is to assess to what extent and how the PCV AMC pilot has achieved its overarching impact goal of reducing rates of morbidity and mortality from pneumococcal disease in developing countries. The intended audiences for this evaluation report are the Gavi Secretariat and Gavi, The Vaccine Alliance – including the donors that funded the PCV AMC pilot. A secondary audience are those stakeholders interested in market shaping.

Methodological overview

To evaluate the outcomes and impacts of the PCV AMC pilot, the independent evaluation team conducted a mixed-methods, theory-based evaluation. The evaluation draws on interviews with 71 experts, review of over 80 documents, and analysis of data from Gavi, UNICEF SD, the Vaccine Impact Modelling Consortium (VIMC), and Institute for Health Metrics and Evaluation (IHME). The evaluation uses the uptake of three other vaccines available through Gavi as counterfactuals for what might have happened without the PCV AMC pilot. These vaccines are Hib/Penta, rota and HPV.

[1] These are the verbatim objectives for the PCV AMC pilot, as reported in the 2020 Pneumococcal AMC Annual Report and elsewhere.
[2] The subsidy associated with doses purchased through the PCV AMC pilot will have been distributed substantially before 2029

There have been no significant departures from the Terms of Reference laid out for the evaluation (See Annex 1).

Summary of conclusions

This Executive Summary discusses the PCV AMC pilot framed around the four objectives as defined by Gavi. These, as ordered by Gavi, are 1) R&D, 2) supply, 3) uptake and then 4) impact and effectiveness.

Conclusions on Objective 1: R&D

The PCV AMC pilot aimed to "Accelerate the development of pneumococcal vaccines that meet developing country needs". However, it was not specified if this meant reducing the time to market of those already in the pipeline, encouraging new entrants to enter the pipeline, or both.

This evaluation did not find evidence that the PCV AMC pilot accelerated new product R&D amongst those in the pipeline, despite one new TPP-compliant PCV product coming to market during the PCV AMC pilot. SII's PCV10 only reached the market in 2020, five years later than estimated. There is no evidence of accelerated progress across pipeline candidates before and after 2010, and the manufacturers interviewed for this evaluation did not state that the pilot had a catalytic effect on R&D.

Taking a broader interpretation of 'accelerating' new product R&D, the PCV AMC pilot was successful at signaling the value of the LMIC PCV market. This may have contributed positively to the large number of firms pursuing PCV vaccines, however it is difficult to be precise about the role the PCV AMC pilot played given the complex firm-level decisions underpinning investment decisions, and the fact that the Gavi-73 market is only ~10% of the value of the global market.

The PCV AMC pilot was very successful at driving presentation innovation, in terms of Multi-Dose Vials (MDVs). These were key to scaling up supply and driving down cost per dose in LIC and LMIC markets. Both Pfizer and GSK developed 4-dose presentations during the PCV AMC pilot, which required new product design, new formulations, clinical studies, and securing WHO-PQ status for the new presentations.

Conclusions on Objective 2: Vaccine supply

The PCV AMC pilot achieved the objective of scaling up PCV supply in Gavi-73 markets – especially between 2010 and 2015/6 – by increasing manufacturer confidence in market demand. Supply increased from 3 million doses per year in 2010 to 150 million doses per year in 2017. GSK and Pfizer invested a combined USD ~500 million to increase their production capacity. These decisions, while informed by the PCV AMC pilot, were at least partially planned prior to the launch of the pilot.

The PCV AMC pilot was not wholly successful at avoiding supply-related and non-supply-related delays common for antigens in Gavi-73 markets – there were significant delays in the first three to four years of the PCV AMC pilot. Full ramp up of supply capacity took until 2015/16. Up to this point, there were countries who were forced to delay introduction of PCV, or who chose to wait for availability of their preferred product. Outside of Penta and measles, however, supply uncertainty is the norm, not the exception, for vaccines in Gavi markets.

Continual structurally optimistic forecasting from Gavi/UNICEF led to unintended consequences for manufacturers and the Gavi markets they aimed to supply, as manufacturers incurred costs and lost confidence in inaccurate Gavi/UNICEF forecasting. Gavi and UNICEF's forecasting is too optimistic both in terms of the total volume of demand, and how soon that will materialize. This led to a loss of confidence amongst manufacturers, as well as unexpected costs from holding over

inventory. While forecasting demand is not specific to the PCV AMC pilot, it is particularly important in an AMC: the instrument works by building manufacturer confidence in demand.

The PCV AMC pilot was relative ineffective at driving price competition, likely due to the late entry of SII's PCV10 and the subsidy design[3]. Different stakeholders had different perspectives on the role of the PCV AMC pilot in driving price competition: some thought the AMC's role was to create a low and stable price, whilst others expected significant price declines over the decade of the instrument to support ongoing affordability of PCV. The PCV AMC pilot was designed under the assumption that a new product would reach the market earlier in the pilot. As this did not happen, the price competition within the PCV AMC pilot was less than originally expected by some stakeholders. In upcoming years, the competitive pressure exerted by SII's PCV10 might cause PCV vaccine prices to decline, if indeed countries' product preferences, and their likelihood to adopt or switch products, are at least partially driven by price.

Conclusions on Objective 3: Vaccine uptake

The PCV AMC pilot achieved the objective of accelerating vaccine uptake, though it is plausible demand for PCV would have been high without an AMC, on account of the disease burden and context. Awareness of the PCV AMC pilot was low amongst country-level decision makers, as befits a manufacturer facing instrument. Similarly, in-country stakeholders did not mention the AMC-*derived* long-term security of supply or AMC-*derived* stability of price as main drivers of PCV uptake.[4] Factors more influential in driving decision-making (burden of disease, Gavi advocacy, short-term security of supply) are though partially or fully linked to the AMC:

- PCV was selected for the AMC pilot partially on account of the high disease burden it represents in Gavi countries, especially in U5 children[5]
- The increase in supply capacity was partially driven by the AMC (Objective 2: Vaccine Supply)
- Gavi Secretariat staff and Gavi partners were advocating for PCV introduction because of the disease burden and the supply availability
- The top-up subsidy on some of the doses inherent in the AMC mechanism has plausibly decreased the prices to Gavi offered by manufacturers, which, in turn, plausibly has increased the likelihood of uptake by price sensitive transitioning countries
- It is possible that the PCV AMC pilot placed additional focus on PCV uptake given the commitments to manufacturers and donors, and desire to demonstrate success for the upcoming replenishment cycle and Strategy 3.0 period that started in 2011. This may have translated into greater country engagement around PCV by Gavi. However, this sentiment has not been corroborated by all stakeholders interviewed

In short, it is likely the PCV AMC pilot accelerated uptake of PCV across the Gavi-73 cohort, although it should be noted that this country demand did not materialize in response to the *predictable* pricing or the *long-term*, sustainable prices.[6]

[3] The PCV AMC pilot sought to offer "low, long term and sustainable prices" rather than specifically to drive price competition. Price competition, however, is relevant because the evaluation specifically asked about whether the PCV AMC pilot created 'affordable and sustainable PCV' (Question 4 in the ToR). PCV is one of the most expensive vaccines in the Gavi portfolio, and this evaluation raised questions about the sustainability of countries' co financing obligations (see Section 3).

[4] There has been significant discussion between the Gavi Secretariat and the evaluators about how much it matters whether in-country decision makers responded to AMC-specific attributes like predictable supply or long-term sustainable prices. The Gavi-approved Theory of Change on which this evaluation was based (see Annex 5) assumed that in-country decision makers were aware of these attributes, and responded to them. They were not – in short, the PCV AMC pilot worked, but not through the causal path assumed by Gavi and therefore tested in this evaluation.

[5] Gavi, The Pilot Advance Market Commitment Concept and Development, 2011.

Conclusions on Objective 4: Impact and effectiveness

The PCV AMC pilot likely was successful at driving higher coverage, and thus an increase in lives saved, from PCV than under counterfactual antigen scenarios. While these comparators are imperfect, Gavi-73 countries introduced PCV more quickly than rota, Hib or HPV.

The big questions, for which a counterfactual approach is unfortunately difficult, are whether the PCV AMC pilot created lower prices than would have been observed without an AMC, and to what extent these lower prices would have altered decisions made by transitioning and fully self financing countries. The strong likelihood of receiving top-up subsidy on some of the doses should have decreased the price to Gavi offered by manufacturers. This, in turn, should have increased the likelihood of uptake by price sensitive transitioning countries, though the exact increase in propensity is very hard to tell. Furthermore whether this propensity actually led to different (binary) introduce or do not introduce decisions is very hard to ascertain due to the lack of a clear counterfactual. India and Indonesia (see Sections VI and VIII) highlight how complicated and country-specific these uptake decisions are.

Gavi decided to offer PCV in 2006, so had already, in effect, made a commitment to support uptake before the PCV AMC pilot. The $1.5bn in additional funds raised for subsidy likely reduced the price-to-Gavi and therefore the donor funding of Gavi needed to cover the share of doses not paid for by countries. Given there was no price to Gavi for PCV before the PCV AMC pilot, it is unfortunately impossible to analyze the efficiency of the PCV AMC pilot vs a hypothetical 'normal' PCV program.

Lessons learned

The PCV AMC pilot has yielded important lessons that can inform future AMC design, and the situations in which an AMC can and should be used. Some lessons emerge from specific conclusions, while other lessons cut across the whole of the PCV AMC pilot. Building on the OECD DAC evaluation definitions, lessons learned are broken down into fundamental lessons (overall lessons about the use of the AMC mechanism), tactical lessons (aimed at improving the *efficiency* of future AMCs), and strategic lessons (aimed at maximizing the *effectiveness* of a future AMC or other market shaping activities).

The fundamental lesson from the PCV AMC pilot is that an AMC mechanism can be an effective intervention in vaccine market shaping. Over the course of the 10-year pilot, Gavi has demonstrated that the legal design and operational delivery are feasible; that the design allows stakeholders to work collaboratively and constructively to achieve objectives; and that the instrument appears to stabilize vaccine markets. As such, it becomes one tool that global health actors can use again (in the right context) to increase access to crucial vaccines or health commodities in developing countries.

There are tactical lessons can inform the design of future AMCs.

- There was less downward pressure on prices than might have been expected by some, likely driven by the combination of late entry of SII's PCV10 and the fact that subsidy levels were linked to volume of doses, not the price per dose. Future iterations of an AMC mechanism could consider adjustments to the subsidy design or R&D incentive structures to drive greater price competition.
- The nature of the Gavi/UNICEF forecasting led to a loss of confidence from manufacturers, which may have decreased the effectiveness of the AMC, and may decrease the efficiency of future Gavi investments in vaccines, through increased prices as perceived risk is priced in. While this risk is close to unknowable, simple adjustments like more transparent communication of the assumptions in the forecast may avert these risks in future.

- The World Bank treasury function and guarantee came with a financial cost perceived to be high relative to its 'value' to the PCV AMC pilot; these costs could be avoided in the future. As noted in Section 9, the Treasury function was considered, in hindsight, to have been necessary at the time of the launch of the AMC, given Gavi's much smaller balance sheet and donor base. As Gavi grew, the 'value' of this function declined.
- The PCV AMC pilot's legal structures were perceived to be very cumbersome (both for implementation of the PCV AMC pilot itself, and around the governance of the PCV AMC pilot), which resulted in high transaction costs for the partners, and reduced strategic flexibility. Future iterations of an AMC mechanism could envisage much more streamlined legal agreements.

There are strategic lessons from the PCV AMC pilot. These relate to how strategic objectives within the PCV AMC pilot traded off against each other, and as such will be relevant for future AMCs and market shaping instruments.

- Gavi did not fully communicate degree of prioritization between scaling up production, and incentivizing R&D amongst new market entrants – achieving one comes at the cost of achieving the other – which may have led to less-than-potential progress against either.
- While the uptake of PCV has been rapid, it is possible it could have been even faster with clearer prioritization of supply. Conversely, the PCV AMC pilot did not accelerate R&D – this would have been possible with a different AMC structure.
- The lack of clear prioritization also led to legitimate grievances from some stakeholders when their individual ambitions from the PCV AMC pilot were only partially met. Future AMCs with clearer objectives should minimize this risk.

Recommendations

This report makes four recommendations, all of which benefitted substantially from the co-creation workshop with Gavi Secretariat staff on 19 August 2021.

AMC-specific recommendations

As the PCV AMC pilot has shown, how an AMC is designed and run – elements which are all inherently choices – will have impacts on the potential for progress against the different objectives of the instrument.

The desire to let countries choose their preferred products, linked to Gavi's overarching objective of "country ownership", can be at tension with achieving supply-related objectives. Importantly, country-led decision-making does not mean that supply objectives *cannot* be achieved; rather, it means that Gavi has very limited ability to control demand and thus Gavi cannot guarantee the achievement of these objectives and take accountability for them.

One way for Gavi to partially circumvent this dilemma and increase the likelihood of achieving both supply and market entry objectives would be "healthy demand" interventions.[6]

[6] Given the current focus on COVAX, readers may be interested to understand how the COVAX AMC is grappling with this challenge. While the COVAX AMC it is called an AMC (see https://www.gavi.org/gavi-covax-amc) and was inspired by the PCV AMC pilot, the instrument is different in material ways. Importantly, the deals under the COVAX AMC are manufacturer-specific, not market wide. Furthermore, the COVAX AMC can offer high confidence in demand to manufacturers because supply is so scarce and because countries are allocated products by WHO through the Fair Allocation Framework, rather than choosing them.

Recommendation 1: Gavi could benefit from adopting a more coordinated and intentional approach to shaping healthy demand – as proposed in the new market shaping strategy[7]. This should increase the effectiveness of future AMCs, expand the potential use cases for an AMC, and decrease the risk associated with interventions like AMCs that shape supply.

Fundamentally, the ability to better shape demand would offer new use cases for an AMC at Gavi. These might include situations where products are more differentiated than they are for PCV, for example. While the PCV AMC pilot has been a success in many ways, how often and when Gavi can deploy an AMC again will depend in large part on decisions around Gavi's operationalization of demand shaping, which is just starting.

- **As the strategy notes, Gavi would benefit from increased capabilities to predict countries' preferences, and the likelihood and likely timing of a country's decision to adopt a new vaccine or switch to a different vaccine product.** Understanding in more detail how demand materializes in different country contexts should help Gavi better understand demand across products, and across timeframes.
- **If there is a mismatch between commitments made on the supply side, and emerging demand, Gavi would benefit from a wider and firmer toolkit to steer and shape demand to avoid misalignment and reduce potential risk.** Gavi does seek to shape demand today, but efforts are somewhat *ad hoc*, and often responsive. The new market shaping strategy states the Alliance will develop "a new demand health intervention framework" but notes demand side interventions would only be 'exceptional'. In essence, increasing ambition to make hard commitments on the supply side need to be matched with increased capabilities to shape preferences on the demand side to avoid unacceptable levels of financial risk. Given the market failures across the antigens Gavi supports, and the increasing complexity of these markets, it feels likely these interventions may be needed in more than 'exceptional' cases.

This approach does raise some fundamental and philosophical questions around how demand shaping integrates with country-led decision-making, and which tools encroach too much into country ownership. Discussions on these issues for the evaluation have highlighted differing views within the Secretariat and across the Alliance. The market shaping strategy announces a roadmap development process: this roadmap would be a natural "venue" to debate these trade-offs and chart a path forward.

Recommendations relevant to future AMCs and other market shaping instruments

Recommendation 2: The design of subsidy mechanisms in future AMCs or other market shaping instruments could benefit from both understanding the incentive structures the mechanism will create if the market develops as expected, and how it will influence market actors in other plausible scenarios. The PCV AMC pilot deployed $1.3bn of subsidy, and while the subsidy design was effective at increasingly supply, in hindsight it could have been more targeted and intentional with respect to price competition[8]. The downward pressure on prices was assumed to come from the market entry of SII, an assumed but fundamentally uncertain market development. While it may not be possible to design a perfect subsidy mechanism, Gavi could benefit from analyzing the 'robustness'

[7] The new strategy defines healthy demand as: "Healthy demand from a market perspective is defined as a state when program demand materializes as expected, when the quantity and timing of demand can be sufficiently predicted and sustained over time, and when country product choices are evidenced-based and implemented with minimal delay, leading to the balanced uptake of appropriate products and the timely uptake of new innovative products. In short, demand should be timely, predictable, sustainable, balanced, and driven by evidence-based decisions and up-to-date policies."

[8] As noted above, some stakeholder expected the price to decline during the course of the PCV AMC pilot, whilst others did not. Those that expected a price decline were disappointed.

of the design – how well it works in multiple plausible scenarios – for future AMCs or other market shaping instruments.

Recommendation 3: Gavi could benefit from delivering more accurate and informative[9] demand forecasts to manufacturers, focusing in particular on when demand is likely to materialize. While forecasting demand is challenging, Gavi's forecasting today is perceived to be structurally too optimistic. The current situation might have two counter-productive and unintended consequences: i) that manufacturers disregard Gavi's data, and actually produce lower volumes than they might have with a well-justified and well-communicated Gavi forecast, and/or ii) that manufacturers price in the costs of holding inventory to future Gavi deals, yielding lower value for money for Gavi than might have been possible through better forecasting.[10],[11]

Recommendation 4: Legal structures of future AMCs could be designed to allow for appropriate flexibility, and to minimize transaction costs for all parties involved. It was necessary to use very robust legal structures for the first AMC, because of the innovative nature of the partnership. However, with Gavi's capabilities, and especially its credibility, now firmly established, Gavi and its partners can take advantage and have a nimbler legal structure that reduces (transaction) costs while still providing the right level of confidence and protection for both sides.

[9] Informative, in this context, means greater transparency around assumptions like the probability of NVI by key countries
[10] The Gavi Alliance Market Shaping Strategy for 2021-2025 includes both a desire to better understand country needs and desires, and a focus on the predictability of demand. Both of these should support improved forecasting.
[11] The co-creation workshop attendees noted the challenges of forecasting demand for a given product when countries are choosing between an increasing number of products to introduce – this will increase uncertainty, but should not drive structural biases in the forecasting

II. Acronyms and Abbreviations

AMC	Advance Market Commitment
APA	Advance-Purchase Agreement
AVI	Accelerated Vaccine Introduction
BMGF	The Bill and Melinda Gates Foundation
CAGR	Compound Annual Growth Rate
DAC	Development Assistance Committee
DALY	Disability-adjusted Life Year
DCVM	Developing Country Vaccine Manufacturer
DTP	Diphtheria-Tetanus-Pertussis Vaccine
EPI	Expanded Program on Immunization
FVP	Fully Vaccinated Person
Gavi	Gavi, The Vaccine Alliance
GNI	Gross National Income
GSK	GlaxoSmithKline
Hib	Haemophilus Influenzae Type B
HIC	High-Income Country
HIV	Human Immunodeficiency Virus
HPV	Human Papillomavirus
HSS	Health System Strengthening
IFPMA	International Federation of Pharmaceutical Manufacturers & Associations
INDEPTH	International Network for The Demographic Evaluation of Populations and their Health
IPD	Invasive Pneumococcal Disease
LIC	Low-Income Country
LiST	Lives Saved Tool
LMIC	Low-To-Middle-Income Country
LSHTM	London School of Hygiene and Tropical Medicine
LTA	Long Term Agreement
M&E	Monitoring And Evaluation
MDGs	Millennium Development Goals
MDV	Multi-Dose Vial
MIC	Middle-Income Country
MNC	Multi-national Corporation
MSF	Médecins Sans Frontières (Doctors Without Borders)
NVI	New Vaccine Introduction
OECD	Organisation for Economic Co-operation and Development
PAHO	Pan American Health Organization
PATH	Formerly Called the Program for Appropriate Technology In Health
PCV	Pneumococcal Conjugate Vaccine
PCV10	10 Valent Pneumococcal Conjugate Vaccine
PCV13	13 Valent Pneumococcal Conjugate Vaccine
PCV7	7 Valent Pneumococcal Conjugate Vaccine
PCV3	Received All Three Doses of Pneumococcal Conjugate Vaccine
PneumoADIP	The Pneumococcal Vaccines Accelerated Development and Introduction Plan
R&D	Research And Development
Rota	Rotavirus
RSV	Respiratory Syncytial Virus
SII	Serum Institute of India

SDF	Gavi Strategic Demand Forecast
SDGs	Sustainable Development Goals
ToC	Theory of Change
TPP	Target Product Profile
TRIVAC	Model Developed by London School of Hygiene and Tropical Medicine
U5	Under Five Years Old
UNICEF	United Nations Children's Fund
US	United States of America
USD	United States Dollar
VIG	Vaccine Introduction Grant
VIMS	Vaccine Information Management System
WHO	World Health Organization
WHO-PQ	World Health Organization Pre-Qualification of Medical Products
WUENIC	WHO and UNICEF Estimates of National Immunization Coverage

III. INTRODUCTION

About Gavi

Gavi, the Vaccine Alliance (Gavi) is a global health partnership comprising public and private sector organizations, with the mission of saving lives and protecting people's health by increasing equitable and sustainable use of vaccines. Since its founding in 2000, Gavi, the Vaccine Alliance has helped vaccinate more than 822 million children in the world's poorest countries which, has prevented an estimated 14 million deaths.[12]

Gavi now supports immunization programs that serve almost half of the world's children, giving it tremendous power to negotiate vaccines at prices that are affordable for the poorest countries and to remove the commercial risks that previously kept manufacturers from serving them.

As a result of market shaping efforts, the cost of fully immunizing a child with all 11 WHO-recommended childhood vaccines now is approximately USD 28 in Gavi-supported countries, compared with approximately USD 1,200 in the United States of America, and the pool of manufacturers producing prequalified Gavi-supported vaccines has grown from five in 2001 (with one in Africa) to 17 in 2019 (with 11 in Africa, Asia and Latin America). Gavi support has resulted in more than 495 vaccine introductions and campaigns, dramatically increasing immunization against virulent diseases worldwide.[13]

About pneumococcal disease

There are an estimated 14.5 million cases of serious pneumococcal disease in under-five (U5) children every year, resulting in approximately 500,000 deaths per year.[14] These cases occur mainly in LICs and LMICs. Pneumococcal infections are caused by Streptococcus pneumoniae bacteria and can lead to bacteremia, meningitis, and pneumonia, as well as other less severe conditions such as sinusitis and otitis. There are over 93 pneumococcal serotypes, of which six to eleven account for over 70% of all pneumococcal disease in children. Pneumococci are typically transmitted from the nasopharynx via respiratory droplets, particularly by infants and young children.[15] Children with chronic medical conditions such as heart disease, lung disease, diabetes, or HIV infection are especially susceptible to pneumococcal disease.[16]

In 2007, WHO made the formal recommendation to include PCV in childhood immunization in all countries with high pneumonia and U5 mortality rates.[17] For administration to infants, a three-dose schedule administered either as two primary doses plus a booster (2p+1 schedule) or three primary doses (3p+0 schedule) is recommended. Primary vaccination series can be initiated as early as at six weeks. WHO also states that, whenever possible, catch-up vaccination at the time of PCV introduction should be used to accelerate its impact on disease in children aged one to five years, particularly in settings with a high disease burden and mortality. Catch-up vaccination should be done with a single dose of vaccine for children aged 24 months and older; and one or two doses in children

[12] Gavi website.
[13] Gavi website.
[14] Centers for Disease Control and Prevention, *New and Underused Vaccines, Pneumococcus*, CDC, Atlanta, July 2017.
[15] World Health Organization, *Pneumococcal Disease*, WHO, Geneva, June 2020.
[16] World Health Organization, *Pneumococcal Conjugate Vaccines in Infants and Children Under 5 Years of Age*, WHO, Geneva, February 2019, p. 90.
[17] MSF, Analysis and Critique of the Advance Market Commitment (AMC) for Pneumococcal Conjugate Vaccines (PCVs) and Impact on Access, 2020.

aged 12–23 months. Gavi supports PCV for administration in infant routine immunization programs, with or without catch-up at introduction.[18]

Recognizing the high pneumococcal disease burden in LICs and LMICs, Gavi began making funding available in 2006 for the introduction of PCV in the 72 countries with the lowest GNI per capita.[19] Prior to introduction of PCV (before 2008), 82% of these countries had a mortality rate of >50 per 1,000 live births among U5 children, and 92% had >10% of deaths in U5 children attributed to pneumonia.[20] To help accelerate uptake and access to needed vaccine products (including PCV) in these countries, a coalition of donors was designing innovative approaches to vaccine financing and market shaping, including the Advance Market Commitment (AMC) pilot. PCV was one of the antigens considered for the pilot AMC mechanism and was ultimately selected due to the high disease burden of pneumococcal disease and the availability of PCV products.

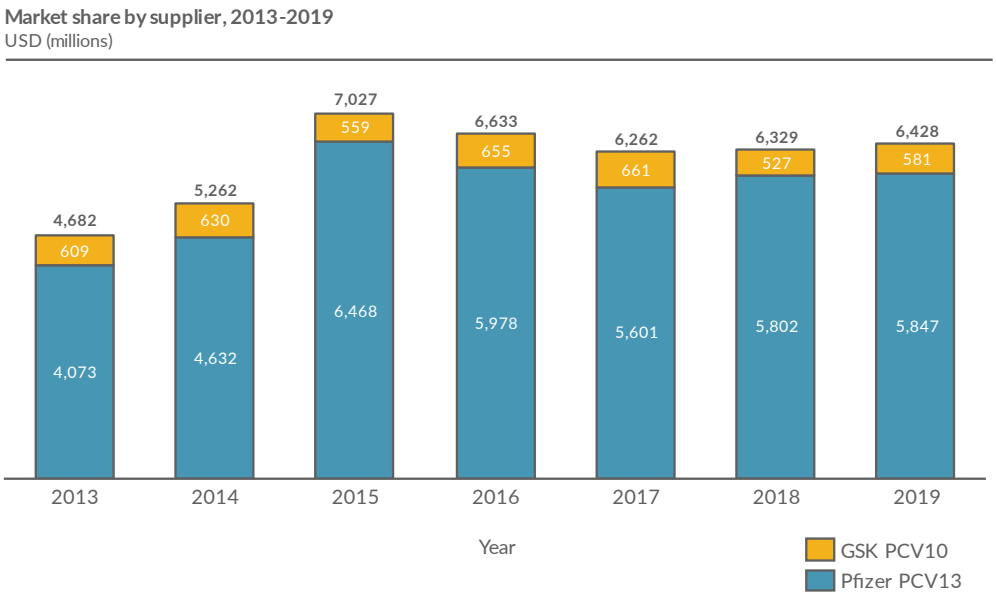
Historical context on the PCV market

In 2006, when Gavi decided to offer PCV to LICs and LMICs, the global PCV market was much smaller with demand concentrated almost exclusively in high-income countries in North America and Europe. At the time, the only available vaccine on the market was Wyeth's[21] seven-valent pneumococcal conjugate vaccine (PCV7). The high vaccine price, driven by the complexity of development and the manufacturer's focus on HICs, impeded inclusion of PCV in the immunization programs of developing countries. In 2009, GSK's Synflorix (PCV10) entered the market, and in 2010 Pfizer's Prevnar (PCV13) was approved by the United States' Food and Drug Administration for use in the United States.[22]

Currently, the global PCV market has estimated annual revenues of between USD 6 to 7 billion. Pfizer is the world's largest producer of PCV, with a 90% market share through its sale of PCV13 (Figure 1). PCV13 dominates the US market, where it is marketed at an indicative price of USD 180.00 per dose. The US market accounts for 55% of global market revenues reaching USD 3.6 billion. GSK occupies second place in the global PCV market, with 10% of global market share by revenue.

[18] UNICEF, "Pneumococcal Conjugate Vaccine: Supply and Demand Update", 2020.
[19] CDC, Progress in Introduction of Pneumococcal Conjugate Vaccine – Worldwide, 2000-2008, 2008.
[20] CDC, Progress in Introduction of Pneumococcal Conjugate Vaccine – Worldwide, 2000-2008, 2008.
[21] Wyeth was acquired by Pfizer in 2009.
[22] MSF, Analysis and Critique of the Advance Market Commitment (AMC) for Pneumococcal Conjugate Vaccines (PCVs) and Impact on Access, 2020.

Figure 1: Global market share USD by supplier, 2013-2019[23]



The PCV market is expected to grow to USD 20.5 billion by 2026, with the Gavi73 market representing ~USD 750 million.[24],[25] This represents a compound annual growth rate (CAGR) of 8.3% from 2017. Market growth is expected to be driven by continued revenue growth in North America with the introduction of PCV in adult populations; and by emerging market vaccine introductions, driven by government and private sector efforts to reduce pneumococcal disease mortality globally. Additionally, there are 'next generation' PCV products (e.g., PCV20) that may come to market in the near future. The supply base for PCV is now increasing with two market entrants in 2019 (SII and Walvax).[26] Moving forward, incumbents are expected to face increasing competitive pressure from new entrants.[27,28]

Background on the PCV AMC pilot

In June 2009, the Governments of Italy, the United Kingdom, Canada, the Russian Federation and Norway, along with the Bill & Melinda Gates Foundation, collectively pledged a total of USD 1.5 billion to fund a pilot AMC against pneumococcal disease. Through forward-looking binding contracts from donors, and international agencies guaranteeing a viable market for target vaccines, the PCV AMC pilot was designed to encourage vaccine makers to develop and build manufacturing capacity to expand PCV access in developing countries.

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

- **"Accelerate the development of pneumococcal vaccines** that meet developing country needs (e.g., in terms of serotype composition and vaccine presentation) as specified in the TPP;

[23] UNICEF, Pneumococcal Conjugate Vaccine: Supply and Demand Update, 2020.
[24] Transparency Market Research, *Global Pneumococcal Vaccines Market*, Transparency Market Research, New York, 2017.
[25] Gavi73 market estimated at ~250m doses (from the UNICEF, Pneumococcal Conjugate Vaccine: Supply and Demand Update, 2020. And USD 3.00 per dose.
[26] Walvax has been developed for use in the domestic Chinese market, not Gavi markets.
[27] Pfizer, *Appendix A: Financial Report 2019*, Pfizer, New York, 2018, p. 26. / Pfizer, *Appendix A: Financial Report 2014*, Pfizer, New York 2015, p. 20.
[28] GlaxoSmithKline, *Annual Report 2017*, GSK, London, 2018, p. 246-247 / *Annual Report 2016*, GSK, London, 2017, p. 62 / *Annual Report 2015*, GSK, London, 2016, p. 58 / *Annual Report 2013*, GSK, London, 2014, p. 62.

- **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 incentivizes manufacturers to invest in scaling up production capacity to meet developing country vaccine demand;
- **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
- **Test the effectiveness of the AMC mechanism** as an incentive for needed vaccines and to learn lessons for possible future AMCs."[29]

The PCV AMC pilot was designed between 2006 and 2008 through an extensive consultation process. An AMC Secretariat was created; a PCV Target Product Profile (TPP) for developing countries was designed to ensure that the candidate vaccines in development would effectively address Gavi-73 contexts in terms of serotype coverage and product presentation;[30] the mechanism design and pricing were developed; an Independent Assessment Committee (IAC) was created to design an M&E framework; and legal agreements with manufacturers were drawn up.

At that time, the private sector was less well recognized as a major player in international development, and there was less experience with public-private partnerships in health. This was the era of the MDGs, not the SDGs. It was an era of much less collaboration between private sector actors and development partners, and Gavi was only six years old. These factors made the PCV AMC pilot highly innovative for its time.

The development and implementation of the PCV AMC pilot also accompanied a strategic shift for Gavi. In 2010, when the PCV AMC pilot was launched, Gavi was transitioning out of its Phase II strategy (2006-2010). During this period two new vaccines were added to its portfolio (PCV and rotavirus) and several fundamental policies and financing mechanisms were developed and reviewed, including the co-financing policy. Gavi's Phase III strategy (2010-2015) had the strategic goals of (i) accelerating the uptake and use of underused and new vaccines; (ii) strengthening the capacity of integrated health systems to deliver immunization; (iii) increasing the predictability of global financing and improve the sustainability of national financing for immunization; and (iv) shaping vaccine markets to provide appropriate and affordable vaccines for the developing world. The ambitious PCV AMC pilot was meant to play a critical role in furthering these new strategic objectives.

The first rollout of PCV under the AMC pilot occurred in Nicaragua in December 2010. As of December 2020, 63 of the 73 AMC-eligible countries have been approved to receive Gavi support for PCV introduction. Of these, five countries are or will be self-funding PCV vaccination and receive support in the form of access to the Gavi PCV AMC prices, the lowest in the world.

From 2010 to 2020, the AMC distributed USD 1.31 billion in subsidy to three manufacturers, and 1.16 billion doses of PCV have been procured for Gavi countries.[31] Donors agreed to allocate the remaining USD ~200 million budget to the COVAX AMCs and to the Gavi PCV program. A further 887 million doses have been contracted though the AMC Long Term Agreements through 2029.

[29] These are the verbatim objectives for the PCV AMC pilot, as reported in the 2020 Pneumococcal AMC Annual Report and elsewhere.
[30] MSF, Analysis and Critique of the Advance Market Commitment (AMC) for Pneumococcal Conjugate Vaccines (PCVs) and Impact on Access, 2020.
[31] Gavi, AMC Secretariat Annual Report, 2020.

Figure 2: The PCV AMC pilot process

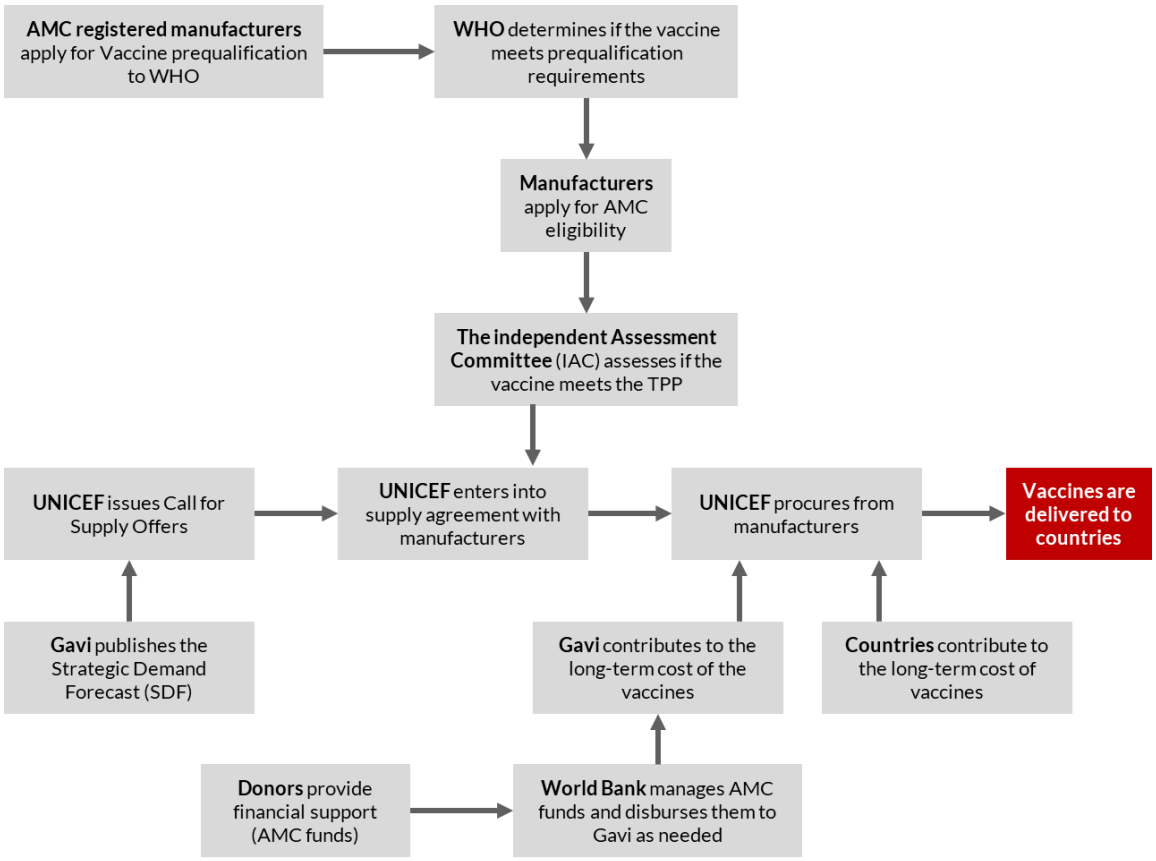
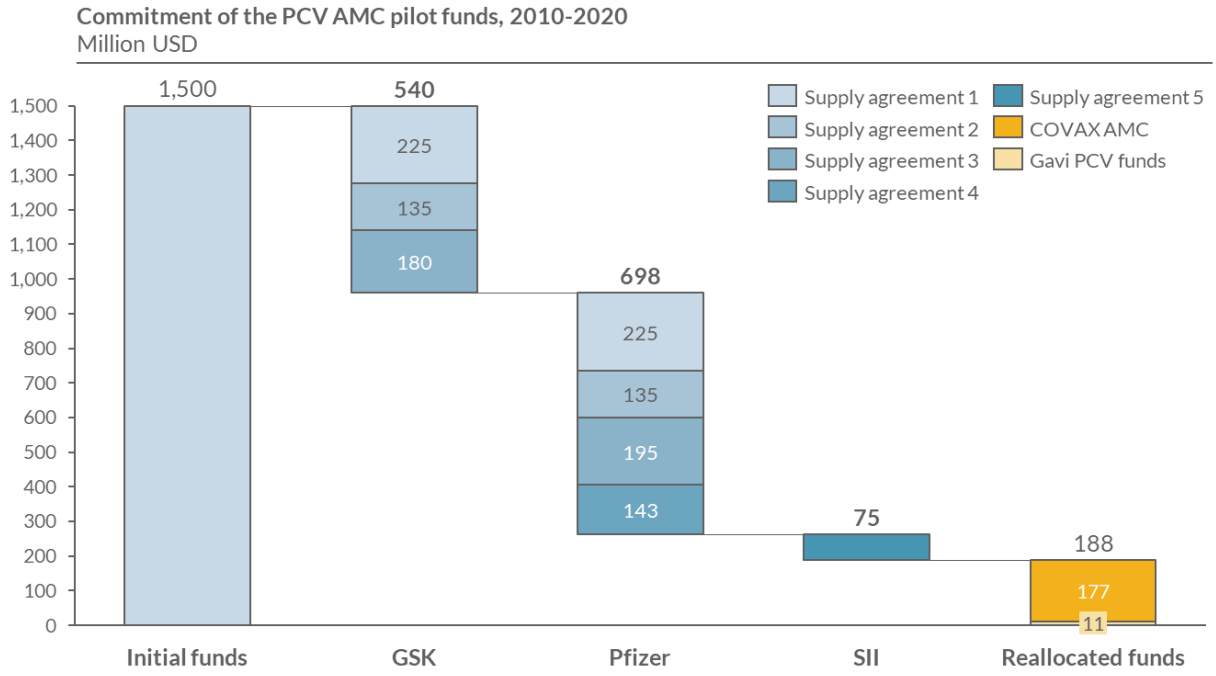


Figure 3: Commitment of PCV AMC pilot funds, 2010-2020



The subsidy is distributed to manufacturers based on demand that materializes from countries. As more demand materialized for PCV13 than PCV10, UNICEF procured more doses from Pfizer than from GSK, and Pfizer received more of the subsidy. The subsidy mechanism 'tops up' the

manufacturer from the price-to-Gavi[32] to USD 7.00 per dose for approximately 20% of the doses procured by UNICEF through the PCV AMC pilot. This price-to-Gavi was originally set at USD 3.50 (meaning USD 3.50 in subsidy per dose). When price-to-Gavi drops below USD 3.50 (for example when SII came to market at USD 2.00 a dose), the subsidy tops the manufacturer up to USD 7.00 for each dose until the agreed volume of subsidy has been paid. The manufacturers do not receive more total subsidy for lower prices – subsidy depends on volume – but rather, the subsidy is paid out more quickly if the price is lower.

Objectives of the evaluation

This is the third evaluation commissioned on the PCV AMC pilot, following the 2012 process and design evaluation and the 2015 midterm evaluation. This final evaluation aims to look back at the whole of the PCV AMC pilot, bringing together the findings, conclusions and lessons learnt from the whole decade to develop recommendations. The primary objective of this evaluation is to assess to what extent the PCV AMC pilot has achieved its overarching goal of reducing rates of morbidity and mortality from pneumococcal disease in LICs and LMICs. The evaluation also seeks to assess to what extent the PCV AMC pilot achieved the four programmatic objectives of (i) accelerating the development of pneumococcal vaccines; (ii) increasing the availability of effective pneumococcal vaccines for developing countries; (iii) accelerate vaccine uptake; (iv) testing the effectiveness of the AMC mechanism. The audiences for this evaluation report are Gavi and Gavi partners, with a secondary audience of those interested in market shaping.

Scope of the evaluation and structure of the report

The scope of this evaluation covers the entire delivery of the PCV AMC pilot, and covers the entire 'results chain' from outputs to outcomes to impacts (see Annex 1 for the ToR and Annex 5 for ToC). The ToR for this evaluation (see Annex 1) also included 11 specific evaluation questions. Some of these were 'big picture' questions: "To what extent can the causal path from the AMC Theory of Change be validated?". Some were more detailed: "What are the learnings at the country level in terms of budgeting and financing?". And some of the questions overlapped: "To what extent can the causal path from the AMC Theory of Change be validated?" vs. "Whether, why and how has the AMC resulted in the availability of affordable and sustainable PCV?"

Given the audiences for this report are both those very close to the AMC, like the Gavi Secretariat, and those with wider interests in market shaping, the evaluation team decided to structure the report around the four publicized objectives of the PCV AMC pilot (see 'Background on the PCV AMC pilot'), not the specific evaluation questions. The contents of this evaluation report do however respond to all evaluation questions (see Annex 2 for a mapping of evaluation questions to report sections).

Building off the OECD DAC standards for evaluations, this evaluation sequentially links the following aspects of the theory-based evaluation methodology (see Annex 4 for a full explanation of the methodology):

- **Findings:** A finding uses evidence from one or more evaluations to allow for a factual statement
- **Conclusions:** Conclusions point out the factors of success and failure of the evaluated intervention, with special attention paid to the intended and unintended results and impacts, and more generally to any other strength or weakness. A conclusion draws on data collection and analyses undertaken, through a transparent chain of arguments.

[32] This is not the same as the price the country pays: that price depends on the co-financing status of the country in question.

- **Lessons learned:** Generalizations based on evaluation experiences with projects, programs, or policies that abstract from the specific circumstances to broader situations. Frequently, lessons highlight strengths or weaknesses in preparation, design, and implementation that affect performance, outcome, and impact.
- **Recommendations:** Proposals aimed at enhancing the effectiveness, quality, or efficiency of a development intervention; at redesigning the objectives; and/or at the reallocation of resources. Recommendations should be linked to conclusions.[33]

In addition to the discussion in the main body of the evaluation, please refer to Annex 7 for a detailed mapping of the evaluation process, findings, and conclusions.

One complication of this objectives-driven structure is that Objective 4 of the PCV AMC pilot[34] includes assessing lessons learned during the pilot. To address this and align the methodological approach with OECD DAC definitions, the evaluation team has chosen to discuss lessons learned in a standalone section, following conclusions and preceding recommendations. Whether the AMC has generated lessons learned is an objective of the AMC in itself (part of Objective 4) and thus answering this evaluation question (and whether this objective of generating useful lessons learned has been achieved) stretches across findings, conclusions and lessons learned, which could result in an unclear chain of logic for the reader if the report followed this path.

The lessons learned – emerging from the conclusions – focus on both efficiency[35] and effectiveness.[36] Within effectiveness, the lessons learned range from potential changes to design, to the 'fundamental' lesson: can an AMC create and or stabilize vaccine markets? As such, lessons learned are organized into three categories to align with this structure:

- **Fundamental lesson learned:** overall lesson about the use and value of the AMC mechanism
- **Tactical lessons learned:** lessons aimed at improving the *efficiency* of future AMCs
- **Strategic lessons learned:** lessons aimed at maximizing the *effectiveness* of a future AMC or other market shaping activities

Finally, recommendations emerge from lessons learned, and focus on broader themes surfaced during the evaluation that aim to improve the efficiency and effectiveness of both future AMCs, as well as Gavi's broader market shaping activities.

Summary of methodology

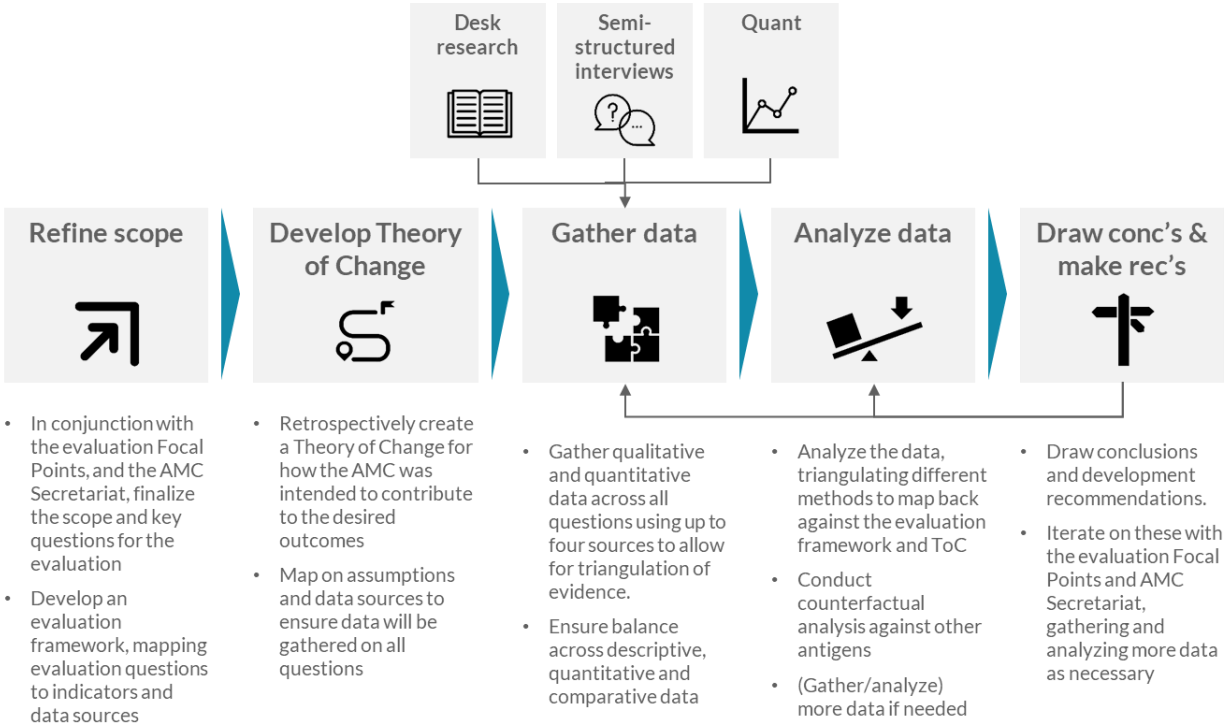
To evaluate the outcomes and impacts of the PCV AMC pilot, Dalberg conducted a mixed-methods, theory-based evaluation. The evaluation draws on the insights of 71 interviewees, review of over 80 documents, and analysis of data from Gavi, UNICEF SD, the Vaccine Impact Modelling Consortium, and IHME. The evaluation uses the uptake of three other vaccines available through Gavi as counterfactuals for what might have happened without the PCV AMC pilot. These vaccines are Hib/Penta, rotavirus and HPV. A full description of the methodological approach can be found in Annex 6, including the Theory of Change[37] (ToC) and evaluation framework.

[33] OEDC, Glossary of Key Terms in Evaluation and Results Based Management
[34] "Test the effectiveness of the AMC mechanism as an incentive for needed vaccines and to learn lessons for possible future AMCs"
[35] OECD DAC definition: A measure of how economically resources/inputs (funds, expertise, time, etc.) are converted to results.
[36] OECD DAC definition: The extent to which the development intervention's objectives were achieved, or are expected to be achieved, taking into account their relative importance.
[37] The theory of change was retrospectively developed by Dalberg through review of Gavi documents and interviews with selected key stakeholders. It received two rounds of review during the inception phase of the evaluation.

Throughout the evaluation process, key stakeholders (Gavi Evaluation Focal Points, Gavi AMC Secretariat, Gavi AMC SteerCo, Gavi EAC, and external experts) have been engaged through structured one-on-one interviews and through group discussions to inform and guide the evaluation process. The independent evaluators have engaged with these stakeholders separately and coordinated with the Gavi Evaluation Focal Points to support outreach when appropriate, in order to maintain independence and navigate potential sensitivities.

There have been no significant departures from the Terms of Reference.

Figure 4: Description of evaluation methodology



IV. Objective 1: Research & Development (R&D)

The first Objective of the PCV AMC pilot was "to accelerate the development of Pneumococcal Conjugate Vaccines that meet developing country needs (e.g., in terms of serotype composition and vaccine presentation), as specified in the TPP". This objective remained unmodified over the course of the PCV AMC pilot

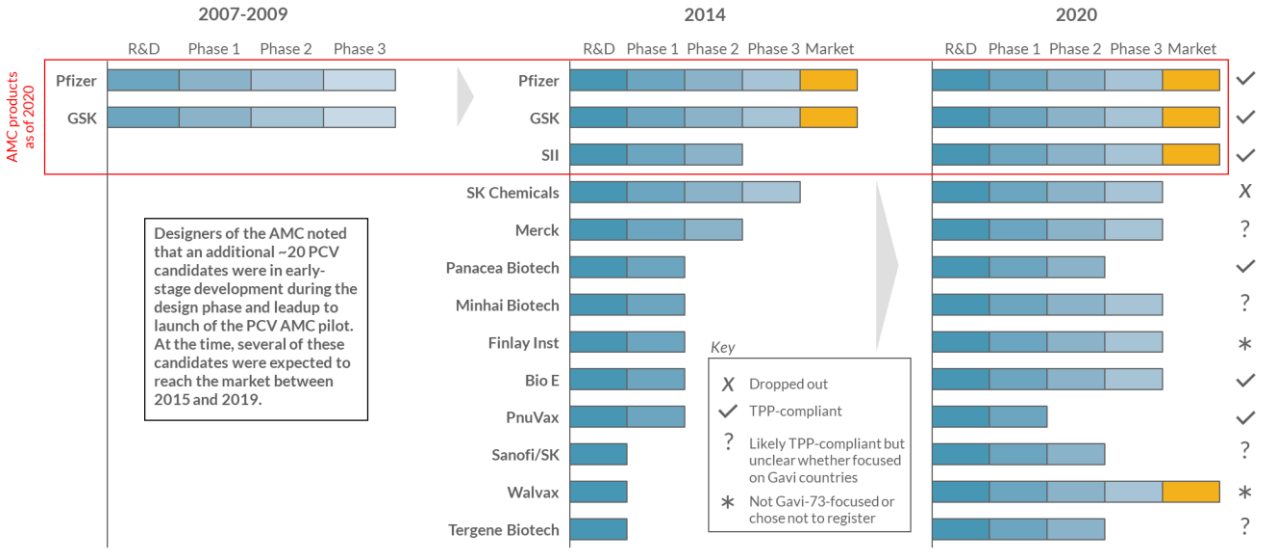
This section is broken down into three parts to understand extent to which the PCV AMC pilot (i) accelerated R&D for manufacturers developing new PCV products; (ii) drove presentation innovation to meet the needs of Gavi-73 countries; and (iii) changed manufacturers' perceptions of the viability of developing country PCV markets.

The TPP ensures that products still in development will have appropriate serotype coverage and product presentation for Gavi-73 markets. In turn, this improves the vaccine efficacy and increase the deaths averted in target geographies. While the TPP did not influence GSK and Pfizer, who reached the market just prior to the launch of the PCV AMC pilot in 2010, it has clarified the path forward for other manufacturers with candidate vaccines, including SII, which launched its PCV10 product in 2020. The development of a TPP for Gavi markets is an example of a successful achievement of the PCV AMC pilot in aligning the parameters of market-wide R&D with the needs of Gavi-73 countries.

Findings on R&D

Since 2010, one new PCV product, SII's PCV10, has become available for Gavi markets. One additional product, Walvax's PCV13 became available, but is focused on the domestic Chinese market, with no immediate indications of interest in entering Gavi-73 markets. Other candidate products have made progress, as well, including BioE's PCV14 and Merck's PCV15 (both are currently in Phase III trials). Other candidate vaccines, however, have stalled or dropped out of development, such as SK Chemicals' vaccine, which dropped out following the loss of a patent dispute with Pfizer. Figure 5, below, shows the progress of relevant PCV pipeline candidates since 2007.

Figure 5: Development phases of PCV candidates, 2014 and 2020



All five vaccine manufacturers interviewed during this evaluation stated that the PCV AMC pilot did not materially accelerate R&D of new PCV products. This echoes the findings of the 2015 midterm evaluation, which stated that none of the PCV candidate products in early or pre-clinical

phase in 2014-2015 entered development due the PCV AMC pilot.[38] At the outset of the PCV AMC pilot, two products were Gavi-approved (Pfizer's PCV13 and GSK's PCV10). Additionally, MNCs, as well as DCVMs had been investing in PCV development far prior to the launch of PCV AMC pilot. Because of this, vaccine manufacturers interviewed do not consider the pilot to have influenced the speed of or resources dedicated to PCV R&D. While SII did bring a new PCV product to market during the PCV AMC pilot, its arrival to market was much slower than anticipated. SII indicated that beyond the technical complexity of PCV development, domestic regulatory issues also slowed its progress during clinical trials, which took eight to nine years to complete.[39] In addition to the market pull provided by the PCV AMC pilot, SII received grant funding from the Bill & Melinda Gates Foundation, which helped accelerate its product development process. The Bill & Melinda Gates Foundation grant was not formally linked to the PCV AMC pilot but did include a (confidential) agreement to make a certain volume of PCV available at a certain price for low-income markets. This makes it difficult to isolate direct causal links between the PCV AMC pilot and SII's market entry.

Selection of PCV as the product for the AMC pilot meant that this vaccine came to Gavi markets only one year after the first approvals by national regulatory agencies, as opposed to an average of seven years for other vaccines like HPV and rota (see Figure 6 below). Historically, new vaccines have been developed and introduced in High Income Country (HIC) markets, with many years of delay before reaching LIC and LMIC markets.

Figure 6: Time lag between vaccine regulatory approval and Gavi country adoption, PCV and counterfactual antigens

Vaccine	Drug name (manufacturer)	FDA/EMA/DCGI approval	Gavi country adoption	Time lag
PCV	PCV10, Pneumosil (SII)	7/2020	2020	1 year
	PCV13, Prevnar (Pfizer)	12/2009	2010	
	PCV10, Synflorix (GSK)	3/2009	2010	
	PCV7, Prevnar (Wyeth)	2/2000	2009	9 years
Hib / Penta	Various	1985	Country intro: 1997 UNICEF: 2001	12 years
Rota	RV5, Rotasiil (SII)	1/2017	2019	2 years
	RV1, Rotavac (Bharat)	1/2014	2019	4-5 years
	RV5, RotaTeq (Merck)	2/2006	2011	
	RV1, Rotarix (GSK)	2/2006	2011	
HPV	HPV9, Gardasil (Merck)	10/2018	N/A	7-8 years
	HPV4, Gardasil (Merck)	6/2006	2013	
	HPV2, Cervarix (GSK)	9/2007	2013	

A review of pipeline candidates suggests that over the timeframe of the PCV AMC pilot, more DCVMs and low-cost vaccine manufacturers are developing PCV products specifically targeted at Gavi-73 markets. For example, SII's and BioE's PCV products have been designed to meet Gavi-73 contexts, including tailoring of the price point, serotype coverage, and MDV presentation.

Findings on presentation innovation

The PCV AMC pilot catalyzed presentation innovations in the form of Multi-Dose Vials (MDVs) that are lower cost and more practical in Gavi-73 markets. During the PCV AMC pilot, both Pfizer and GSK developed a four-dose presentation, while SII came to market with both a one-dose and five-dose presentation. MDV presentations are crucial for reaching the populations of large LICs and LMICs at low cost, and without need for extensive cold chain capabilities. Developing MDVs requires

[38] BCG, The Advance Marked Commitment Pilot for Pneumococcal Vaccines: *Outcomes and Impact Evaluation*, 2015.
[39] Interview, 28 August 2021.

the manufacturers to add preservative to the vial (to reduce cold chain requirements), re-test the stability of the vaccine, and seek new regulatory approval and WHO-PQ status. The fact that both MNCs with products on the market developed MDVs during the PCV AMC pilot does signal their commitment to Gavi-73 markets. One of the MNCs indicated that its MDV presentation was specifically developed for Gavi-73 markets as a means of scaling up production and accelerating expansion.[40] In the absence of the PCV AMC pilot, the manufacturer does not believe it would have invested in developing the MDV presentation.

Looking forward, some manufacturers are already considering Gavi-73-specific presentation innovations. For example, one MNC reported plans to develop an MDV presentation for a future PCV product, regardless of whether an AMC or similar mechanism secures LIC and LMIC demand for the product.[41]

Findings on perceptions of developing country PCV markets

Manufacturers did not indicate that the PCV AMC pilot significantly changed their perceptions of operating in, and providing vaccines to, developing country PCV markets. DCVM perceptions were least affected by the pilot, stating that they already understood Gavi markets, as these are markets that they depend on for long-term profitability and stability. For MNCs, it is difficult to say to what extent their perceptions on the viability of doing business in Gavi markets were affected by the PCV AMC pilot itself, or by other drivers. For example, prior to the 2009 launch of the pilot, Pfizer had already committed to expanding production capacity targeted at Gavi markets. However, this decision was influenced by the long design phase of the PCV AMC pilot, as well as accompanying policy guidance, NVI support, advocacy, and forecasting support that was part of the wider push for PCV adoption pre-PCV AMC pilot.[42]

Further information: *The conclusions on R&D are included in Section VIII. The manufacturers and others interviewed are listed in Annex 10. And Annex 7 describes the theory-based evaluation approach taken for this objective, tracking what analysis was conducted, and how the findings build into conclusions regarding the causal path through which the AMC was envisaged to work.*

[40] Interview, 3 May 2021.
[41] Interview, 3 May 2021.
[42] BCG, The Advance Marked Commitment Pilot for Pneumococcal Vaccines: *Outcomes and Impact Evaluation*, 2015.

V. OBJECTIVE 2: VACCINE SUPPLY

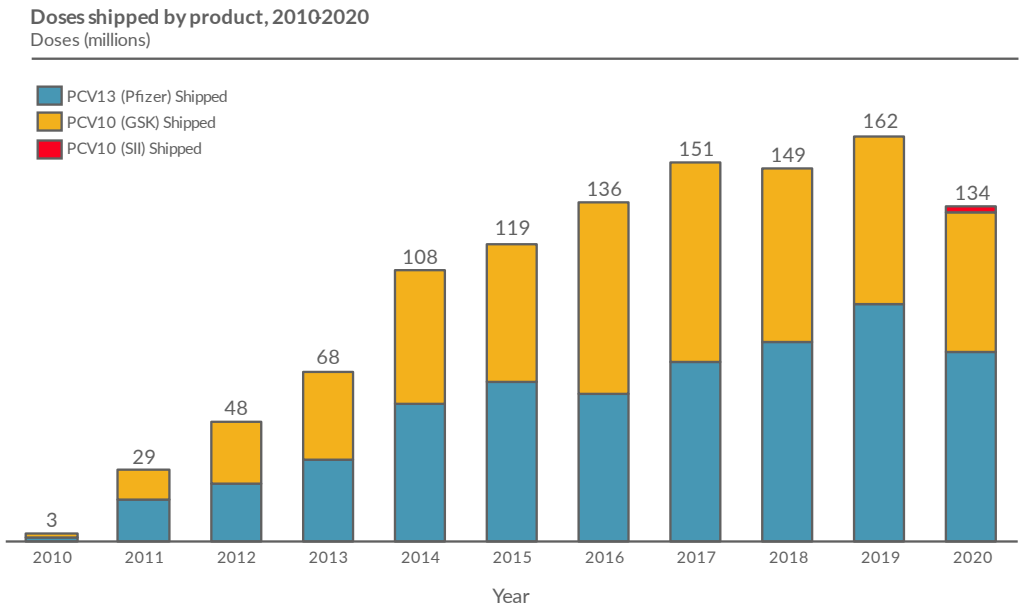
The second programmatic objective of the PCV AMC pilot was to bring forward the availability of effective pneumococcal vaccines for developing countries by guaranteeing the initial purchase price for a limited quantity of new vaccines that represents value for money and incentivizes manufacturers to invest in scaling up production capacity to meet developing country vaccine demand. This objective remained unmodified over the course of the PCV AMC pilot

This section seeks to understand the extent to which the pilot achieved this objective of improving supply, by evaluating (i) the evolution of supply, (ii) security of supply, (iii) alignment between supply and demand, (iv) the effects of supply delays and forecasting on country introduction, and (v) the effects of guaranteeing the initial purchase price for a limited quantity of new vaccines.

Findings on evolution of supply

Supply of PCV to Gavi-73 markets has grown from 3 million doses per year in 2010 to ~150 million doses per year since 2016. Figure 7, below, shows the supply of PCV to the Gavi-73 countries since 2010. A total of 1.16 billion doses had been procured and delivered through the AMC as of 31 December 2020.[43]

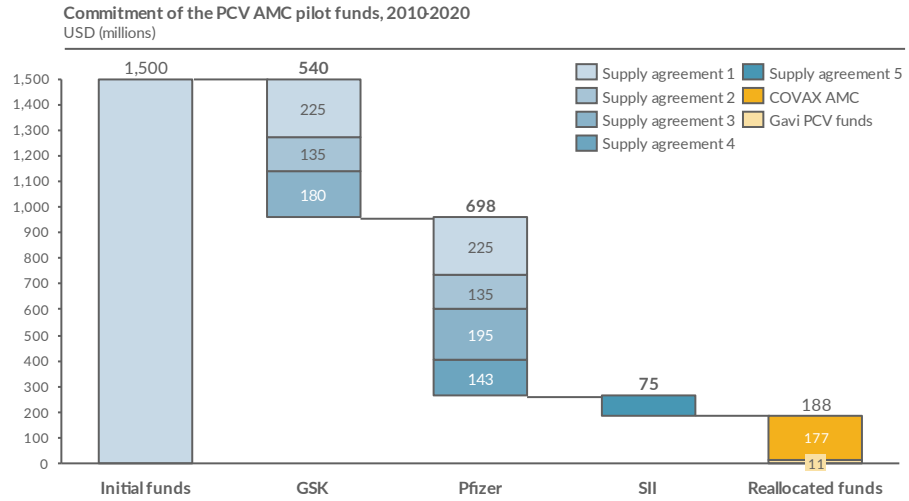
Figure 7 : Supply of PCV through the PCV AMC pilot, 2010-2020



These doses were procured through five Calls for Supply Offers, with Pfizer receiving USD 698 million in subsidy, GSK receiving USD 540 million in subsidy, and SII, contracted for 100 million doses, receiving USD 75 million in subsidy.

[43] Gavi, AMC Secretariat Annual Report, 2020.

Figure 8: Procurement by supply agreement through the PCV AMC pilot



Both GSK and Pfizer state they have invested in production capacity to meet increasing Gavi demand over the course of the PCV AMC pilot. Pfizer state they invested "in excess of the USD 100 million mark",[44,45] while GSK stated they have invested USD 400 million in increasing production capacity**.** However, as stated previously, both MNCs had planned investment in capacity expansion during the design of, and fundraising for, the PCV AMC pilot, making it difficult to isolate what portion of investment was directly due to the AMC mechanism.

Manufacturer quotes on scale up of supply

"The AMC did impact our thinking – it gave us confidence to invest in production, and we invested USD 400m.[46] We had the opportunity to understand that the volumes would become available, and that there was a pricing guarantee. That helped us make the decision: it provided additional confidence".[47]

- *GSK*

"I would not underestimate the signal value of these mechanisms. You are making a pretty big statement that is pretty difficult to walk back. [As a manufacturer] You're going to have your analysts crunch the numbers to make sure you have the IRR to justify it, but the [AMC] launch would give me confidence".[48]

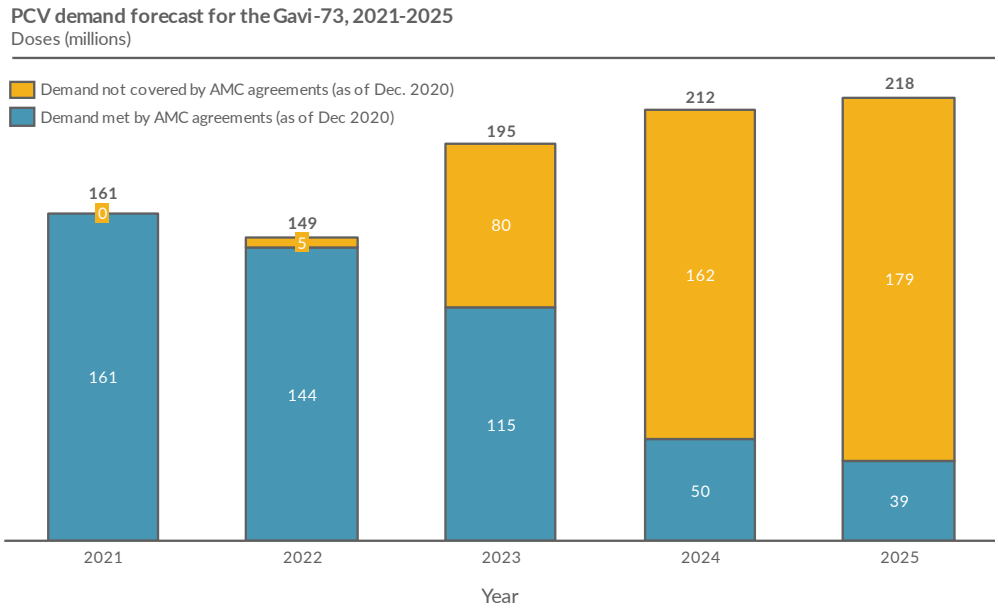
- Donor

Through the AMC's Long Term Agreements (LTAs), another 557 million doses are contracted out to 2025.[49] AMC-procured doses will make up an increasingly smaller share of supply to Gavi markets, which is expected to grow slightly to 220 million doses per year by 2025. While the PCV AMC pilot

[44] At the beginning of the AMC, Pfizer was using existing assets to accommodate the Gavi volume, but have since moved to new assets.
[45] BCG, The Advance Marked Commitment Pilot for Pneumococcal Vaccines: *Outcomes and Impact Evaluation*, 2015.
[46] A new plant in Singapore was also used to produce PCV for non-Gavi markets as well as other vaccines.
[47] Interview, 29 April 2021.
[48] Interview, 25 June 2021.
[49] AMC Secretariat Annual Report, 2020.

has formally closed, the Long Term Agreements will continue until 2029 for SII. Figure 9 below shows the Gavi demand forecast for PCV, and the role that AMC-procured doses will play in meeting demand across the Gavi-73 cohort.

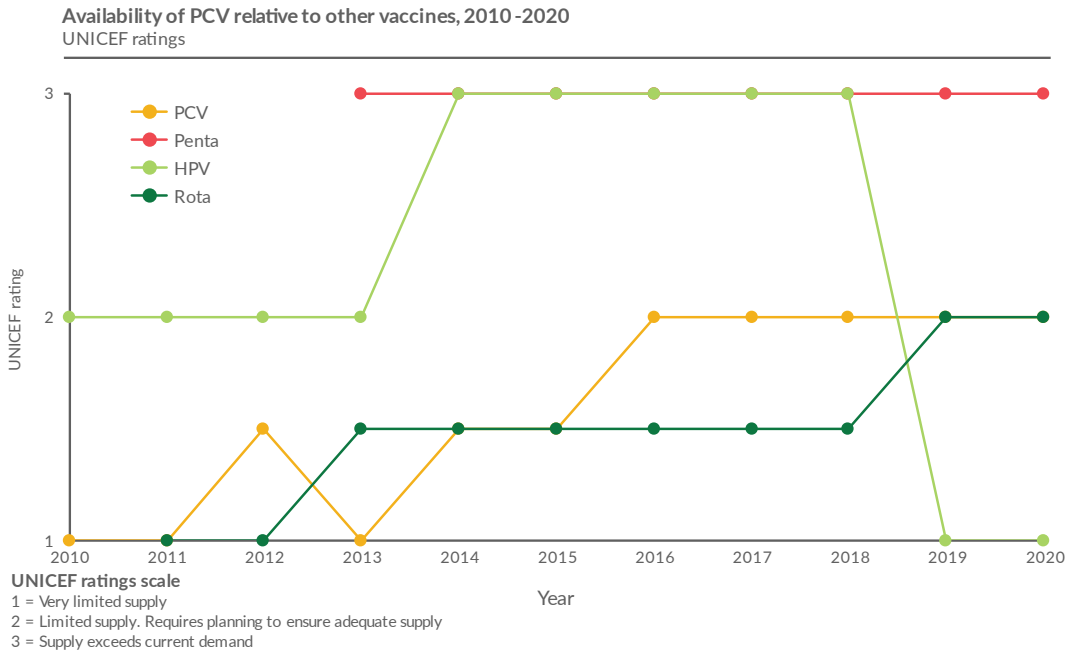
Figure 9 : Forecast demand through the PCV AMC pilot 2021-2025



Findings on security of supply

The UNICEF ratings for supply availability have increased from 1 out of 3, to 2 out of 3, showing greater confidence in the supply of PCV. UNICEF provides a 1-3 rating for supply availability of products supplied to Gavi, where 1 means "Very limited supply" and 3 means "Supply exceeds current demand". UNICEF's rating for PCV has increased from 1 in 2010 to 2 since 2016 – "Limited supply – requires planning to ensure adequate supply". This is shown in Figure 10, below. UNICEF's current assessment shows PCV has greater security of supply than HPV, and the same security of supply as rota. Supply of rotavirus vaccine has increased since 2012/3, whereas supply of HPV has decreased sharply since 2018/19. (Figure 10 below)

Figure 10 : UNICEF Security of supply rankings for PCV, Hib and rota



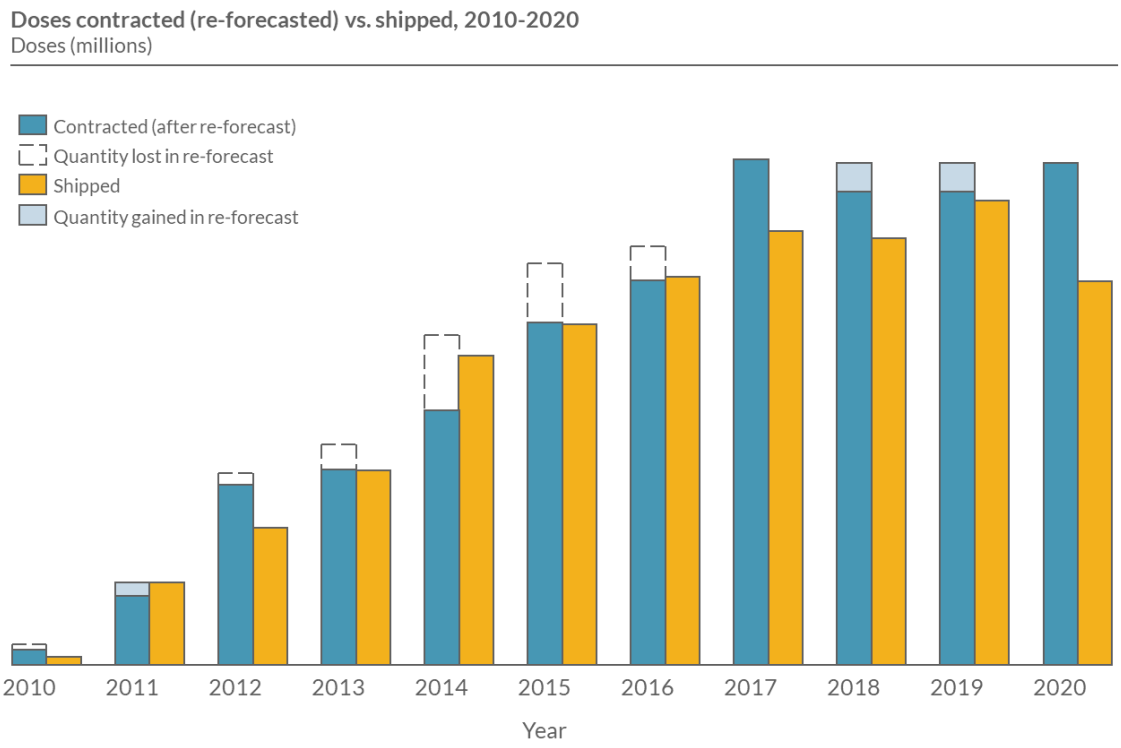
Findings on alignment between supply and demand

As only a small proportion of doses are legally binding under Long Term Agreements (LTAs), New Vaccine Introductions (NVIs) are limited by what manufacturers supply. If supply does not materialize (e.g., if a manufacturer experiences technical problems, or does not allocate the desired volume for Gavi-73 markets), then new demand cannot materialize in response,[50] and both supply and demand are re-forecasted into later years of the LTA. If demand does not materialize (e.g., if a given country is not ready to introduce PCV), that volume is also re-forecasted to a later date in the 10-year agreement. Conversely, if more demand materializes than expected, some doses are brought forwards in the LTA.

Forecasted doses – called 'contracted' by UNICEF – are continuously managed and revised post hoc, making it challenging to assess the alignment between supply and demand solely through procurement and shipping data. Figure 11, below, shows the contracted and shipped from 2010-2020, and revisions to the number of contracted doses *after* the year in question. It is important to note (see Figure 11 below) that the originally forecast doses are higher than what was actually shipped in every year apart from 2011. In some years – e.g. 2018 and 2019, the forecast exceeded what was shipped, and then was revised upwards post hoc (in effect made less accurate) to manage the balance of doses within the 10 year LTAs.

[50] Within Gavi, supply is prioritized for countries who have introduced a vaccine, relative to those who are planning to introduce a new vaccine.

Figure 11 : Doses contracted vs shipped, 2010-2020



In 2012-2014 there were significant supply-related delays to Gavi-73 countries aiming to introduce PCV.

- In 2011 the AMC Secretariat Annual Report noted: "Both suppliers have… communicated the ability to increase such early supplies [beyond the contracted levels], should there be demand."[51] Of the countries that wanted to introduce in 2011, only Pakistan was delayed due to supply shortage.[52]
- However, in 2012, the equivalent report noted "The current scope and pace of vaccine rollouts are unprecedented in GAVI's history. Given the scale up of demand, short-term supply for these vaccines will not be able to meet all requirements, and as a result, some of the countries approved for new GAVI support will be unable to introduce the vaccine in 2012 or 2013."[53]
- In April 2013, GSK experienced production issues with PCV10, resulting in a 14 million dose drop in supply that year. The 2013 AMC Secretariat Report noted the ongoing challenges: "Short-term supply constraints are expected in the next two years, as manufacturers continue to scale up capacity to meet the high-level of demand."[54] Nearly every country that wanted to introduce in 2012 and 2013 was delayed in part due to supply shortages.[55] The delays were particularly acute for large countries: delays of over a year for Bangladesh and Nigeria.
- In March 2014, GSK noted that the production capacity ramp-up was proceeding slower than expected, and that this would affect delivery of doses towards the end of 2014.[56]
- The availability of supply continued to increase in 2015 and was able to meet most of the country demand. Nigeria was the only country where the phased PCV introduction continued to be planned around supply availability, similar to 2014. In mid-2015, GSK confirmed that it

[51] Gavi, AMC Secretariat Annual Report, 2011.
[52] BCG, The Advance Marked Commitment Pilot for Pneumococcal Vaccines: *Outcomes and Impact Evaluation*, 2015.
[53] Gavi. AMC Secretariat Annual Report, 2012.
[54] Gavi, AMC Secretariat Annual Report, 2013.
[55] BCG, The Advance Marked Commitment Pilot for Pneumococcal Vaccines: *Outcomes and Impact Evaluation*, 2015.
[56] Gavi, AMC Secretariat Annual Report, 2014.

would be able to meet demand for the national roll-out in Nigeria from early 2016 onwards, one year ahead of schedule. The additional doses were made available due to introduction delays in large countries (e.g., Bangladesh, Phase 2 of Nigeria) as well as stock adjustments.[57]

Between 2015 and 2019, there were no major supply-related delays. Throughout the PCV AMC pilot, there were delays in planned introduction of PCV caused by factors *unrelated* to supply. Analysis conducted by Gavi in 2015 noted "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 decentralization, for example) and competing priorities at country level, such as multiple concurrent vaccine introductions and campaigns."[58]

Non-supply-related delays can be substantial, lasting up to two years in some cases. Analysis of the intended introduction date relative to the actual introduction date shows delays are very common across Gavi-73 countries. These are usually less than one year, but delays of around two years are not uncommon. DRC, Madagascar, Niger, Lesotho, Guinea Bissau, and Georgia all saw long delays between early ambitions to introduce PCV (aiming for 2011-2013) and actual introduction.[59] In some cases, these delays can serve to better align supply and demand (where supply would have been insufficient to meet total potential demand); in other cases the delays can serve to create 'lumpy' demand, if a number of countries end up introducing PCV at once.

Findings on delays and forecasting

Demand forecasting is critical in helping manufacturers plan annual supply capacity. The Gavi strategic demand forecast helps inform their capacity investment decisions (e.g., building new plants or new lines), and the near-term operational forecasts help inform their one- to two-year production plans (e.g., how much to produce and where to hold inventory). Demand forecast accuracy is extremely important to manufacturers in the context of the AMC, where purchase guarantees were minimal.

Throughout the PCV AMC pilot, the 'contracted' or forecasted doses have almost always been higher than the shipped doses. This can be seen in Figure 11, above, at an aggregate level, and Figure 12, below, at the product level.

[57] Gavi, AMC Secretariat Annual Report, 2015.
[58] AMC Secretariat Annual Report, 2017.
[59] BCG, The Advance Marked Commitment Pilot for Pneumococcal Vaccines: *Outcomes and Impact Evaluation*, 2015.

Figure 12: Difference between doses contracted and shipped by product, 2010-2020

Both manufacturers noted that the Gavi/UNICEF forecasts tended to overestimate volume and underestimate delays. Both manufacturers experienced gaps of up to 20% between what countries estimate as their annual requirement at the beginning of a year versus what they purchased.[60] These challenges with forecasting led both manufacturers to rely on their own forecasts.

Manufacturer quotes on the effects of demand forecasting:

"Gavi's forecast is always bullish – it makes it hard to see what the true needs are. We have a different set of needs, a different lens on the forecasting."[61]

"The timings were certainly not great. They didn't come to fruition when they thought they would."[62]

"There's no real accountability on countries to actually introduce."[63]

"We could never really rely on a forecast from Gavi or UNICEF for actual country demand."[64]

Both manufacturers noted that the dialogue around forecasting had improved, but the quality of forecasting had not. The challenges with forecasting were recognized and discussed in the 2015 evaluation.[65] For this evaluation, one manufacturer stated "The dialogue to improve the forecast got better. Whether or not that changed the outcome, not really."[66] The other said, "If we saw improvements in the forecasting, it was slight. It was too late in the [AMC pilot] process."[67]

Both GSK and Pfizer stated that they have rolled over more doses than expected from year to year, incurring costs. These costs included financial costs of committed resources, opportunity costs

[60] BCG, The Advance Marked Commitment Pilot for Pneumococcal Vaccines: *Outcomes and Impact Evaluation*, 2015.
[61] Interview 29 April 2021.
[62] Interview 29 April 2021.
[63] Interview 3 May 2021.
[64] Interview 3 May 2021.
[65] BCG, The Advance Marked Commitment Pilot for Pneumococcal Vaccines: *Outcomes and Impact Evaluation*, 2015.
[66] Interview, 3 May 2021.
[67] Interview, 29 April 2021.

associated with receiving cashflows later than anticipated, and managerial and coordination costs related to re-forecasting and managing relationships with Gavi/UNICEF. Both manufacturers noted (as in 2015) that the Gavi forecasts were not perceived as credible by their colleagues. "We need something with one foot in realism – the last thing you want is that the forecasts are constantly looked at through another lens."

Manufacturer quotes on the effects of demand forecasting:

"Manufacturing doses which are only suitable for one segment of the market, then holding lots of inventory, does have costs for us that do have to be absorbed elsewhere in the business."

"There is a two-year lag time for PCV – it's an opportunity cost to hold onto all this inventory."[68]

"One of the things we also saw – rollover of doses into the following years. That has made it quite difficult. From Gavi or UNICEF, that's great – you just push the doses. The back of the contract gets quite heavy, whereas the front is quite light. But for us it becomes quite difficult to manage."

Both GSK and Pfizer noted that the Gavi/UNICEF forecasting allocated to their products assumed a third manufacturer would enter the market. The PCV AMC pilot aimed to encourage new manufacturers to supply the Gavi market. SII came to market in 2020, later than had originally been envisaged (see Objective 1: R&D). Both GSK and Pfizer noted that product level forecasting assumed a third manufacturer would come to market and gain market share.

Pfizer and GSK quotes on Gavi supply allocation dynamics:

"It was noticeable that there were volumes kept back for new manufacturers."

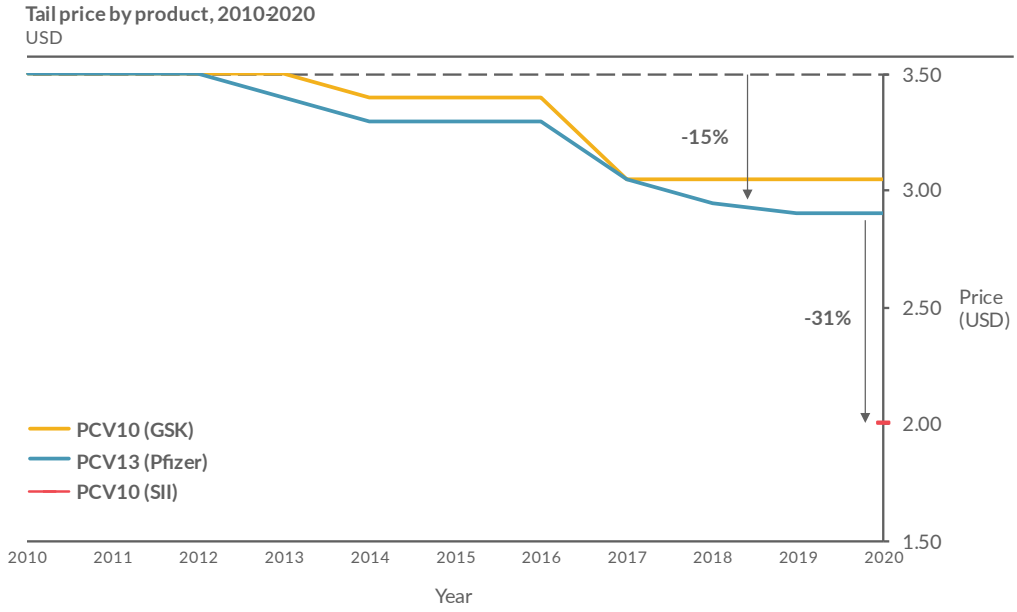
"Yes, we were quite aware that the market dynamics were going to change."

Findings on price

During the PCV AMC pilot, the price of GSK's PCV10 decreased from USD 3.50 to USD 3.05, and Pfizer's PCV13 decreased from USD 3.50 to USD 2.90 per dose.[69] Each manufacturer negotiated a 'Tail Price' with Gavi – this guaranteed a stable price per dose over the course of the PCV AMC pilot. These tail prices were negotiated in advance and decreased throughout the decade in recognition of economies of scale and volumes accruing to manufacturers. Figure 13 below shows the tail price by product throughout the PCV AMC pilot.

[68] Interview, 3 May 2021.
[69] For Multi-Dose Vials (see Objective 1: R&D). The tail price for Single-Dose Vials is USD 3.30.

Figure 13: Price of the products offered through the AMC



SII has entered the market at USD 2.00 per dose;[70] however, it remains to be seen whether this will drive product switch or drive down prices of GSK or Pfizer products. In 2020, SII's PCV10 came to market at a price of USD 2.00 per dose, more than 30% lower than either of the incumbents' tail prices. As of 31 December 2020, one Gavi country (Uzbekistan) had switched to the SII product, and two countries are planning to introduce it – Timor-Leste and India. Indonesia has expressed interest in the product as a second choice to Pfizer's PCV13. It is too early to tell whether the price differential between the SII's PCV10 and the other products will drive countries to switch, and/or will cause downward pressure on prices of GSK's PCV10 or Pfizer's PCV13.[71]

Further information: *The conclusions on vaccine supply are included in Section VIII. The manufacturers, UNICEF staff, and others interviewed are listed in Annex 10. And Annex 7 describes the theory-based evaluation approach taken for this objective, tracking what analysis was conducted, and how the findings build into conclusions regarding the causal path through which the AMC was envisaged to work.*

[70] For a 5-dose vial. The tail price for a Single-Dose Vial is USD 2.95.
[71] As of the publication of this report, August 2021, two further countries (Kenya and Kyrgyzstan) have applied to switch to the SII PCV10

VI. OBJECTIVE 3: VACCINE UPTAKE

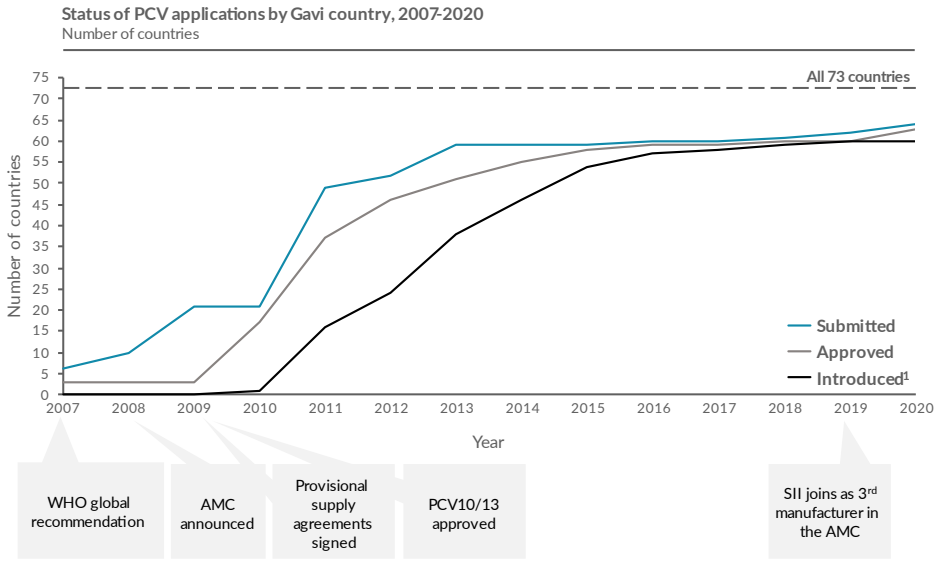
The third programmatic objective of the PCV AMC pilot was to a accelerate vaccine uptake by ensuring predictable vaccine pricing for countries and manufacturers, through binding commitments by participating companies to supply vaccines at low, long-term, and sustainable prices. This objective remained unmodified over the course of the PCV AMC pilot.

To assess the extent to which the PCV AMC pilot contributed to driving country-level uptake, this section examines (i) PCV uptake under the AMC, (ii) PCV uptake versus uptake of a set of counterfactual antigens not available under the AMC; and (iii) sustainability of vaccine co-financing to enable effective uptake.

Findings on uptake across the Gavi-73 cohort

Since the start of the PCV AMC pilot in 2010, 60 of the Gavi-73 countries have introduced PCV. Four further countries have submitted applications for Gavi support, three of which had been approved as of 31 December 2020. Figure 14 below shows the progression of country uptake of PCV, since 2007.

Figure 14: Status of PCV applications by Gavi country, 2007-2020



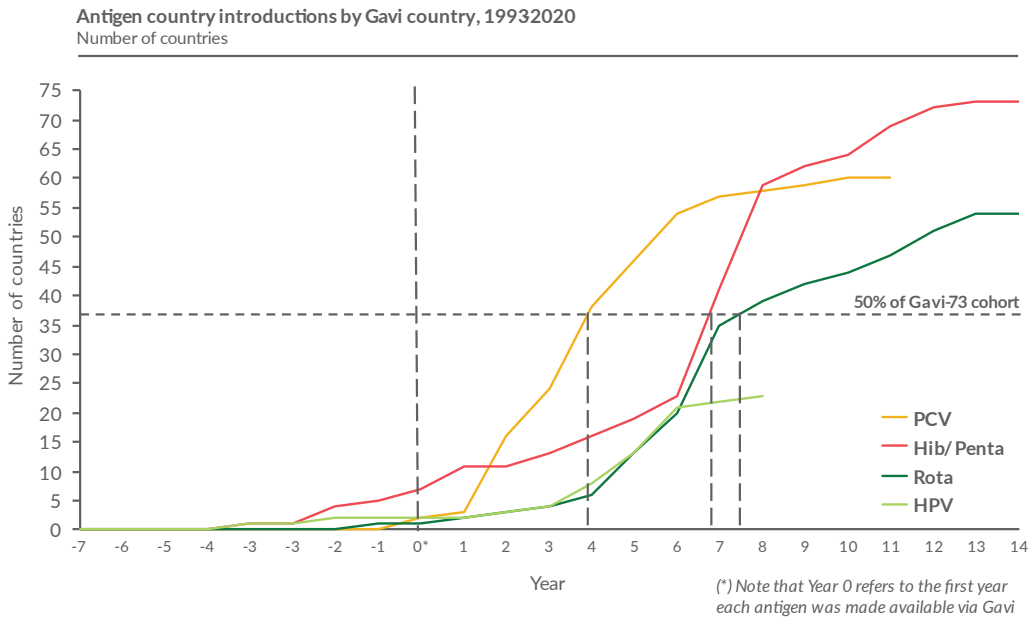
46 of the 60 countries have introduced PCV13; 14 have introduced PCV10. Since original introduction, five countries have switched to PCV 13, while one has switched to SII's PCV10. This means today that 50 countries currently use Pfizer's PCV13, nine use GSK's PCV10, and one uses SII's PCV10. This is more balanced than the global PCV market (see Figure 1) which is dominated by PCV13. However, the Gavi PCV market is still relatively 'fragile'. Demand for PCV10 is anchored in a small number of large Gavi countries. If these countries were to switch to PCV13 or the SII PCV10, then there may be a risk of GSK fully or partially withdrawal from the market. This could lead to dose volume falling below the minimum required for production at the Gavi price point or the market becoming a quasi-monopoly for PCV13. A quasi-monopoly in the PCV market could expose Gavi and global markets to security of supply or price risks.

Eight of the 13 Gavi-supported countries who have not yet introduced PCV are planning to do so. The Gavi-supported countries who did not introduce PCV fall into five groups:

- Three countries who have applied to access the PCV AMC pilot price, have been approved, and are expected to introduce PCV soon. These are Indonesia,[72] Timor-Leste,[73] and Ukraine.[74]
- Four countries who have expressed interest or political will to apply for support in 2021-2025. These are Comoros, Guinea, Somalia,[75] and Tajikistan[76].
- Cuba plans to introduce a domestically developed PCV7 (and has transitioned out of Gavi support), so is not introducing through the PCV AMC pilot.
- There are three countries who were unable to access the PCV AMC pilot because their DTP coverage is below 70%. These are Chad, North Korea, and South Sudan.[77]
- And two further countries who decided not to introduce PCV before they transitioned out of Gavi support. These are Sri Lanka and Vietnam.

Over half of the Gavi-73 countries introduced PCV in the first four years of the PCV AMC pilot. Hib and rota introduction took seven and eight years from introduction, respectively, to reach this level of uptake. Figure 15 below shows the progression of country uptake for PCV and counterfactual antigens, baselined from the time the antigens became available to Gavi markets (Year 0).

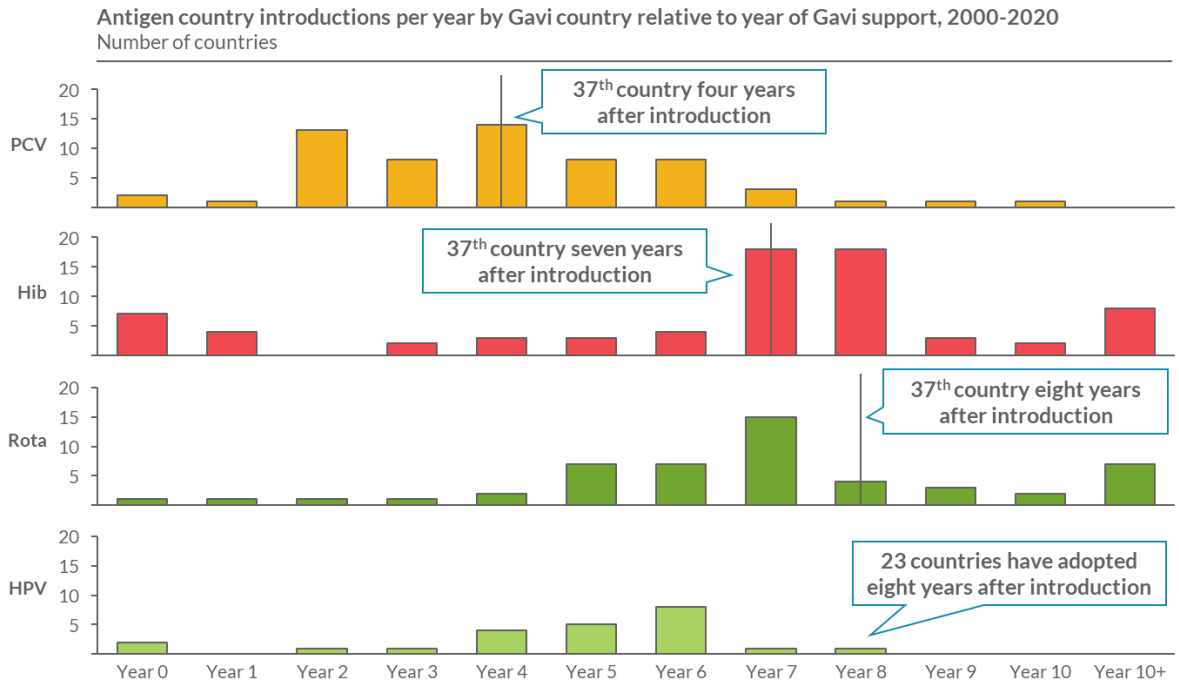
Figure 15: Antigen country introductions by Gavi country, 1993-2020



Introductions of PCV were very rapid in years two to six of Gavi support (2011-2015). Figure 16 below shows the same data as Figure 15, above, highlighting how introduction of PCV accelerated as supply constraints were released (see Objective 2: Vaccine Supply).

[72] Indonesia submitted a request in January 2020, to access the PCV AMC price to scale-up PCV nationwide.
[73] Timor-Leste submitted a request to access the AMC price for routine introduction of PCV in December 2019, with a catch-up campaign (for children aged 1–5 years), for implementation in 2022.
[74] Ukraine submitted a request in September 2020, for routine introduction starting in 2022.
[75] Comoros, Guinea, Somalia had expressed political will to move forward with planning an application for PCV support, and there is expectation for these applications to come forward in the Gavi 2021-2025 strategic period.
[76] Tajikistan has applied in 2021 for support to introduce PCV (with catch-up) in 2022.
[77] The Gavi Board removed the requirement for any application for routine introduction to have DTP3 coverage above 70%, effective June 2020.

Figure 16 : Antigen country introductions per year by Gavi country relative to year of Gavi support, 2000-2020



Other Gavi-supported antigens are not perfect counterfactuals. Hib, rota, and HPV all differ from PCV in ways which likely played a role in driving their speed of uptake, including cultural drivers (e.g., reproductive health perceptions for HPV), and country-level immunization strategies. Please see Annex 8 for further detail on the counterfactual selection.

Findings on uptake in selected case study countries

This evaluation looked in more depth at introduction decisions for PCV across seven transitioning and fully self-financing countries. These case study countries are Nigeria & India (accelerated transition phase), Bangladesh, Cameroon & Pakistan (preparatory transition phase), and Bolivia & Indonesia (fully self-financing). These were selected for their geographical diversity, selection of different PCV products, introduction at different dates during the PCV AMC pilot, and varied co-financing statuses. The full rationale for country selection is included in Annex 8.

Analysis of decision-making across the seven case study countries highlighted (i) the high disease burden from pneumococcal bacteria, (ii) the context in the early-to-mid 2010's, (iii) Gavi support for PCV introduction, and (iv) short-term supply availability as key drivers of PCV uptake.

Of the estimated 5.83 million U5 deaths in 2015, Streptococcus pneumoniae was responsible for an estimated 294,000 deaths, or ~5%.[78] Almost all the stakeholders interviewed for the evaluation, whether Gavi country liaison staff, EPI managers in the selected countries, or other experts (e.g., UNICEF, WHO, Bill and Melinda Gates Foundation staff in country), noted the high disease burden from pneumococcal bacteria as a key driver of vaccine introduction. WHO guidance recommended PCV introduction for all countries in 2007.[79] Both WHO and UNICEF were and are actively encouraging countries to introduce PCV: UNICEF and WHO seek to end preventable child deaths from pneumonia by 2025 through the Global Action Plan for Pneumonia and Diarrhea; UNICEF's

[78] WHO, Pneumococcal conjugate vaccines in infants and children under 5 years of age: WHO position paper, 2019.
[79] WHO global recommendation for PCV through a 2007 position paper, was catalyzed by the output of the PneumoADIP team between 2003 and 2008, and the Accelerated Vaccine Introduction initiative established in 2008.

goal is to have an additional 21 countries introduce PCV into their national immunization programs by 2021,[80] with a focus on bridging the gap in PCV access in MICs.[81]

The period at the start of the PCV AMC pilot was characterized by relative stability in immunization programs and few options for new vaccine introductions, channeling attention towards PCV. Stakeholders interviewed about drivers of PCV introduction in countries earlier in the AMC pilot (Cameroon – 2011, Pakistan – 2012, Bolivia and Nigeria – 2014) noted the relative stability of existing EPI programs, and the desire of EPI managers (then as now) to increase protection against a growing range of diseases. Combined with supply challenges in rota (see Figure 10), this channeled attention towards PCV as the next vaccine to introduce.

Gavi encouraged countries to introduce PCV. Gavi is, and was, actively promoting PCV introduction because of the high disease burden in developing countries, and on account of the availability of the vaccine. Those interviewed both inside the Gavi Secretariat and in case study countries recognized that Gavi advocacy and support played a significant role in the rapid uptake of PCV.

The increasing availability of supply of PCV also drove introduction. Several countries indicated that availability of PCV was a key driver of introduction, particularly given shortages of rota during the same period (see above). While this increasing supply security was driven by the PCV AMC pilot, it is important to note two realities of country-level decision-making. First, most in-country decision makers and their local advisors are not aware of the existence of the PCV AMC pilot, or therefore aware of the impacts of the PCV AMC pilot on price and supply. At the country level, PCV is 'experienced' as (i) a price per dose, as with other Gavi portfolio vaccines; (ii) a set of attributes like presentation and efficacy; and the presence or absence of supply. Second, country decision-making tends to focus on short-term supply, not longer-term security of supply. This is largely a result of the different priorities of those involved in country decision-making. According to multiple experts interviewed for this evaluation, EPI managers are public health-focused, and so want to expand coverage, and are willing to tolerate potential supply risks in future. Wider government actors involved in the NVI decision – such as Ministries of Health or Planning – tend to think in line with political cycles, and so are relatively tolerant of longer-term supply risks (or changes in price). In addition, Gavi Secretariat staff noted that Gavi advocates for introduction of vaccines, whether they can guarantee longer term supply or not.

The low AMC price for PCV did drive uptake, but price is only one variable in country-level decision-making. Several in-country stakeholders stated that price was important, but that it was not as important as, for example, epidemiological evidence and disease burden in decisions around whether, and when, to introduce PCV. For example, the imminent conclusion of the PCV AMC pilot was a key factor in Indonesia's decision to introduce PCV in 2020 – ensuring Indonesia accessed the tail price for ongoing PCV purchases. Indonesia has piloted PCV13, but it was not purchasing through UNICEF. The Indonesian Government was paying close to USD 20.00 per dose and had delayed plans for national rollout. As the end of the PCV AMC pilot drew nearer, the Indonesian government pursued the regulatory changes needed to procure through UNICEF. The 'shutting door' of ability to access PCV13 at USD 2.90 per dose was critical to their decision to roll out PCV, taking place now, and due to cover the whole country by 2022.

It is likely that the low AMC price was necessary for uptake, as indicated by reduced introduction rates among MICs not eligible for the PCV AMC tail prices. PCV prices for MICs can be five to ten times higher compared with the PCV AMC pilot tail prices. The weighted average price for MICs procuring through UNICEF (outside of PCV AMC pilot) has been stable from 2013-2019 at approximately USD 14.00 per dose, although pricing per MIC can now vary significantly and range

[80] UNICEF, Pneumococcal Conjugate Vaccine: Supply and Demand Update, 2020.
[81] UNICEF, UNICEF Deep-dive – Vaccine Industry Consultation, 2020.

from USD 2.90 to USD 25.00 per dose, depending on the manufacturer's pricing policy.[82] Of the 39 non-Gavi-73 countries tracked by LSHTM's TRIVAC Model, only 13 have introduced PCV.

Figure 17 below brings together direct quotes from the interviews focused on uptake in the seven selected transitioning and fully self-financing countries.

Figure 17: Selected interview quotes on country introduction decision-making

Theme 1: Disease burden

"EPI [managers] want to introduce everything, but finance wants to balance."

"The decision-making is not linked to an AMC – mostly the decision making revolved around disease burden."

"Epidemiological evidence of pneumococcal disease and meningitis was main driver of the decision to introduce PCV"

"But I have been involved with other vaccine introductions – it's not the AMC, it's the principle of adding vaccines to the portfolio. Let's be clear that countries don't know about the AMC."

"Of course, the pricing is one factor, but it's not the only factor. All the countries I have worked with past and present, they look at the disease burden, that's the main factor."

"PCV uptake was because countries were quite stable and performing well on the normal vaccines. I think much of the decision was epidemiology and context. The question for them was whether we introduce PCV or rota, based on the epidemiology."

"I don't think [in this country] it's a matter of capacity – there are lots of people with PhDs from Harvard. The problem is that it [economic analysis] has never been suggested, and no one wanted to do something like that to waste time. There's a vaccine that can save lives, someone is paying for it, so let's go. When the minister was just signing because it has been said Gavi will pay."

Theme 2: Era and stability

"PCV supply was available – so there was a push on PCV. Some countries applied for both rota and PCV and there just wasn't rota – so they introduced PCV. It's really nothing more than that."

"It's not like we picked this thing [PCV] out of everything else – we asked the world what they wanted first – Africa said malaria. We told them malaria is not available, but PCV is available – so that's next on the list."

"I've been at Gavi since [2000]. It [PCV] was the only one that was available. It wasn't anything intricate. We only had rota and PCV to offer, and there was no rota supply."

"We were going for a big replenishment. We wanted to show the donors that PCV was the one. There was a bit more push for PCV strategically. We don't want to admit that, but that's what happened."

"We have to also be realistic – it's not about the countries sometimes, it's about what's happening strategically at the global level. PCV was picked up because it was there – the donors had a lot of interest; pharma had a lot of interest. We had a conversation – "Why are we pushing PCV when all the countries said malaria?" PCV is available, donor meetings are coming, replenishment is coming – it really wasn't about the AMC price."

Theme 3: Gavi Alliance support

"This decision is just happening because WHO/UNICEF is pushing."

"Price wasn't what got us over the line – it was a concerted effort speaking to different parts of government – but price really played an element. Because the [Ministry of Finance] drove it, I don't think the element of security of supply was really in there. Because the [Ministry of] Health wasn't making the decision."

"Their political will that we are now running after – this decision has been made because WHO is pushing, UNICEF is pushing. Ministers, they just sign the document and send it to Gavi, and the vaccine has been introduced."

"What I can say about the way decisions are main is very simple. There was no NITAG at that time, so Gavi would like to introduce the vaccine, and the EPI manager wants to push until it was introduced."

[82] Pneumococcal Conjugate Vaccine: Supply and Demand Update, UNICEF Supply Division, July 2020.

"[The country] started to become a defaulter – because of the cost of the co-financing. The country was not prepared enough to put into its budget. Every year we were obliged to run after the government to pay to pay. I went there multiple times with senior staff, speaking to the Minister of Finance, etc."

"One of the consequences of the way we introduced vaccines: We were in too much rush to introduce these vaccines – which were very costly. We don't raise political will for the financing for these vaccines. They become defaulters, they have stock-outs; this can create resistance for circulating serotypes."

"We get [countries] to introduce at a price they can't keep. Then the prices shoot up. We have all these KPIs about NVIs."

Theme 4: Short-term supply availability

"More on a year-to-year basis in terms of its [country] thinking of supply availability."

"I'm not sure how much the question of supply security came in."

"Both of them [countries] do not take a look at [future] supply security when making decisions. They do think about it in the short term because they expect supply [will] help price [come] down."

"We do do that [push NVI even when supply is not secure]. We pushed rota and HPV even though the supply wasn't in place. [The country in question] is a strong enough country with enough capacity [to push back]. With other countries that don't have that level of capacity, you can really frame the discussion, and the role that the others [WHO, UNICEF, etc.] play in country."

"The government would always prefer PCV13 to PCV10 because there is no price difference, more serotype coverage, and can be stored for 28 days in the same presentation."

Theme 5: Price and other factors

"Yes, price plays a role, and it is an issue, but it is not number one priority."

"Price was a key element, but it wasn't what got us over the line. "

"Price is a big consideration for both [countries], especially with large transition countries."

"We were paying USD18.60 per dose, but then you say USD 3.00 per dose. Then USD 2.90 per dose? That really drove it."

"Generally [for two big Gavi countries] price is the large consideration. They don't think about supply security. They don't think about their deep epidemiology."

"With [this transitioning country], we are not sure if the sustainability matters are really considered."

"Countries are very shortsighted. We make it clear in different ways that the prices are going to change – but they are not aware the prices are going to go way up in five years."

"Truth is, when you look at all Gavi countries, you will see price is not an issue. They're not paying for it."

"There is a feeling that this is being dumped on them, and they don't care. For countries in transition – the ability to pay creeps in, and programmatic capacity creeps in, lessons from MICs that are struggling creep in."

"The simple reason is that they know Gavi is there to help them at the end of the day. They have this wrong notion of 'too big to fail'. The government is living under the illusion that they are too big to be allowed to fail."

"You get this rush around Preparatory Transition, with countries doing a bunch of introductions. I don't think the partners who do the financial and technical feasibility studies do enough to make that really clear to them [countries]."

"At that time, there was a conversation around rota – but at that time, PCV was prioritized over rota for so many reasons – capacity of program to manage two introductions at the same time, for example. And that rota requires interventions beyond the health system (WASH, school health etc.,)."

Findings on financial sustainability

Gavi's co-financing strategy is designed to assist developing countries on their path to fully self-financing the cost of domestic immunization. Depending on income level, a country passes through several phases of co-financing support:

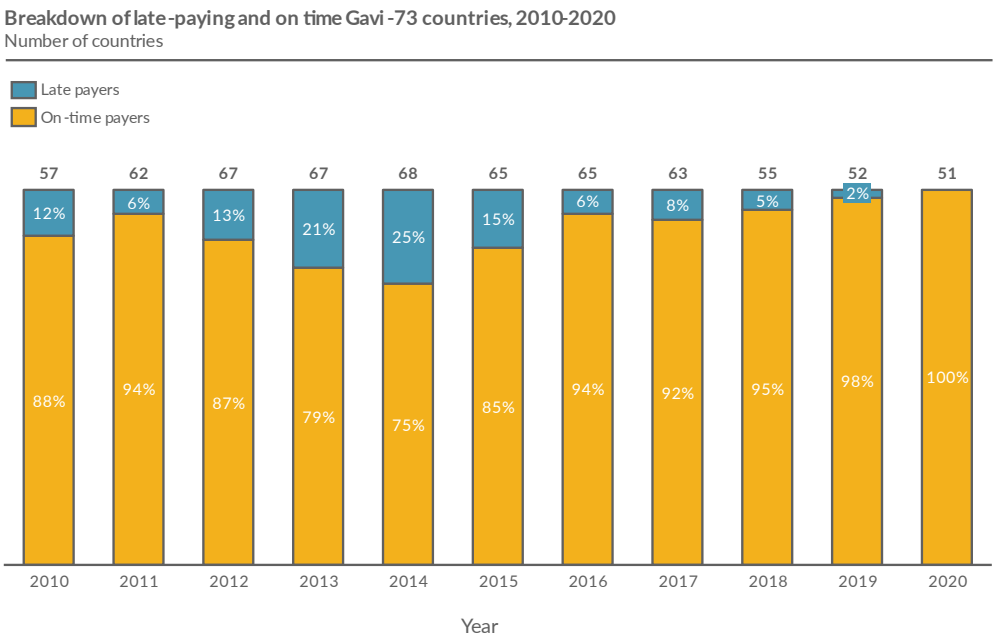
- **Initial self-financing (ISF)**, where a country pays a flat amount of USD 0.20 per dose of Gavi-supported vaccine;
- **Preparatory transition (PT)**, where countries pay a fixed percentage of the price per dose (with that contribution increasing by 15% per year);
- **Accelerated transition (AT)**, where a country transitions to paying 100% of the vaccine cost over five years, starting from the percentage contribution it reached in PT; and
- **Fully self-financing (FSF)**, where a country has graduated from Gavi support and now pays 100% of the cost of vaccines procured through UNICEF

Co-financing results

Most countries meet their co-financing requirements: only 2% were late-paying in 2019. This is the result of a concerted effort to understand drivers of country-level default during Gavi's strategic period 4.0 (2016-2020), following increases in late payments in strategic period 3.0 (2011-2016). These efforts led to a decrease in the percentage of countries with co-financing obligations who were late paying from 25% in 2015, to 2% in 2019.[83] Figure 18 below shows the breakdown of late payers versus on-time payers from 2010 to 2020.

With debt restructuring, all late-paying Gavi-73 countries have repaid their co-financing obligations. From 2010-2020, no country defaulted on restructured obligations for a year in which they initially missed payment.

Figure 18 : Breakdown of late-paying and on time Gavi-73 countries, 2010-2020



Most Gavi-73 countries meet their co-financing obligations through tax revenues. In 2020, for example, 43 of 51 countries met co-financing obligations through federal budgetary resources. Some small and low-income countries receive donor pooled funding and ODA funding to help meet co-financing obligations.[84] One larger, wealthier country, Nigeria, previously met obligations through

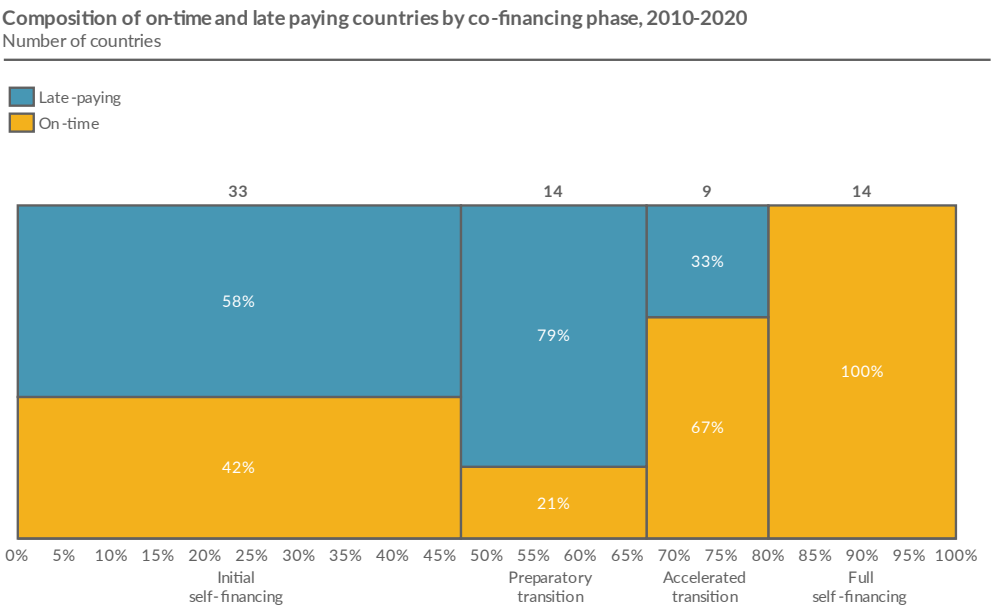
[83] In 2020, none of the Gavi-supported countries was considered late paying; this was due to the issuance of payment waivers (normally granted to infrequently in response to extreme circumstances, such as war or famine) to accommodate the economic impacts of the Covid-19 pandemic.
[84] Gavi co-financing data.

World Bank lending, but in 2019 began to pay through a mix of budgetary funds and World Bank lending.

Initial self-financing (ISF) countries represented the greatest share of countries with at least one incidence of late payment between 2010 and 2020. This is driven by the fact that ISF countries are the largest co-financing cohort, representing 33 of 70 countries with co-financing obligations over the period (see Figure 19 below).

Preparatory transition (PT) countries are most *likely* to pay late, relative to the size of the cohort. From 2010 to 2020, 79% of PT countries experienced late payment at least once (see Figure 19 below). As described in Figure 19 below, and in an evaluation of Gavi's Eligibility and Transition and Co-financing Policies, many countries were not aware of the budgetary implications of transitioning to the next phase of co-financing.[85] This accelerating financial burden may be driving more PT countries to initially pay late on obligations, before recovering as they reallocate or grow their budgetary resources in a more structured manner.

Figure 19 : Composition of late-paying and on time countries by co-financing phase, 2010-2020



Three of the seven case study countries have faced co-financing issues over the course of the PCV AMC pilot. Through restructuring of obligations (typically obligations for the year of late payment are spread over multiple future years), these countries have been able to re-pay obligations.

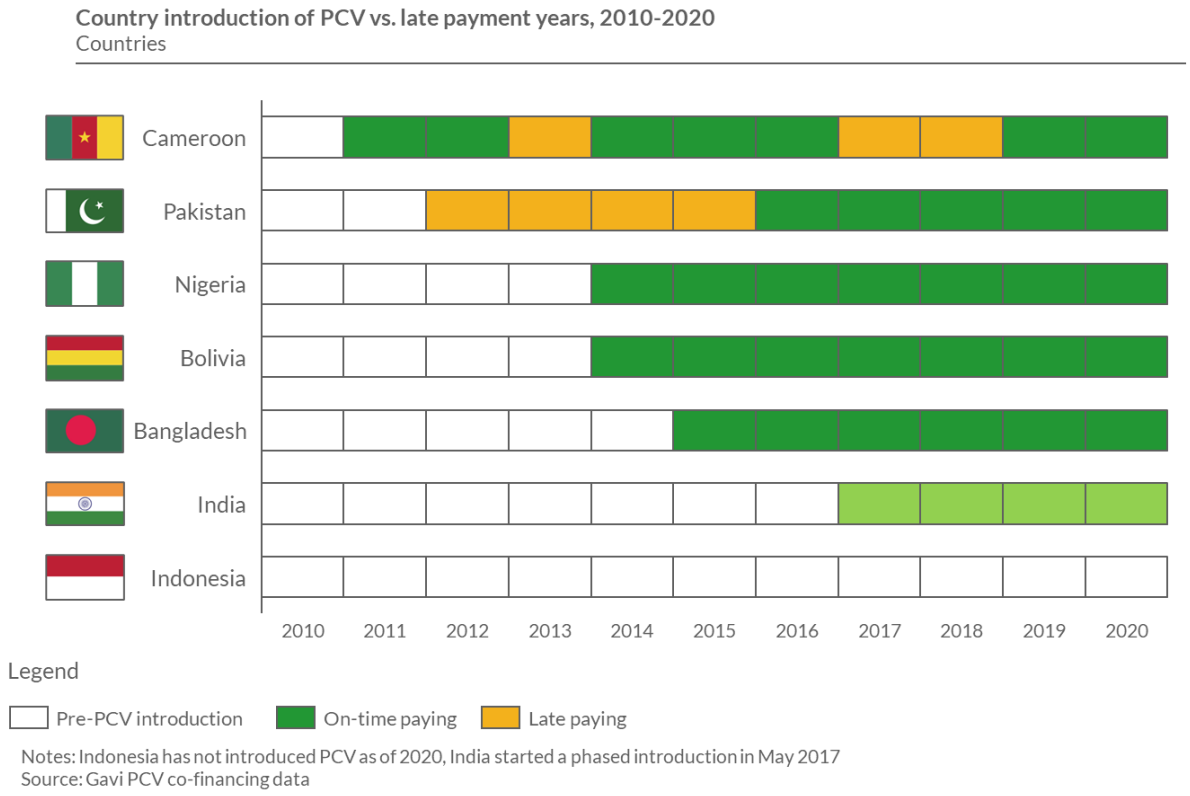
- Cameroon, which introduced PCV in 2011, paid late on its obligations in 2013 (two years post-introduction), as well as in 2017 and 2018.
- Pakistan introduced PCV in 2012 and paid late on its obligations for that same year, as well as the three subsequent years. Interviews with in-country stakeholders revealed that the initial years of late payment following PCV introduction were due to funds not being allocated directly to PCV co-financing obligations. Once funds were properly earmarked (for the 2015-2020 period), Pakistan was able to meet obligations each year.[86] This raises questions around the additional operational support and resources countries may be lacking following Gavi vaccine introduction. Cameroon and Pakistan were in the PT phase during their years of late payment and throughout the PCV AMC pilot years.

[85] CEPA, Evaluation of Gavi's Eligibility and Transition and Co-financing Policies, 2019.
[86] Interview, 2 July 2021.

- Nigeria, while not technically classified as late paying during any year from 2010 to 2020, was exceptionally granted in 2018 an extension of the country's "Accelerated Transition" period from 2021 to 2028.[87]

Figure 20 below shows incidence of late payment relative to PCV introduction year for the case study countries.

Figure 20 : Country introduction of PCV vs. late payment years, 2010-2020



Pakistan was not the only country that introduced PCV while struggling to meet co-financing obligations. Eight additional countries were unable to meet annual co-financing obligations during the same year PCV was introduced, according to Gavi co-financing data.

Further information: *The conclusions on vaccine uptake are included in Section VIII. The in-country decision makers and their advisors interviewed are listed in Annex 10. And Annex 7 describes the theory-based evaluation approach taken for this objective, tracking what analysis was conducted, and how the findings build into conclusions regarding the causal path through which the AMC was envisaged to work.*

[87] Gavi Board, June 2018. See https://www.gavi.org/sites/default/files/board/minutes/2018/Board-2018-Mtg-01-Minutes.pdf .

VII. Objective 4: Testing Impact and Effectiveness

The fourth objective of the PCV AMC pilot was to test the effectiveness of the AMC mechanism as an incentive for needed vaccines and to learn lessons for possible future AMCs. This objective remained unmodified over the course of the PCV AMC pilot. This section covers findings on impacts and effectiveness of the PCV AMC pilot. Lessons learned (part of Objective 4) are discussed in a dedicated section (IX. Lessons Learned).

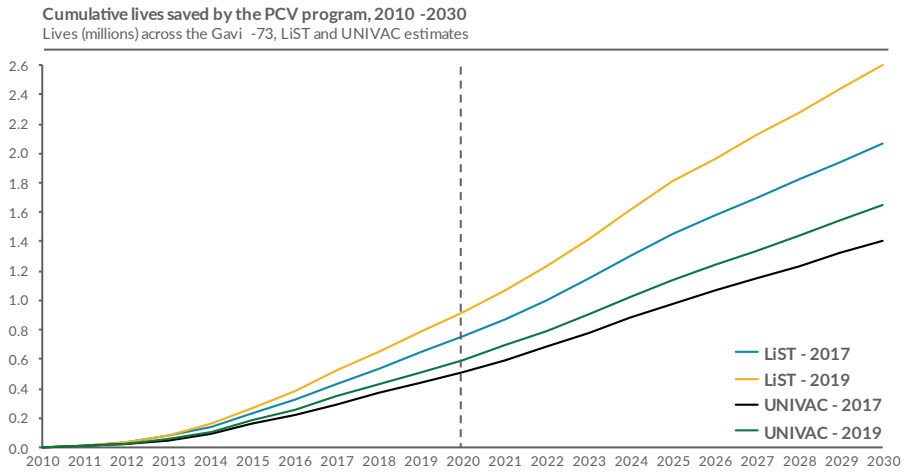
This section seeks to understand the impact and effectiveness of the AMC mechanism for incentivizing expanded access to needed vaccines; and determines whether sufficient lessons have been learned to inform the design of a possible new AMC mechanism in the future.

Findings on impact and effectiveness

Impact of the PCV AMC pilot on mortality and morbidity

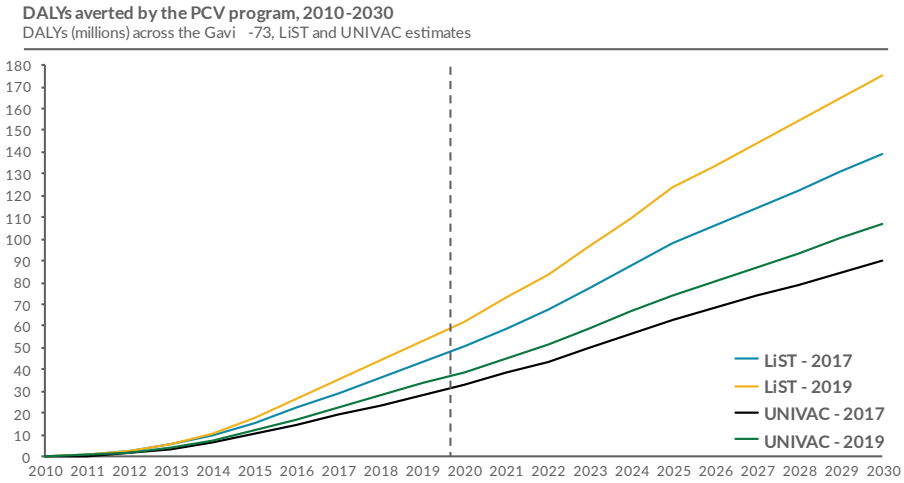
Between 2010 and 2030, the PCV AMC pilot is estimated to save between 1.4 million and 2.6 million cumulative lives, and avert 90 million to 175 million cumulative DALYs.[88,89] See Figures 21 and 22 below for the cumulative estimates of lives saved and DALYs averted through 2030.

Figure 21: Cumulative lives saved by the PCV program, 2010-2030



[88] VIMC, LiST 2017 PCV data, 2020.
[89] The ranges for lives saved and DALYs averted represent the estimates from the LiST and UNIVAC models; model outputs from two separate years of data (2017 and 2019) were used; UNIVAC estimates are more conservative.

Figure 22: Cumulative DALYs averted by the PCV program, 2010-2030



More detailed, country-level studies have shown significant health impacts of PCV introduction in Gavi-73 countries. A non-exhaustive sample of studies and results is included below:

- A study in Lao PDR from 2013-2018 showed that PCV decreased vaccine-type serotype carriage in healthy children aged 12–23 months by 23% in the first three years since PCV introduction.[90]
- In Nepal, a 2013-2021 study (ongoing) indicates that the proportion of children hospitalized with pneumonia who are carrying vaccine-type pneumococcus has nearly halved since PCV introduction in 2015. The study also pointed to significant reductions in pneumococcal carriage among healthy children since vaccine introduction, indicating positive indirect health effects.[91]
- In Kenya, a 2012-2021 study has found that since its introduction in 2011, PCV10 has reduced the incidence of vaccine-type invasive pneumococcal disease by over 90% in children aged under 5 years. Herd effects of the vaccine were also demonstrated by significant declines in PCV10-type IPD in unvaccinated age groups with estimated reductions of 100%, 74% and 81%, in those <2 months, 5–14 years and ≥15 years, respectively.
- In Mongolia, before vaccine introduction, analysis showed the majority (76%) of pneumococci present in the nasopharynx in children hospitalized with pneumonia belonged to serotypes covered by PCV13. One year after PCV introduction, vaccine-type carriage declined by approximately half in both 5–8-week infants and children aged 12–23 months. Non-vaccine type carriage increased 1.5-fold in the 12–23-month age group.

Please refer to the 2020 Pneumococcal AMC Annual Report for a full list of completed and ongoing Gavi impact studies.

IMPACT OF THE PCV AMC PILOT ON EQUITABLE REDUCTIONS IN MORTALITY AND MORBIDITY

Vaccination against pneumococcal disease can promote equitable health and economic outcomes within a given population. At a global level, the PCV AMC pilot has contributed to equitable health and economic outcomes by accelerating uptake amongst lower-income countries, where uptake had previously been close to zero. Even within lower-income countries, vaccination coverage and its associated equity impacts vary across socioeconomic, geographic, maternal, and child characteristics. A study of vaccination coverage in Ethiopia, for example, found that children in the richest quintile

[90] Gavi, PCV AMC Annual Report, 2020.
[91] Gavi, PCV AMC Annual Report, 2020.

were six times as likely to have fill vaccination coverage, relative to the poorest quintile, and that vaccination rates among children in urban areas was more than twice as high as in rural areas.[92] These inequities underscore the importance of increasing vaccine access and equity. This short section summarizes well evidenced pro-equity impacts of vaccination at the country level.

The burden of infectious diseases, including pneumococcal disease, falls disproportionately on lower-income populations. This is driven by factors including increased rates of malnutrition and undernutrition, lack of access to clean water and inadequate hygiene and sanitation. Vaccination, therefore, yields greater benefits for low-income groups than for middle- and high-income groups, on average. An analysis of 41 Gavi-eligible countries found that the poorest quintile accounted for the largest share of deaths averted by all vaccines (23% to 34%), and the poorest two quintiles accounted for over half of the deaths averted by most vaccines. Nearly 50% of pneumococcal disease deaths averted occurred in the bottom two income quintiles.[93] Beyond health, the study showed that most extreme health cost cases would occur in the lowest two income quintiles, in the absence of vaccination.[94]

INDIRECT AND BROADER EFFECTS FROM PCV

Vaccination against pneumococcal disease has several benefits beyond health. This section summarizes the well-evidenced links,[95] drawing on PCV studies in Gavi-73 countries where possible.

Children vaccinated with PCV tend to have better educational outcomes, driven by increased attendance in school and better cognitive performance. Pneumococcal disease may negatively impact cognitive functioning and/or lead to hearing loss. If specific educational support is not available (often the case in Gavi-73 countries), pneumococcal disease can lead to decreases in educational outcomes.[96]

Caregivers (e.g., parents or other family members) also benefit indirectly from PCV uptake, through more time for productive and leisure activities. The burden of caring for a patient with pneumococcal disease can place potentially debilitating demands on the quantity and quality of caretakers' time. The value of reducing these time costs is especially important for caregivers of U5 children with pneumococcal disease, given dedicated care that U5 children require.[97]

Pneumococcal disease has been shown to lead to high degrees of medical impoverishment, which can be avoided through vaccination. For example, in the US, the direct cost of pneumococcal disease among persons of all ages, was an estimated USD 3.5 billion in 2004. Additionally, a study in Taiwan found that families spent an average of USD 653 or USD 218 when their child was diagnosed with IPD or pneumonia, respectively. This represents approximately 27% to 81% of an unskilled worker's monthly salary.[98] An analysis across 41 Gavi-eligible countries estimated that PCV coverage avoided roughly 6.6 million cases of catastrophic health costs (defined as out-of-pocket health spending exceeding 20% of household income) and 0.8 million cases of medical impoverishment attributable

[92] Geweniger, Anne and Abbas, Kaja, Childhood vaccination coverage and equity impact in Ethiopia by socioeconomic, geographic, maternal, and child characteristics, 2020.
[93] Chang et al., The Equity Impact Vaccines May Have On Averting Deaths And Medical Impoverishment In Developing Countries, 2018.
[94] Bloom et al., Commentary: Why has Uptake of Pneumococcal Vaccines for Children been so Slow? The Perils of Undervaluation, 2020.
[95] As discussed in the Methodology (see Annex 4), the spillover impacts of PCV and the equity-dimensions of PCV are both programmatic outcomes from Gavi programming, rather than the AMC itself. As such they have been deprioritized in this evaluation.
[96] *Rodrigues, Charlene and Plotkin, Stanley*, Impact of Vaccines; Health, Economic and Social Perspectives, *2020*.
[97] Bloom et al., Commentary: Why has Uptake of Pneumococcal Vaccines for Children been so Slow? The Perils of Undervaluation, 2020.
[98] Bloom et al., Commentary: Why has Uptake of Pneumococcal Vaccines for Children been so Slow? The Perils of Undervaluation, 2020.

to severe pneumococcal disease. This increase in poverty cases would likely have led to detrimental impacts for the economies and development of these Gavi-eligible countries.[99,100]

METHODOLOGY FOR COUNTERFACTUAL ANALYSIS

This evaluation uses the Vaccine Impact Modelling Consortium's (VIMC) LiST model for counterfactual analysis, comparing the impacts of PCV introduction versus other antigens. The model calculates impacts of PCV introduction based on a multitude of variables, including vaccine coverage. The counterfactual analysis first compared coverage rates across the Gavi-73 cohort for PCV and counterfactual antigens (rota, Hib, and HPV), baselined to the first year of introduction of the antigen in Gavi markets. These coverage rates for the counterfactual antigens were then inputted into the LiST model for PCV, to assess *what the impacts of PCV introduction would have been had it occurred at the rate of the counterfactual antigen coverage over time*. The purpose of this analysis is to try to understand the effects that the AMC mechanism had on driving coverage, and subsequent impacts on lives saved and DALYs averted, relative to coverage rate evolution of antigens that were not introduced under an AMC. However, it should be noted that this is a highly imperfect comparison, as multiple factors influence coverage rates across antigens (e.g., cultural beliefs and country immunization policies), as well as lives saved and DALYs averted (e.g., effectiveness of the vaccine and disease burden of the antigen). In effect, there is selection bias in the control group.

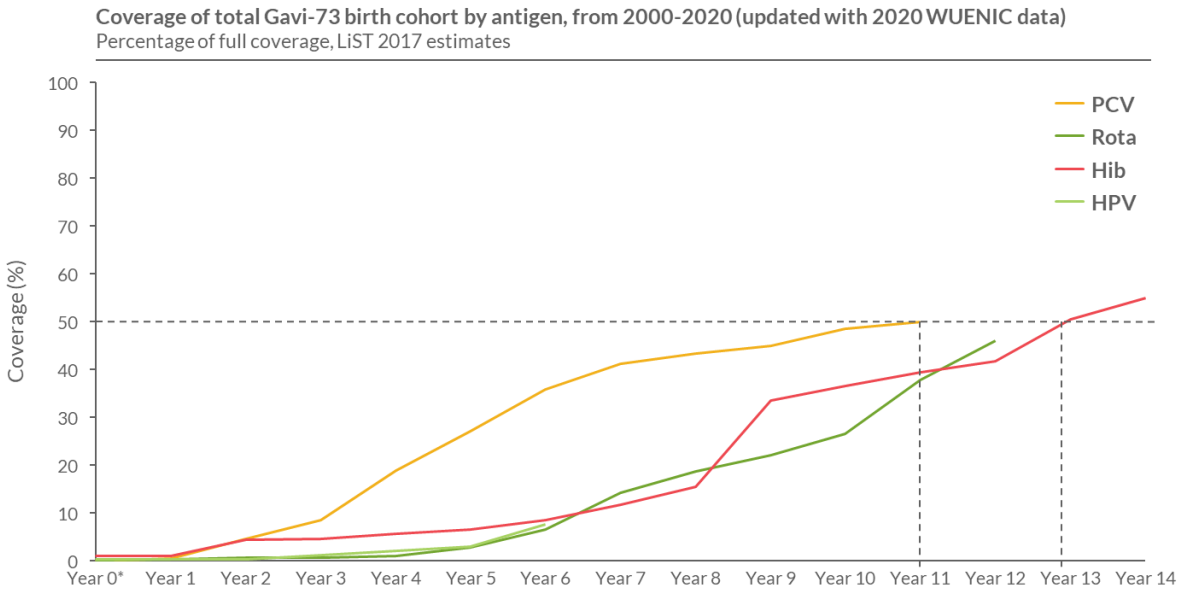
Please see Annex 8 for further detail on the methodology for counterfactual analysis and the rationale for counterfactual selection.

COUNTERFACTUAL ANALYSIS

PCV reached 50% coverage in 11 years, while Hib took around 13 years to reach the same coverage level. Although multiple variables may contribute to the faster coverage growth of PCV following initial availability, the high rate of coverage growth of PCV, particularly from years three to seven (see Figure 23 below), stands out, especially in the context of supply shortages that affected the early years of the PCV AMC pilot.

[99] Bloom et al., Commentary: Why has Uptake of Pneumococcal Vaccines for Children been so Slow? The Perils of Undervaluation, 2020.
[100] Chang et al., The Equity Impact Vaccines May Have On Averting Deaths And Medical Impoverishment In Developing Countries, 2018.

Figure 23: Coverage of total Gavi-73 birth cohort, by antigen



(*) Note that Year 0 refers to the first year each antigen was made available via Gavi

Higher PCV coverage has saved at least 2X the lives and averted 2X the DALYs than it would have with coverage rates of rota, Hib, or HPV. In the 11 years since PCV became available in Gavi-73 countries, it is estimated to have saved a cumulative 752,000 lives. If PCV had experienced the same growth in coverage as Hib over the same period, an estimated 346,000 lives would have been saved. With rota coverage rates, 288,000 lives would have been saved. Because pneumococcal disease primarily leads to deaths in U5 children, the figures for DALYs averted in the PCV and counterfactual coverage scenarios mirror the trend lines for numbers of lives saved, but 'scaled up' to reflect DALYs per life saved. PCV coverage rates led to 50.5 million DALYs averted in 11 years, while Hib and rota coverage rates would have led to DALYs averted of 23.5 million and 19.7 million, respectively. Figures 24 and 25 below show the comparison of lives saved and DALYs averted, respectively, across the antigen comparison scenarios.

Figure 24: Cumulative lives saved estimates, 2000-2020

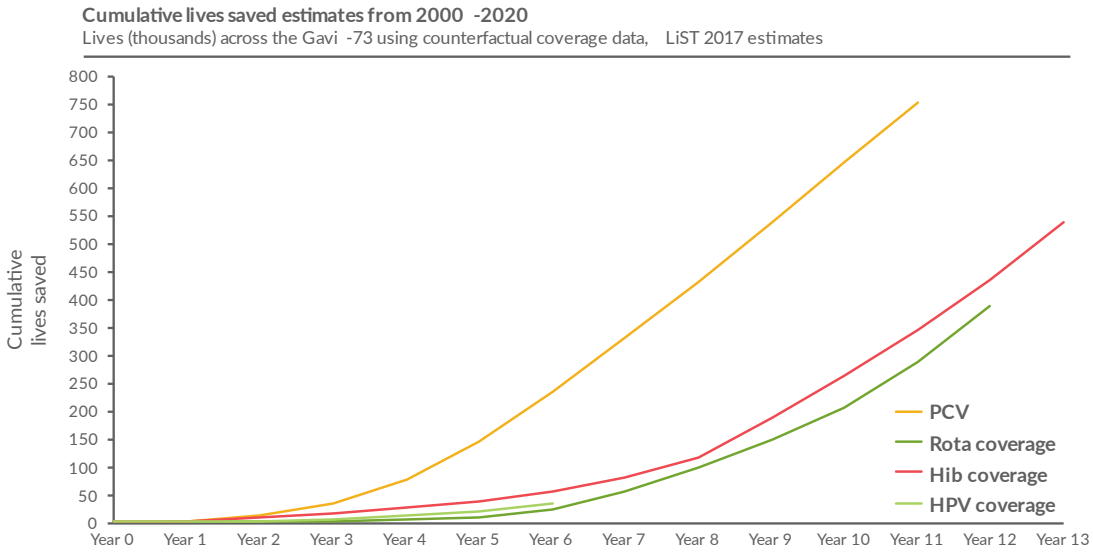
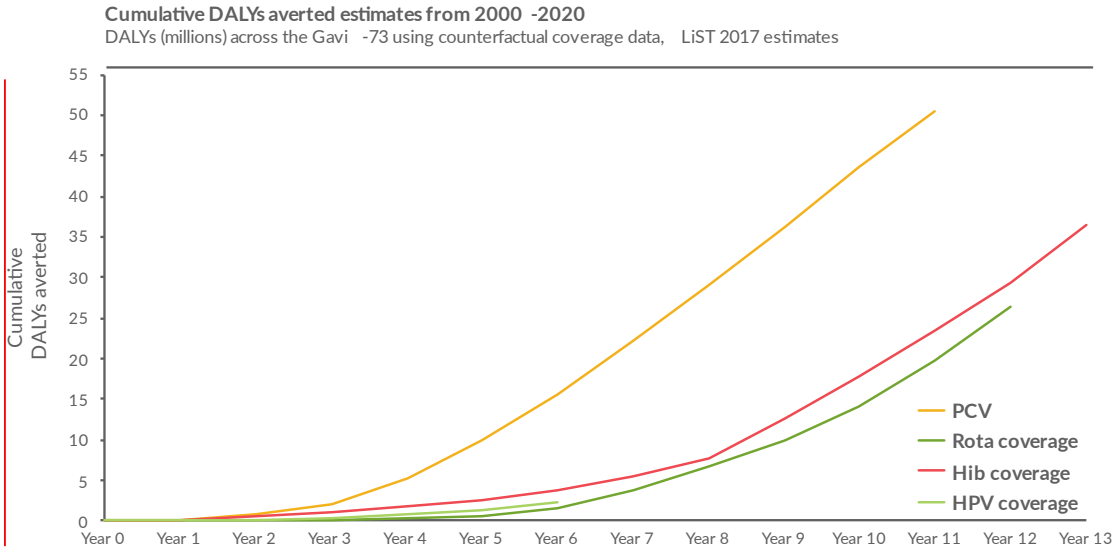


Figure 25: Cumulative DALYs averted estimates, 2000-2020



Further information: *The conclusions on impact and effectiveness are included in Section VIII. Annex 3 contains further information relevant to a specific evaluation question on the methodology used to model the impact of PCV (and other vaccines) by Gavi. Annex 7 describes the theory-based evaluation approach taken for this objective, tracking what analysis was conducted, and how the findings build into conclusions regarding the causal path through which the AMC was envisaged to work. And as mentioned above, Annex 8 contains further detail on the methodology for counterfactual analysis and the rationale for counterfactual selection.*

VIII. CONCLUSIONS

The conclusions discussed below stem from the findings discussed above, and point out the factors of success and failure of the PCV AMC pilot, with special attention paid to the intended and unintended results and impacts, and more generally to any other strength or weakness. Based on the strength and consistency of available evidence, each set of conclusions is assigned a relative 'robustness of conclusions' rating from 1 (most robust) to 4 (least robust) (see Annex 9 for a full description of the framework).

Conclusions on Objective 1: R&D

Robustness of conclusion: 2.

The PCV AMC pilot did not achieve the objective of accelerating new product R&D amongst those in the pipeline, despite one new TPP-compliant PCV product coming to market during the PCV AMC pilot. When PCV was selected as the AMC pilot product in,[101] it was well understood that the mechanism was unlikely to influence the development timelines of the two TPP-compliant candidates (Pfizer's PCV13 and GSK's PCV10) that came to market just prior to the launch of the pilot in 2010. However, only one new product, SII's PCV10, reached Gavi markets between 2010-2020, and only reached the market in 2020, five years later than estimated. Although the PCV AMC pilot likely gave smaller vaccine manufacturers confidence to continue with their R&D processes (see paragraph below), the manufacturers interviewed for this evaluation did not feel that the pilot had a catalytic effect on R&D. In fact, DCVMs continued to experience delays in development, including patent disputes and delays in clinical trials driven by the complexity of PCV development. Manufacturers and other experts noted that to accelerate product R&D (especially for products farther from market), Gavi would likely need to take a longer term, combined approach that includes push and pull elements, similar to the combined support that SII received from the combination of the AMC pilot and the separate BMGF grant.

Taking a broader interpretation of 'accelerating' new product R&D[102], the PCV AMC pilot was successful at signaling the value of the LMIC PCV market. This may have contributed positively to the large number of firms pursuing PCV vaccines, however it is difficult to be precise about the role the PCV AMC pilot played given the complex firm-level decisions underpinning investment decisions, and the fact that the Gavi-73 market is only ~10% of the value of the global market.

The PCV AMC pilot was very successful at driving presentation innovation, in terms of Multi-Dose Vials (MDVs). These were key to scaling up supply and driving down cost per dose in LIC and LMIC markets. Both Pfizer and GSK developed 4-dose presentations during the PCV AMC pilot, which required new product design, new formulations, clinical studies, and securing WHO-PQ status for the new presentations.

Conclusions on Objective 2: Vaccine supply

Robustness of conclusion: 1.

The PCV AMC pilot achieved the objective of scaling up PCV supply in Gavi-73 markets – especially between 2010 and 2015/6 – by increasing manufacturer confidence in market demand. Supply increased from 3 million doses per year in 2010 to 150 million doses per year, just six years later.

[101] Gavi, Pneumococcal AMC Timeline.

[102] In a narrow sense, 'accelerating' could mean speeding up R&D by those in the pipeline, who are hoping to come to market and access the AMC subsidy. In a broader sense, 'accelerating' could mean widening the pipeline (encouraging more players to pursue PCV R&D), which should mean a greater choice of PCV vaccines are available for LMICs earlier than otherwise would have been the case.

GSK and Pfizer invested a combined USD ~500 million to increase their production capacity. These decisions, while informed by the PCV AMC pilot, were at least partially planned prior to the launch of the pilot.

The PCV AMC pilot was not successful at avoiding supply shortage issues common for antigens in Gavi-73 markets – there were significant supply shortages in the first three or four years of the PCV AMC pilot. Full ramp up of supply capacity took until 2015/16. Up to this point, there were countries who were forced to delay introduction of PCV, or who chose to wait for availability of their preferred product. This was particularly noticeable for larger Gavi-73 countries, such as Pakistan and Nigeria. While this misalignment between supply and demand is regrettable, PCV manufacturing is technically complex, and supply shortages occurred for both rota and HPV during the PCV AMC pilot. Outside of Penta, supply uncertainty is more the norm than the exception for Gavi markets.

The Gavi/UNICEF demand forecasts were structurally optimistic, and this has led to a reduction in confidence amongst manufacturers. It is unclear whether the loss of confidence in forecasting is driven by a different balance of perceived costs of under-supply and over-supply between manufacturers and Gavi. However, in the long run, inaccurate forecasts carry risks for all parties. If the forecasts are not perceived as credible, there is a risk that manufacturers will commit far less internal resources and capacity to vaccine production for Gavi markets, to the detriment of supply security and public health. Gavi's forecasting was flagged for improvement in the 2015 mid-line evaluation and was criticized within and outside of Gavi in interviews for this evaluation.

The PCV AMC pilot was relative ineffective at driving price competition, likely due to the late entry of SII's PCV10 and the subsidy design. The PCV AMC was designed under the assumption that a new product would reach the market earlier in the pilot. As this did not happen, the price competition within the PCV AMC was less than originally assumed. In upcoming years, the competitive pressure exerted by SII's PCV10 might cause PCV vaccine prices to decline, if indeed countries' product preferences, and their likelihood to adopt or switch products, are at least partially driven by price.

Conclusions on Objective 3: Vaccine uptake

Robustness of conclusion: 2.

The PCV AMC pilot achieved the objective of accelerating vaccine uptake, though it is plausible demand for PCV would have been high without an AMC, on account of the disease burden and context. Awareness of the PCV AMC pilot was low amongst country-level decision makers, as befits a manufacturer facing instrument. Similarly, in-country stakeholders did not mention the AMC-*derived* long-term security of supply or AMC-*derived* stability of price as main drivers of PCV uptake. Factors more influential in driving decision-making (burden of disease, Gavi support, short-term security of supply) are partially linked to the AMC:

- PCV was selected for the AMC pilot partially on account of the high disease burden it represents in Gavi countries, especially in U5 children[103]
- The increase in supply capacity was partially driven by the AMC (Objective 2: Vaccine Supply)
- Gavi Secretariat staff and Gavi partners were advocating for PCV introduction because of the disease burden and the supply availability
- It is possible that the PCV AMC pilot placed additional focus on PCV uptake given the commitments to manufacturers and donors, and desire to demonstrate success for the upcoming replenishment cycle and Strategy 3.0 period that started in 2011. This may have

[103] Gavi, The Pilot Advance Market Commitment Concept and Development, 2011.

translated into greater country engagement around PCV by Gavi. However, this sentiment has not been corroborated by all stakeholders interviewed

In short, it is likely the PCV AMC pilot accelerated uptake of PCV across the Gavi-73 cohort, but this country demand did not materialize in response to the *predictable* pricing or the *long-term*, sustainable prices.

Conclusions on financial sustainability[104]

Robustness of conclusion: 2.

The sharp increase in late payments during preparatory transition (PT) suggests countries in initial self-financing (ISF) are not fully internalizing the co-financing strategy. There has been a significant increase in late payment rates during PT, suggesting that countries may not have prepared for the budget increases that come with their transition of financing status. One of the case study countries for this evaluation stated that the EPI program and Ministry of Health asked for a budget increase from the Ministry of Planning, in line with the changes in co-financing, but the Ministry of Planning thought that the large jump was a clerical error, so reduced the vaccine budget ten-fold, which triggered late payment. This issue is not specific to the PCV AMC pilot, or to the PCV program, though PCV has one of the highest price points per dose of vaccines available through Gavi.

The drop in late payments during accelerated transition (AT), and the overall reduction in late payments since 2016, suggest that Gavi-73 countries are broadly on track for sustainable co-financing. Most countries pay for their co-financed doses from their own tax base, suggesting real ownership and prioritization of immunization programs.

Gavi's top priority is public health; Secretariat staff and partners expressed concern about potential unintended consequences from the emphasis on New Vaccine Introduction over financing considerations. Pakistan introduced an expensive new vaccine product (PCV) without proper budgetary allocations (which led to immediate late payment) *and* in a co-financing phase that would see steep year-over-year rises in obligations. Several stakeholders interviewed questioned whether countries really understand their co-financing obligations, yet state that Gavi continue to promote new products. As new vaccines tend to be more and more expensive, this tension between public health benefits of protection against new diseases, versus the increasing burden of co-financing, will likely only grow.

Conclusions on Objective 4: Impact and effectiveness

Robustness of conclusion: 2.

The PCV AMC pilot likely was successful at driving higher coverage of PCV than has been seen with other antigens. This increased coverage led to more lives saved. Gavi-73 countries introduced PCV more quickly than rota, Hib or HPV. Despite the imperfect counterfactuals, the difference in uptake is striking, and there is enough circumstantial evidence to be confident in the conclusion.

There are a significant number of non-price sensitive countries who would likely have introduced PCV on account of the disease burden, and Gavi support. As above, the disease burden was a key driver of uptake, as was the engagement from Gavi on PCV. There are a large number of Initial Self Financing Countries who are many years away from paying the full dose price, and so likely would

[104] Evaluation questions 4e and 9a ask specifically about the financial sustainability, in the context of vaccine uptake and future AMC development (see Annex 1).

have introduced PCV whatever the price to Gavi. As such, understanding the increase in rate of uptake of PCV relative to a hypothetical 'normal' PCV program focuses on transitioning countries.

The big questions, for which a counterfactual approach is unfortunately difficult, are whether the PCV AMC pilot created lower prices than would have been observed without an AMC, and to what extent these lower prices would have altered decisions made by transitioning and fully self financing countries. The strong likelihood of receiving top-up subsidy on some of the doses should have decreased the price to Gavi offered by manufacturers. This, in turn, should have increased the likelihood of uptake by price sensitive transitioning countries, though the exact increase in propensity is very hard to tell. Furthermore whether this propensity actually led to different (binary) introduce or do not introduce decisions is very hard to ascertain due to the lack of a clear counterfactual. India and Indonesia (see Sections VI and VIII) highlight how complicated and country-specific these uptake decisions are.

Gavi decided to offer PCV in 2006, so had already, in effect, made a commitment to support uptake before the PCV AMC pilot. The $1.5bn in additional funds raised for subsidy likely reduced the price-to-Gavi and therefore the donor funding of Gavi needed to cover the share of doses not paid for by countries. Given there was no price to Gavi for PCV before the PCV AMC pilot, it is unfortunately impossible to analyze the efficiency of the PCV AMC pilot vs a hypothetical 'normal' PCV program.

The PCV AMC pilot was *perceived* to be a success by almost all stakeholders, which is hugely important given that that making and stabilizing markets is as much about confidence, trust, and signaling as about legal agreements and vaccine procurement. Across 71 interviewees with donors, country stakeholders, and external experts, almost all stakeholders thought the pilot was a success. The importance of this is hard to understate, given the crucial role of confidence, trust and relationships in market shaping. Even the criticisms of PCV AMC pilot do not dispute the fundamental outcomes, but rather than more 'ideological' aspects of the results of the AMC model. Médecins Sans Frontières, for example, named by most stakeholders as the prominent critic of the PCV AMC pilot, did not dispute the AMC mechanism's effect on uptake of PCV, but believe the price of the PCV vaccine is still 'too high' and regret the large volume of subsidy allocated to established multi-national pharmaceutical companies over the course of the pilot.[105,106]

[105] MSF, Analysis and Critique of the Advance Market Commitment (AMC) for Pneumococcal Conjugate Vaccines (PCVs) and Impact on Access, 2020.
[106] MSF were invited to contribute to this evaluation five times, but did not respond to contact from Dalberg.

IX. LESSONS LEARNED

The PCV AMC pilot yielded important lessons that can inform future AMC design, and the contexts in which an AMC can and should be used. Some lessons emerge from specific conclusions, while other lessons cut across the whole of the PCV AMC pilot. Given the complexity of market shaping in vaccines, it is very hard to point to specific, universally applicable lessons from the PCV AMC pilot. Building on the OECD DAC evaluation definitions, lessons learned are broken down into fundamental lessons (overall lessons about the use of the AMC mechanism), tactical lessons (aimed at improving the *efficiency*[107] of future AMCs), and strategic lessons (aimed at maximizing the *effectiveness*[108] of a future AMC or other market shaping activities).

The fundamental lesson from the PCV AMC pilot is that an AMC mechanism can be an effective intervention in vaccine market shaping. Over the course of the 10-year pilot, we have learned that the legal design and operational delivery are feasible; that the design allows stakeholders to work collaboratively and constructively to achieve the objectives; and that the instrument appears to stabilize vaccine markets[109]. As such, it becomes one tool that we can use again (in the right context) to increase access to crucial vaccines or other health commodities in developing countries.

There are tactical lessons that can inform the detailed design of future AMCs. These are discussed below:

There was less downward pressure on prices than might have been expected, likely driven by the combination of the longer-than-expected duopoly and the details of the subsidy design. As noted in the section on Objective 2: Vaccine Supply, production capacity scaled from 3 million doses per year to ~150 million doses per year in six years. However, the price of PCV dropped from USD 3.50 to only ~USD 3.00 over the same period. This is probably for two reasons: first, the delayed entry of SII into the market (first expected in 2015 but only occurring in 2020) meant that the market remained a duopoly for much longer than expected. Secondly, the design of the subsidy mechanism allocated the total dollar value of subsidy on the number of doses contracted, rather than price per dose. If a manufacturer sells at below USD 3.50 per dose, they are 'topped up' to USD 7.00 per dose for each dose until their allocated subsidy runs out – in effect, they receive their subsidy more quickly, but do not receive more subsidy overall. Adjustments to subsidy design and/or R&D incentives could lead to stronger price competition in future AMCs.

The nature of the Gavi/UNICEF forecasting led to a loss of confidence from manufacturers, which may have decreased the effectiveness of the AMC. During the PCV AMC pilot, manufacturers began relying on their own internal forecasts to make decisions around production, after repeated instances of Gavi/UNICEF rolling doses back into later years of the LTAs. This may have reduced manufacturer investment dedicated to vaccine production or allocation for Gavi-73 markets. Continued inaccurate forecasting may decrease the efficiency of future Gavi investments in vaccines (AMCs or other interventions), through increased prices paid by Gavi countries, as manufacturers price in the perceived risks of uncertain demand forecasts. More transparent forecasting with regards to assumptions may avert these risks in future.

The World Bank treasury function and guarantee came with a financial cost, which was perceived to be high relative to its 'value' to the PCV AMC pilot; these costs could be avoided in the future.

[107] OECD DAC definition: A measure of how economically resources/inputs (funds, expertise, time, etc.) are converted to results.
[108] OECD DAC definition: The extent to which the development intervention's objectives were achieved, or are expected to be achieved, taking into account their relative importance.
[109] In this context, stabilize means creating stable, aligned growth in supply and demand that are unlikely to overturn or decline

The World Bank acted as a Treasurer for the AMC and guarantees the AMC funds, in the chance that any donors did not meet their commitments. This was required because UNICEF has made legally binding commitments to manufacturers, but cannot take any financial risk. This World Bank role came with a cost, and interviews during this evaluation recognized that the guarantee was necessary given the context at the time, but probably not necessary going forwards. "If we look at Gavi back in 2007 – Gavi was less than 10 years old. The World Bank was needed to give confidence in the mechanism… It's worth remembering 10 years is a long time, it was a huge amount of money at the time." "If we look at COVAX, there isn't an external treasury. We're at a different place."[110] Following the success of the PCV AMC pilot, as well as the now 20-year track record and balance sheet of Gavi, a third-party guarantee may not be required for a future AMC.

The PCV AMC pilot's legal structures were perceived to be very cumbersome, which resulted in high transaction costs, and reduced strategic flexibility. For future AMCs, much more streamlined legal agreements could be envisaged. Both manufacturers and Gavi noted that the legal agreements were appropriate at the time, given the novelty of what was being attempted, but that they did add costs and reduce flexibility.

Selected stakeholder quotes on the PCV AMC pilot's legal structure:

"We thought manufacturers wouldn't play if they weren't comfortable if this was a legally binding commitment. The offer agreement is not clumsy, but it's difficult to change."[111]

"We certainly made the right decision at the time. Manufacturers had very limited experience with Gavi. Gavi's balance sheet was not what it is today. IFFIm was only set up in 2006."[112]

"The structure was needed, but it did handcuff us – we had to find loopholes. A lot of the strategic discussions were informed by/constrained by the legal structures. A lot of comes down to 'What can we do, based on the legal structure?'. Or 'What do we have to do to get around the constraints in the legal framework?'"[113]

There are strategic lessons from the PCV AMC pilot. These relate to how strategic objectives within the PCV AMC pilot traded off against each other, and as such will be relevant for future AMCs and market shaping instruments.

The objectives of scaling up production, and incentivizing R&D amongst new market entrants trade off against each other – achieving one comes at the cost of achieving the other. Gavi was not clear about the inevitable tensions and internal prioritization between objectives, which may have led to less-than-potential progress against either. In particular, the choice by the coalition designing the AMC pilot of a product with multiple candidates near launch shifted the emphasis away from R&D and towards security of supply and vaccine uptake. However, there were still supply shortages that led to country introduction delays. A clear prioritization of the supply availability might have resulted in different implementation choices. For instance, in seven of eight supply agreements, UNICEF opted not to award the full amount of AMC funds to incumbent manufacturers, in hopes of incentivizing additional manufacturers to accelerate the development of vaccines and improve the likelihood of having a multi-player market with price competition. However, had greater volumes been awarded to the two existing players, they may have been more aggressive with ramping up and allocating capacity between 2010-2015/16 thus avoiding supply shortages and further accelerating uptake.

[110] Interview, 5 May 2021.
[111] Interview, 7 April 2021.
[112] Interview, 7 April 2021.
[113] Interview, 5 May 2021.

Alternatively, if having one additional manufacturer entering the market had been a clear priority, the AMC might have been structured differently. For example, the AMC could have held some portion of the AMC funds in reserve for DCVMs or created an auxiliary fund to help manufacturers overcome technical or regulatory hurdles faced during development. Diverting funds from the incumbents might have had negative short-term consequences on security of supply, but may have led to a lower price in the mid-to-long-term if a third manufacturer had been able to enter the market sooner.

Having competing objectives was a natural outcome of the AMC design process that involved multiple stakeholders and a need to balance competing donor interests. The stated objectives of the PCV AMC pilot spanned the entire delivery chain, from product development to vaccine uptake, and, as a result, it would have been nearly impossible to accomplish all objectives with the time and resources available.

The lack of clear prioritization also led to grievances from some stakeholders when their individual ambitions from the PCV AMC pilot were only partially met. This was brought to light most compellingly around the final tender – the decision to award 100 million doses and USD 75 million in subsidy to SII in 2020.

The final tender: mixed objectives, mixed messages and frustration.

One donor stated that for them, the entrance of SII was "a benefit, not an objective": "I would put it [the entrance of SII] as a benefit or unintended consequence. It was not the objective. It was a desire, we all had, but for me, it wasn't an objective. [The AMC] was open to everybody. If you are not ready you are not ready. That was the idea at least from our part. They [SII] took the last tender, and frankly I didn't think they needed it. There was money left over, so we did it. There were other donors who are more vocal about it [DCVMs], who were trying to put it at the top of the agenda."[114]

Another donor noted "The final tender was a response to political pressure. It didn't influence [production] scale up or product development." The donor opined, "I don't think it made any difference to supply capacity".[115]

For other donors, seeing DCVMs access the AMC *was* a priority, "Our vision of success – DCVMs taking use of the mechanism, not just Pfizer and GSK, but Serum and BioE. That would have made the outcome and the result even stronger."[116] That same donor now has a set of market shaping principles, including explicit support for DCVMs, that have to be met for them to invest in any partnership.

It is important to note that the final tender met the criteria in the legal construct for the AMC, and so its award should be uncontroversial. It was justified based on demand from Indonesia: "Following Indonesia's request in January 2020 to access PCV supply through the Pneumococcal AMC, the demand increase for the following five years was enough to trigger the final AMC Call for Supply Offers (AMC-5)."[117] However, a number of interviewees questioned both whether Gavi *sought* to create that demand, and whether that demand from Indonesia was, in fact, firm demand.

Gavi Secretariat staff recognized they were seeking to influence country-led decision making to assure demand for SII, to be able to trigger this final tender. For some, "It was a very fine line. In terms of whether we were umpiring, we were steering, we were promoting SII or not."[118]. For others,

[114] Interview, 7 May 2021.
[115] Interview, 28 June 2021.
[116] Interview, 5 May 2021.
[117] PCV AMC Pilot Annual Report 2020
[118] Interview, 5 May 2021.

it was less nuanced. One member of country support staff stated "Was there pressure on me/us – to go for the SII vaccine? Yes absolutely. There was a concerted effort on Gavi's part to be pushing this for a large volume country. But Indonesia had already made the decision. They had a NITAG recommendation on PCV13. When we said, "What about SII?", they said "Please don't open this up. Right now, we're not interested".[119]

This lack of neutrality frustrated other manufacturers in the AMC, "In general, we've appreciated with Gavi and UNICEF that they are transparent: they want to ensure market security, having more than one supplier. We don't have any issue with sharing markets. But when Serum was coming online there were lots of proactive measures in countries to try and find a large volume home for SII. I say, 'Let's compete fairly!' We are present in these markets – so we know it's happening."[120]

Overall, SII expressed frustration that they received so little subsidy from the PCV AMC pilot, and that the AMC closed immediately after their first deal[121]. "The objective to start with was very great. But as we experienced commercially, while we came to the end, we found that we had no doses to be allocated for, after putting a lot of strength, finance etc."[122] The Executive Director of SII, speaking in 2020, stated, ""I attended almost each and every meeting of the AMC since the beginning and therefore I feel extremely depressed with the final outcome when even the small amount could not be available for the developing country vaccine manufacturers. Many years ago, someone asked me what I thought would be the fate of the AMC. They asked if I thought Serum would end up getting any money out of it. I said that I was 99% sure that most of the money would go to big pharma with maybe a few crumbs left for us."[123]

This mini case study highlights how the lack of clear prioritization has contributed to frustration amongst stakeholders. Of course, it is impossible to know how fully legitimate these frustrations are e.g., Were verbal assurances [of support] given in contradiction to stated objectives? Or is this frustration about non-AMC related issues – such as delays in coming to market – being focused retrospectively onto the AMC?

All four objectives of the PCV AMC pilot were technically achieved, but not everyone has come away thinking it was a success for them, or that it was 'fair'. This lack of clear prioritization between objectives turned out to benefit Gavi, as it allowed for flexibility and broad buy-in from donors and other stakeholders. However, repeated instances of unclear prioritization with the same stakeholders can undermine engagement, as stakeholders will lose confidence and feel they are constantly 'losing out'.

[119] Interview, 12 May 2021.
[120] Interview, 3 May 2021.
[121] From the outset, the PCV AMC pilot was always scheduled to close at end 2020. There was a discussion about whether to extend it, but Gavi and donors decided against.
[122] Interview, 29 April 2021.
[123] Usher AD. Billion-dollar pneumonia vaccine fund closes after first non-Western firm wins tender. Donors transfer remaining money to COVID19. *Development Today*. [Online] 2020 Jun 16 [Cited 2020 Jun 18]. Available from: https://www.development-today.com/archive/dt-2020/dt-4--2020/billion-dollar-pneumonia-vaccine-fund-closes-after-first-non-western-firm-wins-tender.-donors-transfer-remaining-money-to-covid19.

X. RECOMMENDATIONS

Recommendations

This report makes four recommendations, all of which benefitted substantially from the co-creation workshop with Gavi Secretariat staff on 19 August 2021.

AMC-specific recommendations

As the PCV AMC pilot has shown, how an AMC is designed and run – elements which are all inherently choices – will have impacts on the potential for progress against the different objectives of the instrument.

The desire to let countries choose their preferred products, linked to Gavi's overarching objective of "country ownership", can be at tension with achieving supply-related objectives. Importantly, country-led decision-making does not mean that supply objectives *cannot* be achieved; rather, it means that Gavi has very limited ability to control demand and thus guarantee the achievement of these objectives and take accountability for them.

One way for Gavi to partially circumvent this dilemma and increase the likelihood of achieving both supply and market entry objectives would be "healthy demand" interventions.[124]

Recommendation 1: Gavi could benefit from adopting a more coordinated and intentional approach to shaping healthy demand – as proposed in the new market shaping strategy[125]. This should increase the effectiveness of future AMCs, expand the potential use cases for an AMC, and decrease the risk associated with interventions like AMCs that shape supply.

Fundamentally, the ability to better shape demand would offer new use cases for an AMC at Gavi. These might include situations where products are more differentiated than they are for PCV, or where Gavi needs to make firmer commitments to manufacturers. While the PCV AMC pilot has been a success in many ways, how often and when Gavi can deploy an AMC again will depend in large part on decisions around Gavi's operationalization of demand shaping, which is just starting.

- **As the strategy notes, Gavi would benefit from increased capabilities to predict countries' preferences, and the likelihood and likely timing of a country's decision to adopt a new vaccine or switch to a different vaccine product.** Understanding in more detail how demand materializes in different country contexts should help Gavi better understand demand across products, and across timeframes.
- **If there is a mismatch between commitments made on the supply side, and emerging demand, Gavi would benefit from a wider and firmer toolkit to steer and shape demand to avoid misalignment and reduce potential risk.** Gavi does seek to shape demand today, but efforts are somewhat *ad hoc*, and often responsive. The new market shaping strategy states the Alliance will develop "a new demand health intervention framework" but notes demand

[124] Given the current focus on COVAX, readers may be interested to understand how the COVAX AMC is grappling with this challenge. While the COVAX AMC it is called an AMC (see https://www.gavi.org/gavi-covax-amc) and was inspired by the PCV AMC pilot, the instrument is different in material ways. Importantly, the deals under the COVAX AMC are manufacturer-specific, not market wide. Furthermore, the COVAX AMC can offer high confidence in demand to manufacturers because supply is so scarce and because countries are allocated products by WHO through the Fair Allocation Framework, rather than choosing them.

[125] The new strategy defines healthy demand as: "Healthy demand from a market perspective is defined as a state when program demand materializes as expected, when the quantity and timing of demand can be sufficiently predicted and sustained over time, and when country product choices are evidenced-based and implemented with minimal delay, leading to the balanced uptake of appropriate products and the timely uptake of new innovative products. In short, demand should be timely, predictable, sustainable, balanced, and driven by evidence-based decisions and up-to-date policies."

side interventions would only be 'exceptional'. In essence, increasing ambition to make hard commitments on the supply side need to be matched with increased capabilities to shape preferences on the demand side to avoid unacceptable levels of financial risk. Given the market failures across the antigens Gavi supports, and the increasing complexity of these markets, it feels likely these interventions may be needed in more than 'exceptional' cases.

This approach does raise some fundamental and philosophical questions around how demand shaping integrates with country-led decision-making, and which tools encroach too much into country ownership. Discussions on these issues for the evaluation have highlighted differing views within the Secretariat and across the Alliance. The market shaping strategy announces a roadmap development process: this roadmap would be a natural "venue" to debate these trade-offs and chart a path forward.

Recommendations relevant to future AMCs and other market shaping instruments

Recommendation 2: The design of subsidy mechanisms in future AMCs or other market shaping instruments could benefit from both understanding the incentive structures the mechanism will create if the market develops as expected, and how it will influence market actors in other plausible scenarios. The PCV AMC pilot deployed $1.3bn of subsidy, and while the subsidy design was effective at increasingly supply, in hindsight it could have been more targeted and intentional with respect to price competition[126]. The downward pressure on prices was assumed to come from the market entry of SII, an assumed but fundamentally uncertain market development. While it may not be possible to design a perfect subsidy mechanism, Gavi could benefit from analyzing the 'robustness' of the design – how well it works in multiple plausible scenarios – for future AMCs or other market shaping instruments.

Recommendation 3: Gavi could benefit from delivering more accurate and informative[127] demand forecasts to manufacturers, focusing in particular on when demand is likely to materialize. While forecasting demand is challenging, Gavi's forecasting today is perceived to be structurally too optimistic. The current situation might have two counter-productive and unintended consequences: i) that manufacturers disregard Gavi's data, and actually produce lower volumes than they might have with a well-justified and well-communicated Gavi forecast, and/or ii) that manufacturers price in the costs of holding inventory to future Gavi deals, yielding lower value for money for Gavi than might have been possible through better forecasting.[128],[129]

Recommendation 4: Legal structures of future AMCs could be designed to allow for appropriate flexibility, and to minimize transaction costs for all parties involved. It was necessary to use very robust legal structures for the first AMC, because of the innovative nature of the partnership. However, with Gavi's capabilities, and especially its credibility, now firmly established, Gavi and its partners can take advantage and have a nimbler legal structure that reduces (transaction) costs while still providing the right level of confidence and protection for both sides.

[126] As noted above, some stakeholder expected the price to decline during the course of the PCV AMC pilot, whilst others did not. Those that expected a price decline were disappointed.
[127] Informative, in this context, means greater transparency around assumptions like the probability of NVI by key countries
[128] The Gavi Alliance Market Shaping Strategy for 2021-2025 includes both a desire to better understand country needs and desires, and a focus on the predictability of demand. Both of these should support improved forecasting.
[129] The co-creation workshop attendees noted the challenges of forecasting demand for a given product when countries are choosing between an increasing number of products to introduce – this will increase uncertainty, but should not drive structural biases in the forecasting

ANNEXES

Annex 1: Terms of reference, including evaluation questions

This annex includes the original terms of reference (ToR) for the evaluation. The details of the delivery of the evaluation against the ToR is described in the Inception Report prepared by the independent evaluation team.

Purpose of the evaluation

The purpose of the end line outcomes and impact evaluation of the pilot Pneumococcal vaccines Advance Market Commitment (AMC) is two-fold:

- Summative: Explore the extent to which the pilot AMC has achieved its overarching goal of reducing morbidity and mortality from pneumococcal disease, as well as its four specific objectives, including the unintended effects.
- Formative: Explore the effectiveness and efficiency of the AMC design and implementation to the extent that these processes contribute to explaining the extent that outcomes have been achieved. The evaluation will document lessons learned to improve the design of potential future AMCs or other relevant mechanisms.

The results of this end line evaluation of the pilot AMC mechanism will be critical for both learning and accountability to all AMC stakeholders. The recommendations based on lessons learned will also inform potential AMCs or other relevant mechanisms.

Scope of the evaluation

The evaluation will be retrospective, covering the entire period of the pilot AMC mechanism implementation 2009-2020 and will build upon the M&E work that has already been done, including the outcome and impact study undertaken in 2015.

As proposed in the AMC M&E framework, the second outcomes and impact evaluation will focus on the achievement of AMC outcomes and will assess causal linkages between the AMC intervention and results achieved through comparisons with appropriate counterfactuals. The second outcomes and impact evaluation should be informed by, but is not limited to, the proposed counterfactuals in the baseline study. The evaluation should propose updates to these counterfactuals, or development of new counterfactuals as needed, with justification.

Using a theory-based approach, issues related to AMC design processes, design elements, and implementation should be explored as explanatory factors for observed and estimated changes in outcome and impact measures. As such, the evaluation should build upon rather than replicate work of the process and design evaluation completed in 2013.

The evaluation should explore changes – positive and negative, intended, and unintended – generated by the AMC. As such, it is expected that the evaluation reviews the overall status of key performance indicators related to the AMC outcomes and impact included in the Results Framework for Pneumococcal Conjugate Vaccine.

Counterfactuals	Assessment of the suitability of previously defined counterfactuals and proposing alternatives with justification as needed: • Markets for PCV and other new vaccines in non-AMC-eligible developing countries • Markets for PCV in AMC-eligible countries graduated or graduating from Gavi-support • Markets for other new vaccines in AMC-eligible countries • Modelled market scenario analyses
Outcomes	Progress toward outcomes should be assessed using historical and projected vaccine supply and demand estimates and forecasts, including but not limited to: • Vaccine supply and demand estimates from 2009 to-date • Projected vaccine supply forecasts through 2020 • Projected Gavi demand and coverage forecasts through 2020 • Competition and new manufacturers entering the market
Impact	Comprehensive assessment of existing empirical evidence and model-based estimates of disease burden and vaccination impact, including but not limited to: • Empirical evidence of changes in pneumococcal disease burden and impact of PCV vaccination • Modelled vaccine impact estimates from 2009-2020 • Indirect and broader effects (e.g. herd effects, equity, child mortality, broader social and economic effects)
Lessons learned, replicability and recommendations	• Detailed documentation of lessons learned and considerations for future AMC • Components of the design that are replicable in similar mechanisms • What worked well, why and how? • Evidence based actionable recommendations for future potential AMC or other similar mechanisms

Evaluation questions

Impact

- To what extent has the AMC contributed to the reduction of morbidity and mortality from pneumococcal disease in Gavi eligible countries?
    - During implementation of the project and at the end of current or future agreements with manufacturers?
    - To what extent has the AMC contributed to equitable reduction of morbidity and mortality from pneumococcal disease in Gavi-eligible countries? (Please refer to the equity dimensions represented in the Gavi indicators frameworks for the 2016-2020 period)
    - To what extent has the AMC contributed to indirect and broader effects (e.g. herd effects, equity, child mortality, broader social and economic effects)?
    - What are the identified mechanisms for the proposed impact? How reliable are estimations of impact in terms of other potential factors?

Outcomes

- To what extent can the causal path from the AMC Theory of Change be validated?

    - What were the main contributors (and relative weight of different components) to the long-term outcome of the pilot AMC according to the available data?
    - To what extent have internal and external factors (e.g., changes to Gavi policies, certain elements of AMC design, the role of the Bank) impacted the execution and results of the pilot AMC?
- To what extent has the AMC led to an acceleration of investment in additional manufacturing capacity and availability of supply of suitable pneumococcal vaccines for Gavi-eligible countries?
    - To what extent did the AMC accelerate investments by manufacturers in research and development of pneumococcal conjugate vaccines meeting the Target Product Profile?
    - To what extent did the AMC result in a change to vaccine manufacturer perceptions / assessment of the viability of the market in developing countries?
- Whether, why and how has the AMC resulted in the availability of affordable and sustainable PCV for Gavi-transitioning and transitioned (fully self-financing) countries?
    - To what extent has AMC achieved proper balance between supply and demand for PCV?
    - What factors facilitated or hindered achievement of forecasted targets?
    - Whether and how the AMC contributed to increased uptake of PCV and sustained coverage in countries?
    - To what extent did the AMC mechanism result in a donor-driven prioritization at eligible countries in terms of their budgeting?
    - To what extent did the AMC pilot modify countries policies related to budgeting and financing for health in general and vaccines in particular?
- What were the key positive and negative unintended consequences of the pilot AMC for Gavi, donors, manufacturers and countries and how did they impact AMC objectives?

<u>Lessons learnt</u>

- To what extent is the pilot AMC model still relevant given the changes in the market environment?
- Whether and how changes in the pilot model would have contributed to more effective execution and better results?
- What are the key lessons learned from this pilot that could be used to inform development of similar initiatives in the future?
    - What are the learnings at country level in terms of budgeting and financing?
    - Are there specific lessons that could inform the use of AMC-type mechanisms to meet critical goals for vaccine development, production and rollout related to vaccines against emerging and re-emerging pandemic and epidemic prone diseases like Ebola and Covid-19?
- To what extent is the AMC pilot replicable? Based on the validation of the AMC ToC and causal pathways, are there aspects of the model that are seen to be most critical if replicating for other vaccines?
- To what extent does the AMC pilot compare with other similar mechanisms and what could have been the implication if other mechanisms were tried instead of the AMC approach?

Bidders may propose additional evaluation questions to the above list of evaluation questions as part of their proposals, with justification.

Methodology

In order to respond to the above questions and provide a high-quality report, bidders are expected to employ a range of evaluation methods and to pursue innovation where possible. Firms bidding on the evaluation are strongly encouraged to propose innovative methodological approaches in response to the evaluation questions. They should also describe their strategy for safeguarding the quality and credibility of the evaluation, including their proposed verification strategy and methods for determining and estimating contribution with justification, and strengths and limitations of counterfactuals. As noted above, the evaluation design should demonstrate how it will build upon the previous studies.

Bidders should describe their approach and considerations to overcome the limitations highlighted in the first outcomes and impact evaluation:

- Challenges inherent in isolating the influence of the AMC from all the other concurrent factors
- Limitations to understanding the true and precise mortality and morbidity impact of immunisation

The bidder should include the feasibility of/approach to undertaking a cost-benefit analysis of the AMC in their proposal. At a minimum, bidders should elaborate on the following methods and data collection and suggest additional methods as part of their proposal:

Counterfactuals:

The incremental contribution of the AMC to any observed and estimated changes in outcome and impact measures will be assessed through counterfactual analysis. The bidder should consider a wide range of counterfactuals including but not limited to counterfactuals recommended in previous AMC evaluations. If counterfactuals defined in earlier evaluations are deemed no longer to be suitable

alternatives can be proposed with justification. Criteria for selection of counterfactuals should be stipulated with a description of strengths and limitations.

Impact:

Comprehensive assessment of existing empirical evidence and model-based estimates of disease burden and vaccination impact, including but not limited to:

- Empirical evidence of changes in pneumococcal disease burden and impact of PCV vaccination
- Modelled vaccination impact estimates from 2009-2020.

Outcome:

Progress toward outcomes should be assessed using historical and projected vaccine supply and demand estimates and forecasts, including but not limited to:

- Vaccine supply and demand estimates from 2009 to-date
- Projected vaccine supply forecasts through 2020
- Projected Gavi demand and coverage forecasts through 2020
- Actual vaccine uptake trend in AMC eligible countries
- Competition and new manufacturers entering the market

Review of literature and available data:

This evaluation should capitalise ongoing and past findings. The evaluation should build on the findings and recommendations of all previous AMC assessments and all AMC annual reports available on the Gavi website. The role of the pilot AMC should be interpreted in the context of overall national government and donor support for pneumococcal conjugate vaccine in Gavi-eligible countries, as outlined in the Gavi pneumococcal vaccine Results Framework.

The evaluation should leverage other ongoing complementary work including: pneumococcal impact studies, Gavi transition assessments etc. Broader immunisation and health data should also be utilised. This includes, but should not be limited to:

- WHO-UNICEF and Institute of Health Metrics and Evaluation estimates of national immunization coverage;
- Dates of introduction of new vaccines available at both WHO and Gavi
- Available mortality/morbidity data, including special studies relevant to pneumococcal and other vaccines;
- Disease burden estimates generated by the WHO Global Burden of Disease/Global Health Estimates Project, the Institute of Health Metrics and Evaluation Global Burden of Disease project, and the UN's Inter-agency Group for Child Mortality Estimation.

Interviews:

- Relevant AMC stakeholders (including initial design team) members should be interviewed to ascertain their views and perception on whether the AMC has successfully achieved its objectives and contributed to positive outcomes and impact. Bidders should provide an indication of scope and scale of stakeholder interviews in the proposal.
- Finally, to ensure credibility, the AMC Outcome Evaluation should be conducted in accordance with the following principles: 1) independence and impartiality; 2) involvement of stakeholders (including external participants (countries, manufacturers, CSOs, experts in different AMC fields like economic theory, innovative financing, manufacturing etc.; 3) transparency; and, 4) reference to international norms and definitions such as the OECD Development Assistance Committee (DAC) principles.
- Gavi is committed to learning and adapting based on findings and recommendations from evaluations. Bidders should build a learning approach into the proposal to ensure that opportunities for learning throughout the evaluation, as well as from the findings, lessons learned, and recommendations are maximised. As such, bidders are expected to explicitly describe their communication, learning and engagement modes to foster utility of evaluation results.

Deliverables, management, & oversight

All reports should be provided in English.

Deliverable	Date
Monthly meetings and minutes, including with the Steering Committee of the evaluation	Ongoing throughout the evaluation
Inception Report with Power Point presentation, including a Theory of Change for evaluation purposes, a communication and learning plan for the AMC evaluation	February 15, 2021
Preliminary findings with Power Point presentation Facilitate recommendation cocreation meeting / workshop – Gavi Secretariat	April 30, 2021

Draft Reports (1-2 as needed) with Power Point presentation, including Lessons learned and recommendations co-created with AMC stakeholders	May 31, 2021
Final Report with Power Point presentation	June 30,2021
Presentations of evaluation results at Gavi Secretariat	TBD
Policy Brief summarising the main findings and lessons learnt	June 30, 2021
At least two peer reviewed journal articles	TBD
Other communication, learning and engagement approaches	June 30, 2021
Underlying datasets used for impact estimates	June 30,2021

This evaluation will be outsourced in its entirety to external Service Providers. In accordance with Gavi Board instituted process for conducting evaluations, the Gavi Secretariat will conduct a procurement exercise to recruit the Service Providers and assume responsibility for day-to-day management of the evaluation.

Annex 2: Mapping of evaluation questions to report sections

Evaluation Questions			Corresponding report section(s)	Page number(s)
1		To what extent has the AMC contributed to the reduction of morbidity and mortality from pneumococcal disease in Gavi eligible countries?	VII. Objective 4 > Findings on impact and effectiveness; VII. Conclusions > Conclusions on Objective 4	42-47 50-51
	a	During implementation of the project and at the end of current or future agreements with manufacturers?	VII. Objective 4 > Findings on impact and effectiveness > Impact of the PCV AMC pilot on mortality and morbidity	42-43
	b	To what extent has the AMC contributed to equitable reduction of morbidity and mortality from pneumococcal disease in Gavi-eligible countries? (Please refer to the equity dimensions represented in the Gavi indicators frameworks for the 2016-2020 period)	VII. Objective 4 > Findings on impact and effectiveness > Impact of the PCV AMC pilot on equitable reductions in mortality and morbidity	43-44
	c	To what extent has the AMC contributed to indirect and broader effects (e.g., herd effects, equity, child mortality, broader social and economic effects)?	VII. Objective 4 > Findings on impact and effectiveness > Indirect and broader effects from PCV	44-45
	d	What are the identified mechanisms for the proposed impact? How reliable are estimations of impact in terms of other potential factors?	VII. Objective 4 > Findings on impact and effectiveness > Impact of the PCV AMC pilot on mortality and morbidity	42-43
2		To what extent can the causal path from the AMC Theory of Change be validated?	Entire report is a theory-based evaluation that assesses the causal pathways in the theory of change (see Annex 7 for more information)	N/A
	a	What were the main contributors (and relative weight of different components) to the long-term outcome of the pilot AMC according to the available data?	Entire report is a theory-based evaluation that assesses the causal pathways in the theory of change (see Annex 7 for more information)	N/A
	b	To what extent have internal and external factors (e.g., changes to Gavi policies, certain elements of AMC design, the role of the Bank) impacted the execution and results of the pilot AMC?	Entire report is a theory-based evaluation that assesses the causal pathways in the theory of change (see Annex 7 for more information)	N/A
3		To what extent has the AMC led to an acceleration of investment in additional manufacturing capacity and availability of supply of suitable pneumococcal vaccines for Gavi-eligible countries?	V. Objective 2 > Findings on evolution of supply; VIII. Conclusions > Conclusions on Objective 2	24-26 48-49
	a	To what extent did the AMC accelerate investments by manufacturers in research and development of pneumococcal conjugate vaccines meeting the Target Product Profile?	IV. Objective 1 > Findings on R&D; Findings on presentation innovation; VIII. Conclusions > Conclusions on Objective 1	21-22; 22-23 48

	b	To what extent did the AMC result in a change to vaccine manufacturer perceptions / assessment of the viability of the market in developing countries?	IV. Objective 1 > Findings on perceptions of developing country PCV markets; VIII. Conclusions > Conclusions on Objective 1	23 48
4		Whether, why and how has the AMC resulted in the availability of affordable and sustainable PCV for Gavi-transitioning and transitioned (fully self-financing) countries?	V. Objective 2: Vaccine supply; VI. Objective 3: Vaccine uptake; VIII. Conclusions > Conclusions on Objective 2; Conclusions on Objective 3	24-32 33-41 48-49;49-50
	a	To what extent has AMC achieved proper balance between supply and demand for PCV?	V. Objective 2 > Findings on alignment between supply and demand; VIII. Conclusions > Conclusions on Objective 2	27-29 48-49
	b	What factors facilitated or hindered achievement of forecasted targets?	V. Objective 2 > Findings on security of supply; Findings on alignment between supply and demand; Findings on delays and forecasting; VIII. Conclusions > Conclusions on Objective 2	26-27; 27-29; 29-31 48-49
	c	Whether and how the AMC contributed to increased uptake of PCV and sustained coverage in countries?	VI. Objective 3: Vaccine uptake; VIII. Conclusions > Conclusions on Objective 3	33-41 49-50
	d	To what extent did the AMC mechanism result in a donor-driven prioritization at eligible countries in terms of their budgeting?	VI. Objective 3: Vaccine uptake > Findings on financial sustainability; VIII. Conclusions > Conclusions on Objective 3 > Conclusions on financial sustainability	38-41 50
	e	To what extent did the AMC pilot modify countries policies related to budgeting and financing for health in general and vaccines in particular?	VI. Objective 3: Vaccine uptake > Findings on financial sustainability; VIII. Conclusions > Conclusions on Objective 3 > Conclusions on financial sustainability	38-41 50
5		What were the key positive and negative unintended consequences of the pilot AMC for Gavi, donors, manufacturers and countries and how did they impact AMC objectives?	IV. Objective 1 > Findings on R&D; Findings on presentation innovation; VI. Objective 3: Vaccine uptake > Findings on uptake in selected case study countries	21-22; 22-23 35-38

6		To what extent is the pilot AMC model still relevant given the changes in the market environment?	IX. Lessons learned	52-55
7		Whether and how changes in the plot model would have contributed to more effective execution and better results?	IX. Lessons learned	52-55
8		How has the model for assessing PCV impact evolved and to what degree does the current VIMC model address the weaknesses identified by stakeholders in the previous model?	Annex 3	67-68
9		What are the key lessons learned from this pilot that could be used to inform development of similar initiatives in the future?	IX. Lessons learned	52-55
	a	What are the learnings at the country level in terms of budgeting and financing?	VI. Objective 3: Vaccine uptake > Findings on financial sustainability; VIII. Conclusions > Conclusions on Objective 3 > Conclusions on financial sustainability	38-41 50
	b	Are there specific lessons that could inform the use of AMC-type mechanisms to meet critical goals for vaccine development, production and rollout related to vaccines against emerging and re-emerging pandemic and epidemic prone diseases like Ebola and Covid-19?	IX. Lessons learned	52-55
10		To what extent is the AMC pilot replicable? Based on the validation of the AMC ToC and causal pathways, are there aspects of the model that are seen to be most critical if replicating for other vaccines?	IX. Lessons learned	52-55
11		To what extent does the AMC pilot compare with other similar mechanisms and what could have been the implication if other mechanisms were tries instead of the AMC approach?	IX. Lessons learned	52-55

Annex 3: Supplementary Evaluation Question

This section includes one evaluation question in the Terms of Reference that could not be answered within the overall narrative of the main report.

How has the model for assessing PCV impact evolved and to what degree does the current VIMC model address the weaknesses identified by stakeholders in the previous model?

There are two models used for by Gavi to estimate the impact of PCV vaccination – UNIVAC and LiST. UNIVAC is a static cohort model based in R. The model was originally developed to provide national ministries of health in LMICs with conservative estimates of the impact and cost-effectiveness of routine Hib, rotavirus and pneumococcal vaccination. It is managed by LSHTM. It is described in further detail in Annex 4 and online.[130] The Lives Saved Tool (LiST) is a multi-cause model that estimates the impact of scaling up more than 70 evidence-based health and nutrition interventions, including vaccines, on maternal mortality, neonatal mortality, child mortality, and stillbirths. LiST has been characterized as a linear, mathematical model that is deterministic. It was developed by the Johns Hopkins Bloomberg School of Public Health. It is described in further detail in Annex 4 and online.[131] As you can see in Figures 21 and 22, these models provide a range of outputs, based on the model, and the 'touchstone' – the update to the inputs.

THE RATIONALE FOR THE VIMC

The Vaccine Impact Modelling Consortium coordinates the work of several research groups modeling the impact of vaccination programs worldwide. The Consortium was established at the end of 2016, brings together 18 modeling groups, and is coordinated by a secretariat based at Imperial College London. The Consortium is funded by Gavi and the Bill & Melinda Gates Foundation.

The VIMC was set up for two main reasons: to simplify contracting for Gavi and BMGF, and to drive alignment and improvement amongst the various vaccine models through standardized inputs and peer to peer feedback.[132] Before the VIMC, the M&E team at Gavi contracted all the academic modeling groups directly, which was hugely time intensive for the Secretariat. In addition, the lack of standardized inputs made it very challenging to understand what proportion of the differences between results could be attributed to the inputs vs structural differences between the models. Now, the central VIMC team at Imperial College manages all the contracting within the consortium. The team also facilitates coordination and collaboration between the different modeling groups: establishing working groups working on similar problems; providing standardized data, to allow for comparison of outputs and running an annual light touch peer review process.

PROGRESS AGAINST THE WEAKNESSES IDENTIFIED IN PREVIOUS MODELS[133]

The use of standardized input data has been recognized as hugely helpful by the modelers themselves and by Gavi. However, some stakeholders interviewed noted a pressure towards

[130] https://www.vaccineimpact.org/models/hib/ and https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32657-X/fulltext

[131] https://www.vaccineimpact.org/models/hib/#jhu and https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32657-X/fulltext

[132] Formal objectives, as stated on the VIMC website, are: "As its core objective, the Consortium aims to deliver a more sustainable, efficient, and transparent approach to generating disease burden and vaccine impact estimates. Furthermore, the Consortium works on aggregating the estimates across a portfolio of twelve vaccine-preventable diseases and further advancing the research agenda in the field of vaccine impact modelling."

[133] These weaknesses were not specified in the ToR for the evaluation, so have been inferred from interviews with key stakeholders.

minimizing differences between results through the VIMC peer to peer conversations, rather than recognizing these differences may result from equally valid modeling choices between LiST and UNIVAC.

The annual peer review of the models works well, though the VIMC may want to add disease-experts to modeling experts in the peer review process. Those interviewed for this evaluation noted the annual review sessions have broadly worked well. Some stakeholders noted that the reviews are conducted by another modeler, rather than someone who necessarily understands the antigen being modelled – so some of the feedback can be badly targeted/irrelevant. As a result, the VIMC may want to add or pair up a disease expert and modeling expert in the annual review process.

The PCV models under the VIMC do not currently report on many of the equity indicators in the Gavi 5.0 strategy. This is more often because high quality input data does not exist, than because the models cannot compute the results. The LiST and UNIVAC models are relatively similar to each other, compared to the broader stable of models under the VIMC. Many of the proposed improvements to the models (aligned to Gavi 5.0) are technically feasible already: input data is more of a constraint. Please see Table 1 below.

Table 1: Proposed improvements to the VIMC PCV models aligned with the Gavi 5.0 strategy

<table>
<tr><th>Potential improvement</th><th>UNIVAC (LSHTM)</th><th>LiST (JHU)</th></tr>
<tr><td>Herd effects</td><td>A semi-dynamic version of the model is due imminently</td><td>Functionality exists, but JHU have been asked not to use, to ensure consistency with the UNIVAC estimate</td></tr>
<tr><td>Effect of partial coverage</td><td colspan="2" rowspan="4">Functionality exists in the model, but standardized data does not</td></tr>
<tr><td>Inputs/outputs by sub-national groups</td></tr>
<tr><td>Inputs/outputs by socio-economic status</td></tr>
<tr><td>Inputs/outputs by gender</td></tr>
<tr><td>Impact on over 5s</td><td>Functionality exists, but LSHTM have been asked not to use, to ensure consistency with the LiST estimates</td><td>Not possible – LiST focuses on mothers, and children U5</td></tr>
</table>

Annex 4: Methodology and Data Sources

Mixed-methods approach

Dalberg used a mixed-methods, theory-based evaluation approach. A theory-based evaluation tests the 'Theory of Change' (ToC) underpinning a policy or program, unpacking the relationships between foreseen activities, outputs, outcomes, and impacts. It helps to understand which parts of the results chain are working and which are not, the reasons for this and whether, overall, the logic behind the ToC is robust.

Mixed-methods, theory-based evaluations work well for complex programs because they provide a more complete, nuanced and context-based answer than other methods (e.g., difference-in-differences). We used the Theory of Change to identify key hypotheses that were tested to answer priority evaluation questions. We tested these hypotheses across different contexts and built an informative picture of where and how the program has worked best, and what lessons that yields for future AMCs.

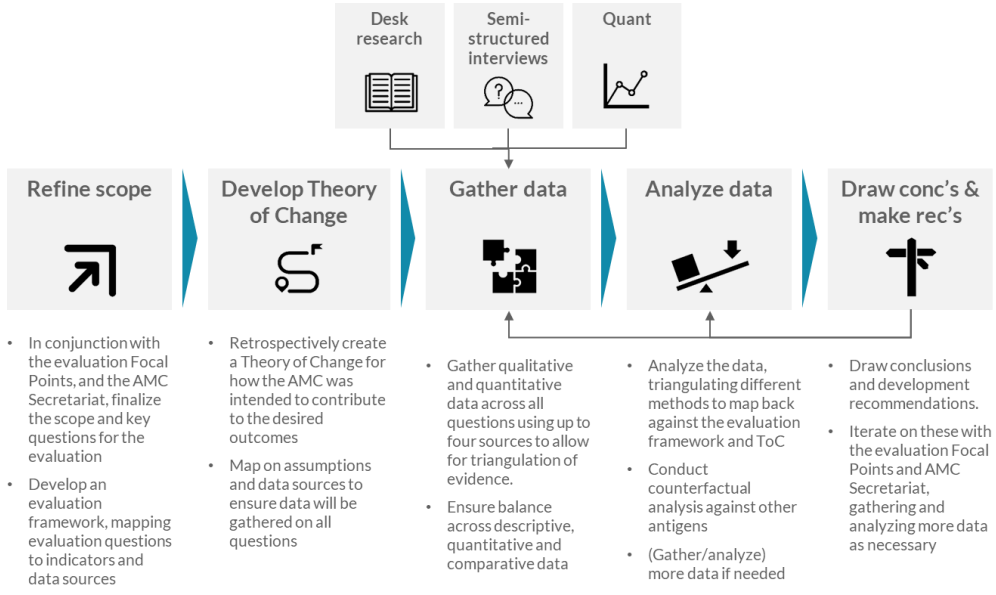
The evidence informing the evaluation questions at both global and national level was fragmented in terms of providing a comprehensive contribution story that can be linked to Gavi (and partner) activities. We have taken a conservative view to contribution vs attribution.

For all conclusions, we adopted a four-point scale for robustness rating. Robustness in the strength of conclusions is based on several factors, including the quantity of evidence, its alignment to other pieces of evidence, as well as the source and centrality of stakeholders to the evidence content area. All robustness rankings are relative robustness rankings and will be ultimately judgement-based. The robustness ratings are presented alongside key conclusions within this report.

Our research was conducted within and across methods (e.g., desk research, interviews) to reach coherent findings and achieve analytic saturation or sufficient burden of proof. These findings may not be fully consistent and there are differences of opinion between stakeholders. We have looked into these to try to understand and explain them, keeping in mind the limit of our engagement's timeframe.

The figure below describes the overall methodology.

Figure 26: Summary of evaluation methodology



To aid the evaluation process, the Evaluation Framework (Annex 6) identifies the data sources we proposed to use (at the Inception of the evaluation) to answer each of the evaluation questions and associated sub-questions, and potential indicators to look for in the evidence.

To arrive at a judgement concerning any ethical considerations that arose during the evaluation, the independent evaluation team used the UNEG Ethical Guidelines as the point of reference.

Mixed-methods in more detail: Desk research

Desk research was one of the primary methods used in this evaluation, allowing us to track outputs and outcomes and identify the main contributors to the outcomes of the PCV AMC pilot. We used a snowball, or chain-referral, sampling approach for identifying relevant documents for desk research. We started with a draft list of documents in the Dalberg proposal, and built on these with Gavi during the Inception Phase. From these documents we then identified relevant further documents, and 'snowballed' from there.

The chain referral method can be highly effective within a limited timeframe, as it focuses on relevance not comprehensiveness or systematicity. However, it can bring in an element of bias: documents tend to refer to/cite those that support their viewpoint, for example. To mitigate this, we made sure we included external voices/sources where possible (e.g., CGD analysis of AMCs) or voices known to be critical (e.g., MSF, and make sure we ask for further data suggestions from them).

Our robustness ranking approach includes the extent to which we reached analytical saturation, and is informed by the extent to which we exhausted the snowballing (documents referring to ones we have already analyzed, vs. new documents that were not possible to analyze during the evaluation timeframe).

The key information sources reviewed include:

- AMC Secretariat Annual Reports
- AMC Monitoring & Evaluation Study (2008)
- AMC baseline study (2010)
- AMC process and design evaluation (2013)
- AMC first outcomes and impact evaluation (2015)
- Gavi annual progress reports
- Gavi Mid-Term Review report (2016-2020)
- Gavi country data: progress reports, fact sheets, and full country evaluations
- IRC reports
- PCV impact studies (e.g., Bangladesh, Mozambique, Kenya)
- DFID Annual Reviews of the PCV AMC pilot
- Evaluate Pharma database
- Clinicaltrials.gov
- UNICEF documents on shipping data, supply availability data, product menu, etc.
- Gavi market shaping strategies for Gavi 4.0 and 5.0
- Gavi guidelines for AMC price request from transitioned countries
- Gavi demand forecast projections
- Gavi documentation from the 2019 AMC stakeholder meeting
- CGD's Blueprint for a Market-Driven Value-Based Advance Commitment (MVAC) for Tuberculosis
- MSF's Analysis and Critique of the Advance Market Commitment (AMC) for Pneumococcal Conjugate Vaccines (PCVs) and Impact on Access
- ViewHub by IVAC
- LiST impact model
- UNIVAC impact model

- Industry and press searches
- Academic literature searches on indirect effects of vaccination, or equity impacts

Analytical approach: Thematic analysis

For both the interview and desk research data, we used thematic analysis, after Braun and Clarke.[134] This follows six stages:

i) **Familiarization with the data.** This phase involves reading and re-reading the data, to become immersed and intimately familiar with its content.
ii) **Coding.** This phase involves generating succinct labels that identify important features of the data that might be relevant to answering the research question. It involves coding the entire dataset, and after that, collating all the codes and all relevant data extracts, together for later stages of analysis.
iii) **Generating initial themes.** This phase involves examining the codes and collated data to identify significant broader patterns of meaning (potential themes). It then involves collating data relevant to each candidate theme, so that we can work with the data and review the viability of each candidate theme.
iv) **Reviewing themes.** This phase involves checking the candidate themes against the dataset, to determine that they tell a convincing story of the data, and one that answers the research question. In this phase, themes are typically refined, which sometimes involves them being split, combined, or discarded.
v) **Defining and naming themes**. This phase involves developing a detailed analysis of each theme, working out the scope and focus of each theme, determining the 'story' of each. It also involves deciding on an informative name for each theme.
vi) **Writing up**. This final phase involves weaving together the analytic narrative and data extracts, and contextualizing the analysis in relation to existing literature.

We took a latent [vs. semantic] approach to the thematic analysis. While this does include a risk of bias (filtering the subtext and assumptions of the speaker or author through the evaluation team's assumptions), we feel that this approach is merited for this evaluation. The 'community' around the PCV AMC pilot is small, and truly independent stakeholders are few. As such, we believe subtext and assumptions are key to drawing out more critical perspectives from within Gavi and from its partners.

We used a mix of coding approaches akin to deductive and inductive reasoning (e.g., per Fereday and Muir-Cochrane, 2006)[135] depending on the evaluation question to be answered:

i) We used a coding approach akin to deductive reasoning for questions like *"Did the PCV AMC pilot lead [your company] to make additional investments in R&D and/or product presentation innovations for TPP-compliant PCV?"* or *"Without the PCV AMC, would your company have continued R&D on TPP-compliant vaccines?"* Here, themes included "investments aligned with our pre-existing strategy", or "[long] investment horizon" or "de-risking investment". These tended to be the more structured questions and/or those where we had greater clarity on emerging findings from initial desk research or interviews.
ii) We used a coding approach akin to inductive reasoning for questions like *"Are there specific lessons that could inform the use of PCV AMC-type mechanisms…."* Here we wanted the themes to emerge fully from the interviews or desk research. Coding akin to inductive reasoning tended to

[134] Virginia Braun & Victoria Clarke (2006) Using thematic analysis in psychology, Qualitative Research in Psychology, 3:2, 77-101, DOI: 10.1191/1478088706qp063oa.
[135] Fereday, Jennifer, and Eimear Muir-Cochrane. "Demonstrating rigor using thematic analysis: A hybrid approach of inductive and deductive coding and theme development." International journal of qualitative methods 5.1 (2006): 80-92.

be more suitable for the unstructured interview questions, or the more open evaluation questions.

The strengths and weaknesses of thematic analysis have been documented thoroughly in academic literature:[136]

- It is a useful method for examining the perspectives of different research participants, highlighting similarities and differences, and generating unanticipated insights.
- It is also useful for summarizing key features of a large data set, as it forces the researcher to take a well-structured approach to handling data, helping to produce a clear and organized final report
- However, the flexibility inherent in thematic analysis can lead to inconsistency and a lack of coherence when developing themes derived from the research data. It can be hard to interpret what data is or is not important to emphasize.
- It can have limited interpretive power if not grounded in a theoretical framework [this evaluation has a ToC so this is not a major concern here]
- Finally, since thematic analysis focuses on looking for patterns across interviews, phenomena that occur in only one individual account can be overlooked.

On balance, we believed (and still believe) it to be the most appropriate approach, given the scope of the evaluation, the timeframe, and the expertise and experience of the evaluation team.

Mixed-methods in more detail: Stakeholder interviews

Throughout the evaluation, Dalberg conducted semi-structured interviews with 71 topic experts and relevant stakeholders. This allowed us to gather a range of perspectives on the pilot PCV AMC and multiple data points from the same organization while remaining feasible within the timeline of the evaluation. These interviews were used to review and validate our findings from desk research, collect additional data and technical information, identify lessons learned, and support buy-in for the conclusions and recommendations from key stakeholders. We asked stakeholders both whether they made the best decisions *given the information available at the time* as well as now, with the benefit of hindsight, what they might have done differently. Evidence from stakeholder interviews was used to map onto indicators associated with the evaluation questions and supplement data with qualitative sentiments, opinions, and comparisons.

Inevitably, some of the stakeholders we interviewed may carry biases, may only be exposed to partial information, or may unconsciously filter information based on their positions or preferences. We sought to mitigate these risks by interviewing as broad range of stakeholders representing a diversity of positions and experiences as possible. Information furnished by others is believed to be reliable but will not be independently verified, unless expressly indicated. To account for the long 10-year duration of the PCV AMC pilot, we emphasized the importance of gathering the perspectives of those that were involved early in the PCV AMC pilot process, including stakeholders that might have left Gavi since the start of the PCV AMC pilot.

We have protected key informants' confidentiality.[137] Insights and quotes from the interviews are used in the report, but key informants are only mentioned by their high-level stakeholder group (e.g., multinational manufacturer). If we have received the consent of key informants, we have disclosed their names in the Annex 10.

[136] See, for example, Nowell LS, Norris JM, White DE, Moules NJ. Thematic Analysis: Striving to Meet the Trustworthiness Criteria. International Journal of Qualitative Methods. December 2017. doi:10.1177/1609406917733847.
[137] Confidentiality is the main ethical consideration to be addressed in this evaluation, given there was no human research.

We have tried to use a transparent approach to address conflicting guidance. Where we uncovered conflicting insights, we triangulated the evidence by discussing the issue with other key informants. We do not dismiss any insight from key informants, unless deemed unreliable, and have acknowledged in the report if an issue is divisive.

We developed the interview guide together with the Evaluation Focal Points in the Inception Phase of the evaluation. We pre-tested (pilot tested) the design and flow of the interview guide with both the Gavi team and a small sub-set of interviewees (field pre-testing). The interview guide included structured questions, follow-up or probing questions, and open questions. Overall interviews took one hour. The interviews included:

i) **Structured questions**. We asked certain questions in a clear and consistent format, using the same language for each respondent, to obtain answers to the evaluation questions in a systematic and structured manner. An example question that fits this format is: "*Did the PCV AMC pilot lead [your company] to make additional investments in R&D and/or product presentation innovations for TPP-compliant PCV?"*

ii) **Follow-up or probing questions.** These questions aimed to elicit further information on the rationales that informed the structured questions. Following on the example above, probing questions might include, *"Without the PCV AMC, would your company have continued R&D on TPP-compliant vaccines? Why / why not? How did the AMC play into the investment decision making?"*

iii) **Open-ended questions.** There are some evaluation themes and topics that can only be addressed in open-ended questions. An example of such a question is "*Are there specific lessons that could inform the use of PCV AMC-type mechanisms to meet critical goals for vaccine development, production and rollout related to vaccines against emerging and re-emerging pandemic and epidemic prone diseases like Ebola and Covid-19?"*

Selection of participants and stratification of participants

i) We aimed to achieve two objectives in selecting participants for interviews. For the structured questions, our main objective was to obtain a sufficiently sized and representative sample in total and in the different sub-groups or strata (e.g., different stakeholder groups) (e.g., per Gentles, 2015.)[138] For the open questions, we strove for thematic saturation (e.g., Saunders, 2018; Fusch and Ness, 2015,)[139] which (informally) means that further data collection would be unlikely to lead us to obtain new themes, insights or findings but would likely merely repeat earlier findings.[140]

ii) The majority of interviews included the structured, probing and open components and contribute to both objectives, but some interviews only included structured and probing components. Within the timeframe constraints, we believe we were able to access a sufficiently sized and representative sample for the structured questions, and we carefully drew up the interviewee list, and associated country and manufacturer shortlists, during Inception to achieve this.

[138]Gentles, Stephen J., et al. "Sampling in qualitative research: Insights from an overview of the methods literature." The qualitative report 20.11 (2015): 1772-1789.

[139] Fusch, Patricia I., and Lawrence R. Ness. "Are we there yet? Data saturation in qualitative research." The qualitative report 20.9 (2015): 1408; B Saunders, J Sim, T Kingstone, S Baker, J Waterfield, B Bartlam, Saturation in qualitative research: exploring its conceptualization and operationalization, Quality & Quantity, 1-15 (2018).

[140] More formally - The criterion for judging when to stop sampling the different groups pertinent to a category is the category's theoretical saturation. Saturation means that no additional data are being found whereby the sociologist can develop properties of the category. As he sees similar instances over and over again, the researcher becomes empirically confident that a category is Glaser, B.G., Strauss, A.L.: The Discovery of Grounded Theory: Strategies for Qualitative Research. Aldine, Chicago (1967).

However, we the evaluation timeframe was short, and stakeholders were very busy with the Covid-19 response so access to data/stakeholders, especially in-country stakeholders, was somewhat limited.

iii) Finally, both for the structured and open questions we ensured that we had representative participation on several important dimensions, including both internal and external stakeholders, representation from different organizations and different roles within the Alliance, variation in tenure and seniority, balance in geography, and balance in gender.

For analysis of interview findings, please see above on thematic analysis.

Mixed-methods in more detail: Quantitative analysis

We used quantitative analytical methods as the primary approach to answering the impact-focused evaluation questions.

Contribution to reduction in mortality and morbidity

We used the existing LiST and UNIVAC models to generate estimates of lives saved and DALYs averted up until the latest available data for the PCV AMC period. We also projected forwards to the close of the supplier agreements (2029) for a second estimate. We used the March 2021 Interim update estimate from each model, as it based on the latest WUENIC coverage data and Gavi forecasts.

The methodology and structure of both models is well-documented in separate publications.[141,142] These models were chosen for this evaluation for three main reasons:

- **Credibility:** Their application to immunization programs in Gavi countries have been peer reviewed and well accepted.
- **Not re-inventing the wheel.** The level of effort required to develop new models from scratch within the evaluation timeframe would require a significant tradeoff against the depth of analysis possible in other areas. Furthermore, the existing country-level inputs and assumptions for the two models, while not perfect, will be more accurate than those Dalberg could develop from scratch during the timeframe.
- **Ranges:** Having two models can provide a range of estimates, helping to convey appropriate levels of uncertainty inherent in the modeling process.

However, these models do have several well-understood drawbacks:

- **Partial vaccination:** The effect of partial vaccination is not included in either model.
- **Herd immunity:** Protections from herd immunity are not included in either model.
- **Over-five deaths:** Both models focus on the under-five population, but there is evidence that deaths over the age of five represent a significant portion of childhood pneumococcal deaths.
- **Country-level data only.** Neither of these models provide outputs broken down by gender, socio-economic groups, or by sub-regional geography (e.g., rural vs urban). While the VIMC team is developing improvements to the models, their current state makes it relatively challenging to understand the equity impacts of PCV coverage in a quantitative way.

[141] Clark A, Jauregui B, Griffiths U, Janusz C Bolanos-Siera B, Hajjeh R, Andrus J, Sanderson C. TRIVAC decision -support model for evaluating the cost-effectiveness of Haemophilus influenzae type b, pneumococcal and rotavirus vaccination. Vaccine. 2013 Jul: 31 (Suppl 3): C19 – C29.
[142] Walker N, Tam Y, Friberg I. Overview of the Lives Saved Tool (LiST). BMC Public Health. 2013: 13 (Suppl 3): S1.

On balance, we felt (and feel at the conclusion of the evaluation) the pros outweigh the cons for these models.

Equitable contribution to reduction in mortality and morbidity

The evaluation asked to understand the contribution of the AMC to *equitable* reductions in mortality and morbidity. The dimensions of equity listed[143] are:

- **Geographic distribution:** Average percentage of coverage for sub-national districts across the countries being supported.
- **Wealth distribution:** Average difference in full coverage between the poorest and richest quintiles across countries being supported.
- **Maternal education:** Average difference in coverage between non-educated mothers or female caregivers and mothers who have at least completed secondary school.

We conducted a brief literature review and signposted well-evidenced links between coverage and equity outcomes and impacts. We did not conduct bespoke quantitative analysis for two reasons:

- **Feasibility and accuracy.** Unfortunately, the LiST and UNIVAC models currently only produce national level outputs, and this is not disaggregated by gender or socio-economic status. It would not be feasible within the timeframe to develop new models, nor as mentioned previously, sensible to duplicate the ongoing, and much more substantial, effort of the VIMC to include equity.
- **Scope.** Equity dimensions are primarily programmatic outcomes, not PCV AMC outcomes. Beyond the actual point of purchase, these vaccines are treated the same way as other vaccines, so it is unlikely to have any influence on coverage amongst boys vs. girls, rural vs. urban, or the education level of the mother.

Indirect and broader effects

The evaluation also asked for contribution to "indirect and broader effects (e.g., herd effects, equity, child mortality, broader social and economic effects)?" As above, these are primarily programmatic outcomes, not outcomes related to price or security of supply of PCV. We signposted plausible impact pathways where rigorous academic literature exists but did not conduct bespoke quantitative modeling for these questions. Particularly, proposed to not calculate broader economic effects like the value for money or return on investment (ROI).

Mixed-methods in more detail: Survey

Following discussions with the evaluation Focal Points, we decided not to conduct a survey as part of our mixed-methods approach.[144] We did not see the survey being additive for two reasons:

1. In defining the evaluation framework (see Annex 6), there were no evaluation questions where the survey was going to be the primary source of data: it was always a supplement to desk research *and* interviews.
2. There is a material risk of low responses from surveyed participants as relevant stakeholders are occupied with the Covid-19 response.

[143] https://www.gavi.org/our-impact/measuring-our-performance/2016-2020-indicators/vaccine-goal
[144] The proposal submitted to Gavi suggested we might include a survey.

Country selection

We answered the majority of the evaluation questions at a whole of cohort level (e.g., we did not produce country-level estimates of lives saved). However, there are 10 specific questions and sub-questions that focus on the role of the PCV AMC in catalyzing uptake of PCV amongst transition countries:

Framework number	Question
1b[145]	To what extent has the AMC contributed to equitable reduction of morbidity and mortality from pneumococcal disease in Gavi-eligible countries? (Please refer to the equity dimensions represented in the Gavi indicators frameworks for the 2016-2020 period)
2a	What were the main contributors (and relative weight of different components) to the long-term outcome of the pilot AMC according to the available data?
2b	To what extent have internal and external factors (e.g. changes to Gavi policies, certain elements of AMC design, the role of the Bank) impacted the execution and results of the pilot AMC?
4a	To what extent has AMC achieved proper balance between supply and demand for PCV?
4b	What factors facilitated or hindered achievement of forecasted targets?
4c	Whether and how the AMC contributed to increased uptake of PCV and sustained coverage in countries?
4d	To what extent did the AMC mechanism result in a donor-driven prioritization at eligible countries in terms of their budgeting?
4e	To what extent did the AMC pilot modify countries policies related to budgeting and financing for health in general and vaccines in particular?
5	What were the key positive and negative unintended consequences of the pilot AMC for Gavi, donors, manufacturers and countries and how did they impact AMC objectives?
9a	What are the learnings at the country level in terms of budgeting and financing?

Here, we focused on a sub-set of countries to understand whether the theory held true across countries, and to what extent it might be generalizable to other transitioning countries. We hypothesized that the PCV AMC may have worked through three interacting effects. This overarching framing has informed our country shortlisting, below.

We focused on Bangladesh, Cameroon and Pakistan, Nigeria and India, Bolivia, and Indonesia. The table below describes the variables informing the country selection, and how each one influenced the final mix of countries proposed. It is important to note that country selection is always contested within Gavi – every country has valid claims for meriting study, but also valid claims for being a weak starting point for generalization. As such there is no perfect mix of countries.

Variable	Intended outcome	Influence on final selection mix
Co-financing status	To have a mix of transitioning countries, including PT, AT and FSF countries (e.g., assumed differences in price sensitivity and donor funding)	The shortlisted evaluation questions focus specifically on transitioning and Fully Self-Financing Countries (not Initial Self-Financing Countries). AT countries (Nigeria, India) and FSF countries (Bolivia, Indonesia) are more likely than PT countries (Bangladesh, Cameroon, Pakistan) to pay the full 'tail price'[146] within the time frame of the AMC.

[145] Note that we will generate country by country estimates but plan to present the data at a cohort level

[146] Each manufacturer must commit to supply its annual share of doses for 10 years at a maximum price of US USD 3.50 per dose to be paid by Gavi and Gavi-eligible countries.

		However, AT and FSF countries have very little donor funding, making it hard to answer question 4d "To what extent did the PCV AMC mechanism result in a donor-driven prioritization at eligible countries in terms of their budgeting?" We have therefore included three PT countries.
NVI dates	To balance across NVI dates over the PCV AMC timeframe as a proxy for receptiveness to Gavi guidance	(Partly in tension with the current/recent decision-making variable below). Assuming that Gavi engages with all countries relatively equally, earlier NVI dates within the window could be a proxy for country level amenability to Gavi focus (Pathway 4 in the ToC). As such, we wanted to include Cameroon, who NVI'ed in 2011, Pakistan in 2012 and Indonesia, below, who have delayed their introduction multiple times.
Access to information	To consider countries who are currently or have recently made NVI decision decisions	Unpacking the role of price, stability of supply and Gavi engagement will not be easy. Accessing this information should be easier for countries who are making NVI decisions now, rather than those who NVI'ed nearly a decade ago. As such, we propose to include Indonesia who are piloting PCV currently and making decisions on scale up.
Geography	To have a range of geographical regions	We wanted to ensure a mix of countries across Asia (n=4), sub-Saharan Africa (n=2), and Latin America (n=1).
PCV product selection	To balance uptake across the three PCV products	We have ensured a balance across manufacturers (five countries using/who want to use Pfizer[147] and two using GSK[148]).
Engagement timeframe	To be feasible within the engagement timeframe and scope	We proposed seven countries for study. In each country we need to speak to the EPI Manager/former EPI manager from the time of the NVI, as well as the SCM and potentially donor representatives. This was hard and time consuming (especially with the current Covid-19 context), and then we needed multiple rounds of conversations to triangulate findings (see below on Limitations). As such, seven is the most countries we could commit to within the timeframe and scope of the evaluation.
Share of birth cohort	To ensure selected countries are credible in terms of representing a high proportion of the Gavi73 birth cohort	Nigeria and India are often referred to as 'unique' or 'special cases' within the Gavi73 but they represent 39%[149] of the birth cohort, so whether they choose to NVI/roll out PCV has a substantial bearing on reductions in mortality and morbidity. As such, we believe they merit study despite the perceived lack of generalizability.

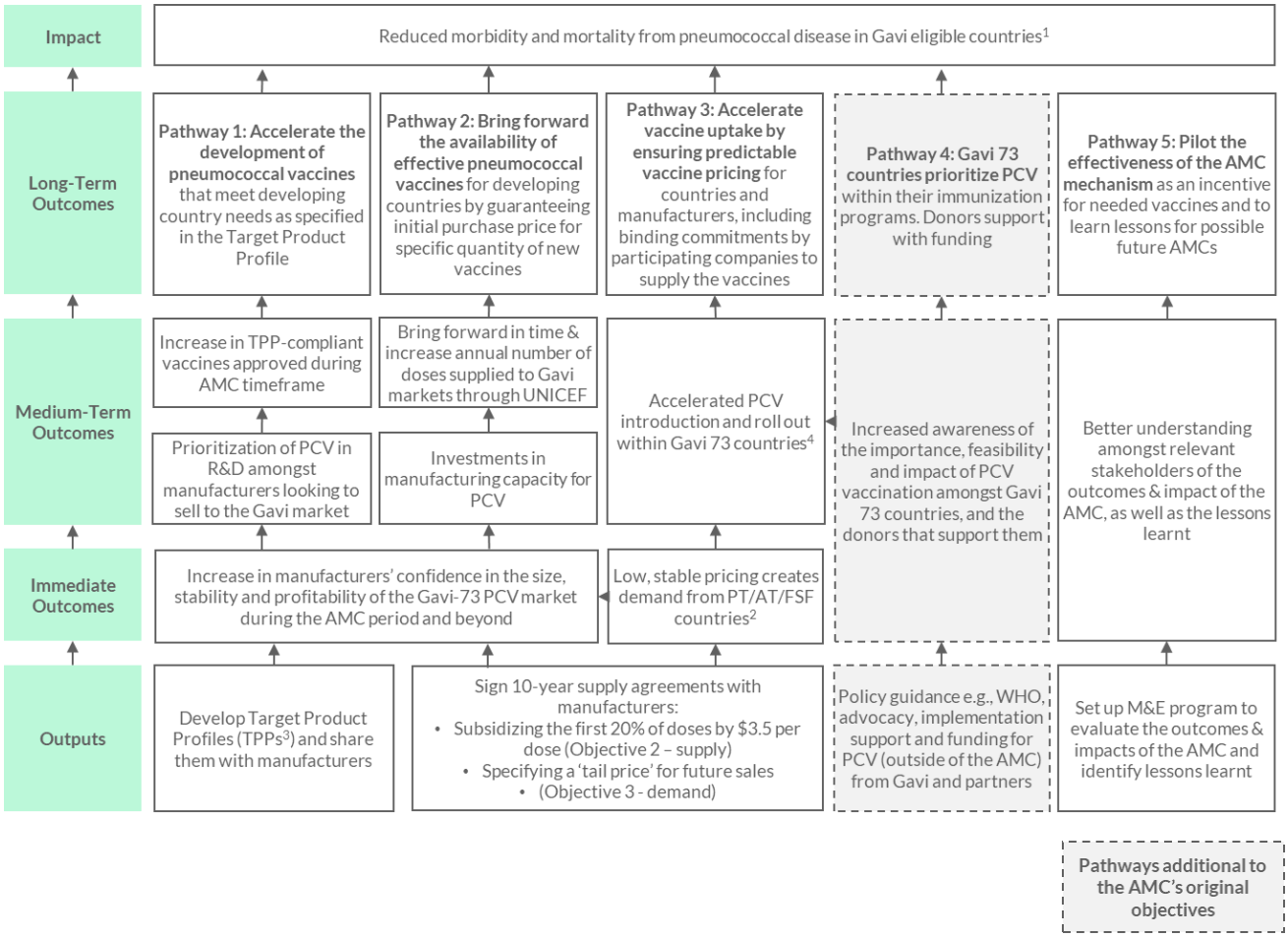
Throughout our country engagement we remained hyper conservative on potential for generalizability from specific Gavi countries. These issues are important – especially given the evaluation questions on replicability of an AMC – but we wanted to be very careful not to overstate similarities where they may not exist.

[147] Cameroon, Pakistan, India, Bolivia, Indonesia.
[148] Bangladesh, Nigeria.
[149] https://www.gavi.org/programmes-impact/country-hub

Annex 5: Theory of Change

The evaluation team reconstructed a Theory of Change (ToC) which sets out the steppingstones Gavi (and partners) envisaged in the implementation of the PCV AMC pilot. It is built from the background information provided on the PCV AMC pilot, as well as a small set of key informant interviews with PCV AMC Secretariat members and UNICEF Supply Division. For the reconstructed ToC to work as intended, the outputs must have happened, and the assumptions linking the outputs to outcomes and impact must hold true.

Figure 27: Retrospective Theory of Change (ToC) for the PCV AMC pilot



The PCV AMC pilot has been evaluated against its four objectives of the PCV AMC (note how pathways 1, 2, 3, and 5 map almost exactly to the formal four objectives). The role of this additional pathway (pathway 4) was to test the 'theory'/how change happened: Did the outcomes and impacts come from the AMC itself, or from external factors? As such, this pathway is key for the process of the evaluation but will not be prominent in the final report.

ToC pathways

The ToC comprises five main pathways. From left to right, these are:

Pathway 1, which relates to accelerating the development of TPP-compliant PCV vaccines. The ambition of the PCV AMC pilot was that, through the development of TPPs and the long-term tenders for TPP-compliant PCV vaccines, manufacturers would become more confident in the size, stability, and profitability of Gavi-73 PCV markets. This would lead them to prioritize R&D on TPP-compliant PCV vaccines, as well as production presentation innovations for Gavi countries. This would then result in an increase in the number of TPP-compliant PCV vaccines approved during the PCV AMC timeframe.

Pathway 2, which relates to bringing forward the availability of effective PCV vaccines in Gavi countries. The ambition of the PCV AMC pilot was that, through signing 10-year supply agreements with manufacturers and subsidizing the first 20% of doses, manufacturers would become more confident in the size, stability, and profitability of Gavi-73 PCV markets. This would lead them to make additional investments in manufacturing capacity for TPP-compliant PCV vaccines. At a whole of market level, this would then bring forward in time and increase the number of PCV doses supplied to Gavi markets. On a country-by-country basis we hypothesize that the low stable price brought about by the AMC supply agreements influenced price sensitive countries to bring forwards introduction or roll out of PCV.

Pathway 3, which relates to accelerating PCV vaccine uptake in Gavi countries. The ambition of the AMC was that, through signing 10-year supply agreements with manufacturers which specify a low, stable "tail price", demand amongst preparatory transition/accelerated transition/fully self-finance countries would both be created earlier in time, as well at greater volume. On a country-by-country level we hypothesize that the PCV AMC-catalyzed manufacturer investment in capacity influences countries to bring forwards introduction or roll out of PCV as they are more confident of getting the doses they need. This increase in demand would also lead manufacturers to be more confident in the market, which would support Pathway 1 and 2.

Pathway 4, which relates to Gavi countries prioritizing PCV within their immunization programs and donors providing them with the appropriate funding to support this ambition. This was not formally an objective of the PCV AMC pilot but we hypothesize that the PCV AMC itself (responsibilities to donors, responsibilities to manufacturers, publicity, CSO advocacy and accountability, status as flagship initiative within Gavi) led to a greater focus on PCV by Gavi. This could take the form of incremental increases in policy guidance, advocacy, and implementation support (e.g., health systems strengthening support) relative to vaccine programs without an AMC. This may have accelerated uptake and rollout amongst Gavi-73 countries.

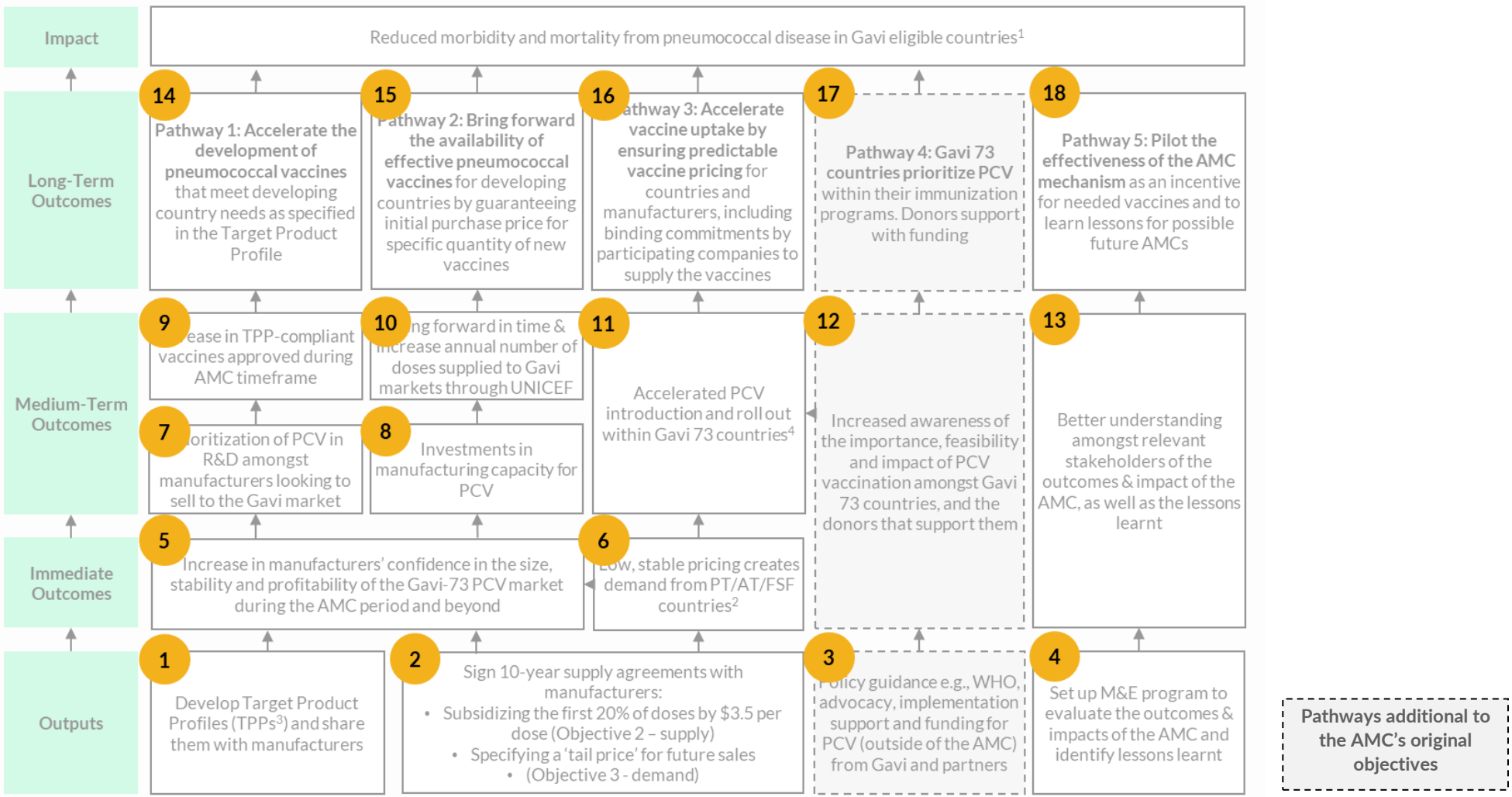
Pathway 5, which relates to piloting the effectiveness of the PCV AMC pilot mechanism. The ambition of the PCV AMC pilot was that, through setting up a detailed M&E program and publishing evaluations of the mechanism, relevant stakeholders would gain a better understanding of its outcomes and impact, as well as lessons learned for possible future AMC.

Annex 6: Evaluation Framework

The evaluation framework in tables below tie the evaluation questions and methodology to the ToC. The table is organized by the five pathways in the ToC. The columns are as follows:

- **Causal pathway:** We have numbered the ToC (see below) to facilitate tracking the causal pathway and assumptions that are being mapped to the evaluation questions
- **Assumptions to be tested:** Each causal pathway (arrows in the ToC) is supported by assumptions that we are seeking to either validate, challenge, or qualify within our evaluation. The numbers in the 'causal pathway' column can help indicate where the assumption drives the program theory. These assumptions are key to a theory-based evaluation
- **Key evaluation questions:** This column maps the ToC pathway back to the priority evaluation questions to demonstrate comprehensive coverage of the questions put forward by Gavi. Note that these evaluation questions are directly taken from the Terms of Reference for the evaluation.
- **Evidence:** This column outlines what evidence was reviewed to validate or refute the outputs, outcomes and impacts for that causal pathway.
- **Indicators:** This column outlines what we looked *for* within the evidence. Please note, for almost all of the evaluation questions, there are no simple 'Yes'/'No' indictors that point to the success or failure of the PCV AMC pilot
- **Data sources to triangulate:** For particular questions, there was a higher need to triangulate evidence (e.g., whether the drivers of uptake at country level are the same between shortlisted countries, and whether they are generalizable to the whole Gavi cohort). This column highlights questions where triangulation was key to test the underlying program theory[150]

[150] Please note triangulation/coherence of evidence checks were conducted for all questions, as part of the strength of evidence framework. This column highlights where we suspect the underlying program theory will be hardest to test, and therefore where triangulation within and across methods will be particularly valuable.



[1]This is the overarching goal of the PCV program at Gavi of which the AMC is one part, [2]Transitioning and FSF countries can apply to access the AMC price, [3]The Target Product Profiles outline the desired characteristics of PCV vaccines for Gavi countries, [4]Refers to roll-out within [big] countries (e.g., India or Indonesia, which can often be more important than NVIs for driving demand).

Causal pathway		Assumption to be tested	Key eval. questions	Evidence *(What did we look at?)*	Key indicators: *(What did we look for?)*	Data sources to triangulate
From	To					
Pathway 1						
1,2	5,7	That the long-term supply agreements and TPPs were necessary and did contribute to incentivizing manufacturers to accelerate PCV R&D (e.g., That the manufacturers did it, and did not do it on account of other factors)	2a, 2b, 3a, 3b	• Progress of R&D from desk research (e.g., clinical trials announcements) • Acceleration of R&D from interview questions	• Interview findings stating that the various manufacturers did accelerate R&D, and it was on account of the PCV AMC	Between manufacturers, triangulating 1) whether AMC did drive acceleration, and 2) what other factors were also contributing to prioritization (or not) of PCV R&D
7	9,14	That prioritization of R&D leads to new TPP compliant PCVs (new presentations and products) coming to market within the timeframe of the PCV AMC pilot (e.g., that the R&D is successful for at least one manufacturer beyond Pfizer and GSK).[151]	2a, 2b, 3a, 3b	• PQ announcements/ AMC Secretariat reports/ regulatory approval of vaccines	• Pipeline progress combined with evidence (above) that the acceleration in R&D was due to the PCV AMC pilot	
14	19	That the newly qualified PCV (presentation or product) has been rolled out and was efficacious within the timeframe of the evaluation so that it contributed to reducing mortality and morbidity	1a, 1b, 2a, 2b	• UNICEF shipping data • Coverage data by country • Gavi impact models (e.g., LiST and UNIVAC)	• Indication from UNICEF shipping data that the new to market vaccine was or was not shipped within the timeframe of the PCV AMC pilot, and therefore can/cannot be plausibly considered to have contributed to reductions in mortality and morbidity	

[151] Note that from pre-testing, we find this assumption to be contested in findings.

					• Shipment data showing volume uptake for new presentations (MDVs), and in sync with price decrease to show a virtuous cycle	

Causal pathway		Assumption to be tested	Key eval. questions	Evidence *(What did we look at?)*	Key indicators: *(What did we look for?)*	Data sources to triangulate
From	To					
Pathway 2						
1, 2	5,8	That the long-term supply agreements and TPPs were necessary and contributed to confidence amongst manufacturers in the LMIC PCV market, and thus investment in increased manufacturing capacity for PCV (e.g., manufacturer confidence in the PCV market did not stem from factors outside the AMC)	2a, 2b, 3a, 3b	• PCV AMC funding allocated to manufacturers • Manufacturer investment in PCV production capacity	• Interview findings that state that investment in production capacity by manufacturers was influenced by the PCV AMC, both directly (incentives) and indirectly (market creation) • Annual contracted PCV supply for Gavi, 2010-2029 (doses in millions)	Between manufacturers, triangulating 1) investments in PCV capacity, and 2) other drivers of investment in supply capacity outside the PCV AMC
8	10,15	That investments in manufacturing of fill and finish capacity for PCV brought forward an increased annual number of doses supplied to Gavi markets through UNICEF, giving Gavi-eligible countries greater availability of effective PCVs (e.g., that the increase in doses produced did not supply non-Gavi markets)	2a, 2b, 3a, 3b, 4a	• Annual contracted PCV supply with manufacturers • Annual shipped PCV supply by product • UNICEF rankings on security of supply	• Doses procured vs shipped, whole market and by product 2010-2020 (doses in millions) • Availability of PCV relative to other vaccines, 2010-2020 (UNICEF ratings)	
15	19	That the increased availability of effective PCVs in Gavi-eligible countries led to increased coverage, and so ultimately to reductions in morbidity and mortality (e.g., that the PCVs were rolled out effectively, and the products themselves were effective)	1a, 1b, 2a, 2b	• UNICEF shipping data • Coverage data by country • Gavi impact models (e.g., LiST and UNIVAC)	• Coverage rates, 2010-2020, relative to other vaccines (%) • Lives saved and DALYs averted from PCV (millions), relative to what would have been realized with the coverage rates of other vaccines (see methodology and key exhibits)	

Causal pathway		Assumption to be tested	Key eval. questions	Evidence *(What did we look at?)*	Key indicators: *(What did we look for?)*	Data sources to triangulate
From	To					
Pathway 3						
2	6,11,16	That aspects of the long-term supply agreements (e.g., tail prices and subsidies) were necessary and did contribute to decreasing and stabilizing PCV pricing for PT/AT/FSF countries, which then drove demand and accelerated PCV introduction/rollout (e.g., demand and rollout were not exclusively driven by external factors such as WHO guidance)	2a, 2b, 4a, 4b	• Manufacturer tail prices • PCV submissions/ approvals/ introductions by Gavi country • Counterfactual data from Hib, rota, and HPV (e.g. introduction dates and roll out progress)	• Annual announced tail price by manufacturer, 2010-2020 (USD) • Status of PCV applications by Gavi country, 2007-2020 (number of countries) • Vaccine country introduction by Gavi country, 1993-2020 (number of countries)	Triangulation between countries as to 1) the core drivers of NVI – what role does price/price stability play, and 2) the relative influence of the other factors
16	19	That the increased uptake of effective PCVs in Gavi-eligible countries led to increased coverage, and so ultimately to reductions in morbidity and mortality (e.g., that the PCVs were rolled out effectively, and the products themselves were effective)	1a, 1b, 2a, 2b, 4a, 4b, 4c	• UNICEF shipping data • WUENIC Coverage data by country • Gavi impact models (e.g., LiST and UNIVAC)	• Coverage rates, 2010-2020, relative to other vaccines (%) • Lives saved and DALYs averted from PCV (millions), relative to what would have been realized with the coverage rates of other vaccines (see methodology and key exhibits)	Quantitative modeling of country introductions and coverage to understand reductions in mortality and morbidity from supply

Causal pathway		Assumption to be tested	Key eval. questions	Evidence *(What did we look at?)*	Key indicators: *(What did we look for?)*	Data sources to triangulate
From	To					
Pathway 4						
3	12,17	That non-PCV AMC factors (e.g., WHO guidance, Gavi support and others) did contribute, but were not sufficient, to drive uptake of PCV without the low stable price achieved through the AMC[1]	2a, 2b, 3b, 4a, 4b, 4c, 4d, 4e, 5, 9a	• Interviews with EPI managers, donors and SCMs for selected countries to understand the drivers of PCV introduction • Desk review of policy documents, and/or Gavi application documents to understand the drivers of PCV introduction	• Interview findings that indicate the level of balance between Pathways 2, 3 and 4 (e.g., estimates of the weight of non-AMC factors in driving uptake) • Policy guidance and regulation for PCV by country government, WHO, and Gavi 2010-2020 (number and nature interventions)	Triangulation between the selected case study countries to understand, 1) whether the AMC did drive acceleration, and 2) what other factors were also contributing to PCV rollout. The coherence, or lack of, of these factors within types of countries (co-financing statuses) and across all the case study countries will determine the generalizability of the findings from the case studies.
17	19	That the increased prioritization of PCV within Gavi-73 country immunization programs and donor support programs does, or will, contribute to the reduced morbidity and mortality of pneumococcal disease	1b, 2a, 2b, 4a, 4b, 4c, 4d, 4e, 9a	• UNICEF shipping data • WUENIC Coverage data by country • Gavi impact models (e.g., LiST and UNIVAC)	• Coverage rates, 2010-2020, relative to other vaccines (%) • Lives saved and DALYs averted from PCV (millions), relative to what would have been realized with the coverage rates of other vaccines (see methodology and key exhibits)	

Causal pathway		Assumption to be tested	Key eval. questions	Evidence *(What did we look at?)*	Key indicators: *(What did we look for?)*	Data sources to triangulate
From	To					
Pathway 5						
4	13	That the M&E program's monitoring and evaluations of the PCV AMC pilot help develop a better understanding amongst relevant stakeholders of the outcomes, impact, and lessons learned of the PCV AMC pilot (e.g., that the evaluations are insightful, and are read and discussed by the relevant people)	5, 6, 7, 8, 9a, 11	• Desk review of previous M&E data (e.g., review of previous evaluation lessons learned) • Interviews with stakeholders who were involved in the PCV AMC pilot and then in subsequent market shaping initiatives	• Evidence based modifications in the design and implementation of AMC or uptake of lessons learned in the PCV AMC or other similar mechanisms • Proof of concept, by achievement of each objective (quotes from interviewees)	
13	18	That it is possible to prove (or disprove) the concept of the PCV AMC and that its core mechanisms (supply acceleration, demand creation, etc.) are not exclusive to PCV and can work across vaccines so that these learnings can feed into other possible future AMCs[152]	5, 6, 7, 8, 9a, 9b, 10, 11	• Interviews with Gavi Secretariat and donor representatives that are involved in other relevant financing mechanisms • Desk review of the lessons learned from the AMC in annual reports and strategy documents	• Evidence or lack of evidence that the documented lessons learned over the course of the PCV AMC has impacted other similar mechanisms (quotes from desk research and interviews)	

[152] Note that from pre-testing, we find this assumption to be controversial in upholding the causal pathway.

Recap: Evaluation Questions		
1		To what extent has the AMC contributed to the reduction of morbidity and mortality from pneumococcal disease in Gavi eligible countries?
	a	During implementation of the project and at the end of current or future agreements with manufacturers?
	b	To what extent has the AMC contributed to equitable reduction of morbidity and mortality from pneumococcal disease in Gavi-eligible countries? (Please refer to the equity dimensions represented in the Gavi indicators frameworks for the 2016-2020 period)
	c	To what extent has the AMC contributed to indirect and broader effects (e.g., herd effects, equity, child mortality, broader social and economic effects)?
	d	What are the identified mechanisms for the proposed impact? How reliable are estimations of impact in terms of other potential factors?
2		To what extent can the causal path from the AMC Theory of Change be validated?
	a	What were the main contributors (and relative weight of different components) to the long-term outcome of the pilot AMC according to the available data?
	b	To what extent have internal and external factors (e.g., changes to Gavi policies, certain elements of AMC design, the role of the Bank) impacted the execution and results of the pilot AMC?
3		To what extent has the AMC led to an acceleration of investment in additional manufacturing capacity and availability of supply of suitable pneumococcal vaccines for Gavi-eligible countries?
	a	To what extent did the AMC accelerate investments by manufacturers in research and development of pneumococcal conjugate vaccines meeting the Target Product Profile?
	b	To what extent did the AMC result in a change to vaccine manufacturer perceptions / assessment of the viability of the market in developing countries?
4		Whether, why and how has the AMC resulted in the availability of affordable and sustainable PCV for Gavi-transitioning and transitioned (fully self-financing) countries?
	a	To what extent has AMC achieved proper balance between supply and demand for PCV?
	b	What factors facilitated or hindered achievement of forecasted targets?
	c	Whether and how the AMC contributed to increased uptake of PCV and sustained coverage in countries?
	d	To what extent did the AMC mechanism result in a donor-driven prioritization at eligible countries in terms of their budgeting?
	e	To what extent did the AMC pilot modify countries policies related to budgeting and financing for health in general and vaccines in particular?

5		What were the key positive and negative unintended consequences of the pilot AMC for Gavi, donors, manufacturers and countries and how did they impact AMC objectives?
6		To what extent is the pilot AMC model still relevant given the changes in the market environment?
7		Whether and how changes in the plot model would have contributed to more effective execution and better results?
8		How has the model for assessing PCV impact evolved and to what degree does the current VIMC model address the weaknesses identified by stakeholders in the previous model?
9		What are the key lessons learned from this pilot that could be used to inform development of similar initiatives in the future?
	a	What are the learnings at the country level in terms of budgeting and financing?
	b	Are there specific lessons that could inform the use of AMC-type mechanisms to meet critical goals for vaccine development, production and rollout related to vaccines against emerging and re-emerging pandemic and epidemic prone diseases like Ebola and Covid-19?
10		To what extent is the AMC pilot replicable? Based on the validation of the AMC ToC and causal pathways, are there aspects of the model that are seen to be most critical if replicating for other vaccines?
11		To what extent does the AMC pilot compare with other similar mechanisms and what could have been the implication if other mechanisms were tries instead of the AMC approach?

Annex 7: Mapping of assumptions to evaluation process, findings, and conclusions

This table builds on the evaluation framework (Annex 6), and describes how the theory-based evaluation methodology was deployed against each Objective/evaluation question, tracking what process was undertaken, what findings were generated, and therefore what (theory-based) conclusions were drawn.

		Evaluation process							Findings		Conclusions				
Causal pathway		**Assumption to be tested**	**Key eval. questions**	**Evidence *(What did we look at?)***	**Key indicators: *(What did we look for?)***	**Data sources triangulated**	**Did the evaluator conduct the evaluation as planned?**	**Did the objective change?**	**Did the objective achieve what was intended?**	**Robustness of findings rationale for sub-Objective**	**Did the assumption of the pathway hold? (Held, Partially held, Did not hold) OR To what degree did the impact pathway operate as assumed?**	**What are the implications if the assumption did not hold?**	**Are there other assumptions that are key to performance that came to light during the evaluation?**	**Unintended and unexpected findings at level of pilot sub-Objective**	**Implications of the context for lesson learning**
From	**To**														
Pathway 1															
1,2	5,7	That the long-term supply agreements and TPPs were necessary and did contribute to incentivizing manufacturers to accelerate PCV R&D (e.g., That the manufacturers did it, and did not do it on account of other factors)	2a, 2b, 3a, 3b	· Progress of R&D from desk research (e.g., clinical trials announcements) · Acceleration of R&D from interview questions	· Interview findings stating that the various manufacturers did accelerate R&D, and it was on account of the PCV AMC	Between manufacturers, triangulating 1) whether AMC did drive acceleration, and 2) what other factors were also contributing to prioritization (or not) of PCV R&D	Yes	No	No	2 - most interviews and data sources aligned, but there was some variability	Did not hold - The PCV AMC pilot was not successful at accelerating new product R&D, despite one new TPP-compliant PCV product coming to market during the PCV AMC pilot.	Possibilities: timeframe too short, incentive not big enough, R&D already moving as fast as possible.	Yes - interviews highlighted the importance of public comms/signaling for de -isking investment, as much as the LTAs	Yes - see left (assumption did not hold)	1. At point of selecting PCV, two products were nearly on the market, which led to implicit emphasis on supply scale-up 2. PCV is a very complicated product to develop and manufacture

7	9,14	That prioritization of R&D leads to new TPP compliant PCVs (new presentations and products) coming to market within the timeframe of the PCV AMC pilot (e.g., that the R&D is successful for at least one manufacturer beyond Pfizer and GSK).[1]	2a, 2b, 3a, 3b	· PQ announcements/ AMC Secretariat reports/ regulatory approval of vaccines	· Pipeline progress combined with evidence (above) that the acceleration in R&D was due to the PCV AMC pilot		Yes	No	Partially	2 - most interviews and data sources aligned, but there was some variability	Partially held - The PCV AMC pilot was not successful at accelerating new product R&D, despite one new TPP-compliant PCV product coming to market during the PCV AMC pilot. (~5 years later than originally anticipated) The PCV AMC pilot was very successful at driving presentation innovation, through MDVs, which were key to scaling up supply and driving down cost per dose in LIC and LMIC markets.	While partially successful, the experience of SII reveals that market pull via an AMC may not be sufficient to accelerate R&D for an antigen that has products already on the market (e.g., PCV). It is also possibly that the timeframe was too short or R&D was already moving as fast as possible (e.g., SII received grant funding from BMGF to further support their R&D process and still came to market 5 years later than expected)	Yes - as per left, both 'push' and 'pull' funding may be needed for R&D focused AMCs, or specific support on things like tech transfer or clinical trials (a cause of the delays for SII)	Yes - see left (assumption only partially held)	1. PCV is a very complicated product to develop and manufacture
14	19	That the newly qualified PCV (presentation or product) has been rolled out and was efficacious within the timeframe of the evaluation	1a, 1b, 2a, 2b	· UNICEF shipping data	· Indication from UNICEF shipping data that the new to market vaccine was or was not shipped within the timeframe of the PCV AMC pilot, and		Yes	No	Yes	1 - Both LiST and UNIVAC models are peer reviewed, and further studies showed country level impacts	Held - The PCV AMC pilot will have contributed greatly to reducing mortality and morbidity by 2030. While SII's PCV10 only came to market in	N/A	No	N/A	N/A

		so that it contributed to reducing mortality and morbidity		· Coverage data by country · Gavi impact models (e.g., LiST and UNIVAC)	therefore can/cannot be plausibly considered to have contributed to reductions in mortality and morbidity · Shipment data showing volume uptake for new presentations (MDVs), and in sync with price decrease to show a virtuous cycle					from the PCV coverage. E.g., The evaluators have every reason to believe increasing PCV coverage does contribute to reductions in mortality and morbidity	2020, and therefore had minimal impact on reducing mortality and morbidity from PCV during the timeframe of the PCV AMC pilot, it should reduce mortality and morbidity out to 2030 Furthermore, multiple experts indicated that the MDV presentations developed by GSK and Pfizer were crucial to scaling up production and simplifying logistics of vaccine delivery (e.g., reduced cold chain requirements) for Gavi markets, which in turn contributed to reducing mortality and morbidity				

		Evaluation process							Findings		Conclusions				
Causal pathway															
From	**To**	**Assumption to be tested**	**Key eval. questions**	**Evidence** ***(What did we look at?)***	**Key indicators:** ***(What did we look for?)***	**Data sources triangulated**	**Did the evaluator conduct the evaluation as planned?**	**Did the objective change?**	**Did the objective achieve what was intended?**	**Robustness of findings rationale for sub-Objective**	**Did the assumption of the pathway hold? (Held, Partially held, Did not hold) OR To what degree did the impact pathway operate as assumed?**	**What are the implications if the assumption did not hold?**	**Are there other assumptions that are key to performance that came to light during the evaluation?**	**Unintended and unexpected findings at level of pilot sub-Objective**	**Implications of the context for lesson learning**
Pathway 2															
1, 2	5,8	That the long-term supply agreements and TPPs were necessary and contributed to confidence amongst manufacturers in the LMIC PCV market, and thus investment in increased manufacturing capacity for PCV (e.g., manufacturer confidence in the PCV market did not stem from factors outside the AMC)	2a, 2b, 3a, 3b	· PCV AMC funding allocated to manufacturers · Manufacturer investment in PCV production capacity	· Interview findings that state that investment in production capacity by manufacturers was influenced by the PCV AMC, both directly (incentives) and indirectly (market creation) · Annual contracted PCV supply for Gavi, 2010-2029 (doses in millions)	Between manufacturers, triangulating 1) investments in PCV capacity, and 2) other drivers of investment in supply capacity outside the PCV AMC	Yes	No	Yes	1 - high level of consistency between interviews	Partially held - The PCV AMC pilot was very successful at scaling up PCV supply in Gavi-73 markets through LTAs and TPP that helped give confidence to manufacturers that demand for PCV would materialize in Gavi markets. However, Pfizer and GSK had plans to expand into LMIC markets that predate the PCV AMC pilot, and likely would have gone through with these plans in the absence of an AMC for PCV. The PCV AMC pilot, then, helped	The PCV AMC pilot was an intervention that operated in a multi-variable / high context environment, making it difficult to isolate the effect of the pilot on Manufacturers' capacity expansion decision-making	Manufacturer investment decisions were also influenced by the long design phase of the PCV AMC pilot, as well as accompanying policy guidance, NVI support, advocacy, and forecasting support that was part of the wider push for PCV adoption pre-PCV AMC pilot. The public signaling value of the PCV AMC mechanism also turned out to be as important as the LTAs in terms of inspiring manufacturer confidence in	Yes - see left (assumption only partially held)	Particularly for large MNCs, an AMC mechanism in isolation may not be enough to influence decision-making around LMIC market entry and capacity expansion, although it can further de-risk the decision for MNCs by helping secure future demand

											to 'solidify' the market, but scale-up would have likely happened without an AMC.		the Gavi-73 PCV market.		
8	10,15	That investments in manufacturing of fill and finish capacity for PCV brought forward an increased annual number of doses supplied to Gavi markets through UNICEF, giving Gavi-eligible countries greater availability of effective PCVs (e.g., that the increase in doses produced did not supply non-Gavi markets)	2a, 2b, 3a, 3b, 4a	· Annual contracted PCV supply with manufacturers · Annual shipped PCV supply by product · UNICEF rankings on security of supply	· Doses procured vs shipped, whole market and by product 2010-2020 (doses in millions) · Availability of PCV relative to other vaccines, 2010-2020 (UNICEF ratings)	1. Interviews with manufacturers and experts 2. Review of investments in capacity made my MNCs	Yes	No	Yes	1 - high level of consistency between interviews	Mostly held - The PCV AMC pilot helped drive investments in capacity from MNCs (although not fully driven by the PCV AMC pilot), which contributed to rapid scaleup in supply over the course of the pilot, from ~30 million doses per year in 2010 to ~150 million doses per year from 2017 to present. There were some supply shortages in early years, but it is impossible to know whether these were exclusively manufacturing shortages, or prioritization of other markets on the part of the manufacturer	N/A	The AMC drove greater, but not total, security of supply. Total security of supply may only be available with 'hard' contracts, not the Gavi/UNICEF forecasting approach deployed under the AMC	N/A	Even with a long AMC-design phase (during which manufacturers invested in production capacity) there is only so fast they can ramp up (as is being seen today with Covid-19)

15	19	That the increased availability of effective PCVs in Gavi-eligible countries led to increased coverage, and so ultimately to reductions in morbidity and mortality (e.g., that the PCVs were rolled out effectively, and the products themselves were effective)	1a, 1b, 2a, 2b	· UNICEF shipping data · Coverage data by country · Gavi impact models (e.g., LiST and UNIVAC)	· Coverage rates, 2010-2020, relative to other vaccines (%) · Lives saved and DALYs averted from PCV (millions), relative to what would have been realized with the coverage rates of other vaccines (see methodology and key exhibits)	1. Interviews with manufacturers and experts 2. Gavi-73 cohort-level estimates of reduction of mortality and morbidity (VIMC modeling)	Yes	No	Yes	1 - high level of consistency between interviews	Held - The PCV AMC pilot will have contributed greatly to reducing mortality and morbidity by 2030. While SII's PCV10 only came to market in 2020, and therefore had minimal impact on reducing mortality and morbidity from PCV during the timeframe of the PCV AMC pilot, it should reduce mortality and morbidity out to 2030 Furthermore, multiple experts indicated that the MDV presentations developed by GSK and Pfizer were crucial to scaling up production and simplifying logistics of vaccine delivery (e.g., reduced cold chain requirements) for Gavi markets, which in turn contributed to reducing mortality and morbidity	N/A	No	N/A	N/A

		Evaluation process							Findings		Conclusions				
Causal pathway		**Assumption to be tested**	**Key eval. questions**	**Evidence** *(What did we look at?)*	**Key indicators:** *(What did we look for?)*	**Data sources triangulated**	**Did the evaluator conduct the evaluation as planned?**	**Did the objective change?**	**Did the objective achieve what was intended?**	**Robustness of findings rationale for sub-Objective**	**Did the assumption of the pathway hold? (Held, Partially held, Did not hold) OR To what degree did the impact pathway operate as assumed?**	**What are the implications if the assumption did not hold?**	**Are there other assumptions that are key to performance that came to light during the evaluation?**	**Unintended and unexpected findings at level of pilot sub-Objective**	**Implications of the context for lesson learning**
From	**To**														
Pathway 3															
2	6,11,16	That aspects of the long-term supply agreements (e.g., tail prices and subsidies) were necessary and did contribute to decreasing and stabilizing PCV pricing for PT/AT/FSF countries, which then drove demand and accelerated PCV introduction/rollout (e.g., demand and rollout were not exclusively driven by external factors such as WHO guidance)	2a, 2b, 4a, 4b	· Manufacturer tail prices · PCV submissions/ approvals/ introductions by Gavi country · Counterfactual data from Hib, rota, and HPV (e.g. introduction dates and roll out progress)	· Annual announced tail price by manufacturer, 2010-2020 (USD) · Status of PCV applications by Gavi country, 2007-2020 (number of countries) · Vaccine country introduction by Gavi country, 1993-2020 (number of countries)	Triangulation between countries as to 1) the core drivers of NVI – what role does price/price stability play, and 2) the relative influence of the other factors	Yes	No	Partially - the PCV AMC pilot drove vaccine uptake, but predictable vaccine pricing was likely not the main enabler of this uptake	2 - most interviews and data sources aligned, but there was some variability	Partially held - The PCV AMC pilot was successful at accelerating vaccine uptake, but in-country decision makers did not report the AMC mechanism itself as a major driver of uptake. Most in-country stakeholders pointed to epidemiological evidence as the main driver of PCV introduction. Many stakeholders did list the low, stable price of PCV as a factor, but not the main factor in decision-making. Some stakeholders commented that for many	Possible implications: - Gavi's current co-financing policy make countries 'price inelastic', especially in cases where countries are not aware of the increasing financial obligations as the transition towards FSF. - This ToC assumed countries make decisions in a relatively technocratic and informed way e.g. being aware of the AMC and understanding the tail price for PCV is more stable than for e.g., rota - this is not the case	Country decision making is more organic and less well understood than Gavi assumed at the start of the AMC - a more realistic theoretical framework underpinning country decision making may support better predictability of demand and uptake in future	Yes - see left (assumption only partially held)	As left, country decision-making may be more complex and 'reactionary' then previously thought. Under Gavi's current co-financing policy, PT countries are incentivized to introduce vaccines through low co-financing commitments, but may not always be aware of increasing commitments over time, or may initially lack the operational capacity to manage co-financing (e.g., budget allocation)

											PT countries, price was not a strong consideration given the low co-financing obligation at the time of introduction.					
16	19	That the increased uptake of effective PCVs in Gavi-eligible countries led to increased coverage, and so ultimately to reductions in morbidity and mortality (e.g., that the PCVs were rolled out effectively, and the products themselves were effective)	1a, 1b, 2a, 2b, 4a, 4b, 4c	· UNICEF shipping data · WUENIC Coverage data by country · Gavi impact models (e.g., LiST and UNIVAC)	· Coverage rates, 2010-2020, relative to other vaccines (%) · Lives saved and DALYs averted from PCV (millions), relative to what would have been realized with the coverage rates of other vaccines (see methodology and key exhibits)	Quantitative modeling of country introductions and coverage to understand reductions in mortality and morbidity from supply	Yes	No	Yes - the PCV AMC pilot led to rapid uptake in Gavi-73 countries, with 60 of the 73 cohort countries introducing PCV by the end of the pilot period	2 - most interviews and data sources aligned, but there was some variability	Held - The PCV AMC pilot contributed to reduced morbidity and mortality though increased PCV coverage. Multiple experts indicated that the MDV presentations developed by GSK and Pfizer were crucial to scaling up production and simplifying logistics of vaccine delivery (e.g., reduced cold chain requirements) for Gavi markets, which facilitated uptake, and in turn contributed to reducing mortality and morbidity	N/A	No	N/A	N/A

		Evaluation process							Findings		Conclusions				
Causal pathway															
From	To	Assumption to be tested	Key eval. questions	Evidence *(What did we look at?)*	Key indicators: *(What did we look for?)*	Data sources triangulated	Did the evaluator conduct the evaluation as planned?	Did the objective change?	Did the objective achieve what was intended?	Robustness of findings rationale for sub-Objective	Did the assumption of the pathway hold? (Held, Partially held, Did not hold) OR To what degree did the impact pathway operate as assumed?	What are the implications if the assumption did not hold?	Are there other assumptions that are key to performance that came to light during the evaluation?	Unintended and unexpected findings at level of pilot sub-Objective	Implications of the context for lesson learning
Pathway 4															
3	12,17	That non-PCV AMC factors (e.g., WHO guidance, Gavi support and others) did contribute, but were not sufficient, to drive uptake of PCV without the low stable price achieved through the AMC[1]	2a, 2b, 3b, 4a, 4b, 4c, 4d, 4e, 5, 9a	· Interviews with EPI managers, donors and SCMs for selected countries to understand the drivers of PCV introduction · Desk review of policy documents, and/or Gavi application documents to understand the drivers of PCV introduction	· Interview findings that indicate the level of balance between Pathways 2, 3 and 4 (e.g., estimates of the weight of non-AMC factors in driving uptake) · Policy guidance and regulation for PCV by country government, WHO, and Gavi 2010-2020 (number and nature interventions)	Triangulation between the selected case study countries to understand, 1) whether the AMC did drive acceleration, and 2) what other factors were also contributing to PCV rollout. The coherence, or lack of, of these factors within types of countries (co-financing statuses) and across all the case study countries will determine the generalizability of the findings from the case studies.	Yes	No	NA - this ToC pathway was inserted by the evaluators to test the different drivers of country level uptake, so does not formally link to an overarching objective	2 - most interviews and data sources aligned, but there was some variability	Partially held - Countries did prioritize PCV when offered through Gavi, regardless of the AMC-specific factors, such as the LTAs under Pathway 3. The causal chain in the pathway was more linked with the high disease burden of PCV in country, rather than donor prioritization (as stated in the ToC), though the high disease burden was one driver	The drivers of uptake at country level are complicated and vary by country. Countries are often not aware of the specifics of financing arrangements e.g. the presence of absence of an AMC, so the effects of the instrument are 'filtered' through increased emphasis from donors, in-country advisors etc.	Country decision making is more organic and less well understood than Gavi assumed at the start of the AMC - a more realistic theoretical framework underpinning country decision making may support better predictability of demand and uptake in future	Yes - see Pathway 3	PCV was a high priority disease for Gavi73 countries - Gavi should not propose an AMC for non-priority vaccines

											of donor interest.				
17	19	That the increased prioritization of PCV within Gavi-73 country immunization programs and donor support programs does, or will, contribute to the reduced morbidity and mortality of pneumococcal disease	1b, 2a, 2b, 4a, 4b, 4c, 4d, 4e, 9a	· UNICEF shipping data · WUENIC Coverage data by country · Gavi impact models (e.g., LiST and UNIVAC)	· Coverage rates, 2010-2020, relative to other vaccines (%) · Lives saved and DALYs averted from PCV (millions), relative to what would have been realized with the coverage rates of other vaccines (see methodology and key exhibits)	Triangulation between the selected case study countries to understand, 1) whether the AMC did drive acceleration, and 2) what other factors were also contributing to PCV rollout.	Yes	No	NA - this ToC pathway was inserted by the evaluators to test the different drivers of country level uptake, so does not formally link to an overarching objective	2 - most interviews and data sources aligned, but there was some variability	Held - Increased prioritization of PCV in Gavi-73 countries led to increased uptake, which in turn led to reductions of morbidity and mortality.	N/A	No	N/A	N/A

		Evaluation process							Findings		Conclusions				
Causal pathway															
From	To	Assumption to be tested	Key eval. questions	Evidence *(What did we look at?)*	Key indicators: *(What did we look for?)*	Data sources triangulated	Did the evaluator conduct the evaluation as planned?	Did the objective change?	Did the objective achieve what was intended?	Robustness of findings rationale for sub-Objective	Did the assumption of the pathway hold? (Held, Partially held, Did not hold) OR To what degree did the impact pathway operate as assumed?	What are the implications if the assumption did not hold?	Are there other assumptions that are key to performance that came to light during the evaluation?	Unintended and unexpected findings at level of pilot sub-Objective	Implications of the context for lesson learning
Pathway 5															
4	13	That the M&E program's monitoring and evaluations of the PCV AMC pilot help develop a better understanding amongst relevant stakeholders of the outcomes, impact, and lessons learned of the PCV AMC pilot (e.g., that the evaluations are insightful, and are read and discussed by the relevant people)	5, 6, 7, 8, 9a, 11	· Desk review of previous M&E data (e.g., review of previous evaluation lessons learned) · Interviews with stakeholders who were involved in the PCV AMC pilot and then in subsequent market shaping initiatives	· Evidence based modifications in the design and implementation of AMC or uptake of lessons learned in the PCV AMC or other similar mechanisms · Proof of concept, by achievement of each objective (quotes from interviewees)	1. interviews with expert stakeholder, both internal to Gavi, and external 2. Review of past evaluations of the PCV AMC pilot and M&E framework	Yes	No	Yes	2 - most interviews and data sources aligned, but there was some variability	Held - The PCV AMC pilot has yielded important learnings on how an AMC mechanism functions, its possible use cases, and areas of adjustment or improvement in design for future iterations.	N/A	No	N/A	While important lessons have been learned through the PCV AMC pilot's evaluation and M&E processes, it is difficult to isolate the causal links between the AMC mechanism and results of the pilot

13	18	That it is possible to prove (or disprove) the concept of the PCV AMC and that its core mechanisms (supply acceleration, demand creation, etc.) are not exclusive to PCV and can work across vaccines so that these learnings can feed into other possible future AMCs[1]	5, 6, 7, 8, 9a, 9b, 10, 11	· Interviews with Gavi Secretariat and donor representatives that are involved in other relevant financing mechanisms · Desk review of the lessons learned from the AMC in annual reports and strategy documents	· Evidence or lack of evidence that the documented lessons learned over the course of the PCV AMC has impacted other similar mechanisms (quotes from desk research and interviews)	1. interviews with expert stakeholder, both internal to Gavi, and external 2. Review of data on evolution of supply, PCV demand, and PCV introduction over the course of the PCV AMC pilot	Yes	No	Partially - it seems likely that the AMC mechanism will work in other contexts. However, it is important to keep in mind the multi-variable context of any global health market shaping activity. This complex context makes isolating the direct effects of the AMC mechanism from antigen selection impossible. Furthermore, the Gavi-specific use cases will be different again (see main report) because of Gavi's position on country-led decision making and demand shaping	2 - most interviews and data sources aligned, but there was some variability	Partially held - Proving causality of the AMC mechanism itself is difficult given the simultaneous interventions and influences that were present alongside the PCV AMC pilot	Possibilities: - An AMC either has a limited set of use cases, or the potential objective and results of an AMC must be adjusted given the antigen context (e.g., PCV which had products on the market vs. malaria which does not have a vaccine that has been developed yet)	No	Yes - see left (assumption only partially held)	While important lessons have been learned through the PCV AMC pilot's evaluation and M&E processes, it is difficult to isolate the causal links between the AMC mechanism and results of the pilot

Annex 8: Counterfactuals

Approaches to the counterfactual

To rigorously evaluate the outcomes and impacts catalyzed by the PCV AMC pilot, we needed to understand what would have likely happened if the PCV AMC pilot had not existed. Being a real-world scenario, the ideal 'control group' – identical to the 'treatment group' in every way apart from the PCV AMC pilot – does not exist. As per the Proposal and Inception Report, we considered a variety of approaches to counterfactual analysis,[153] shortlisting two:

- By looking at antigens beyond PCV supported by Gavi,
- By looking at countries outside of Gavi support

Antigen-based counterfactual

Both shortlisted approaches have strengths and weaknesses. We primarily proposed to use an antigen-based counterfactual, comparing uptake of PCV relative to other vaccines (e.g., Hib, rota, HPV), that are available with Gavi support under normal co-financing arrangements.

These antigens are different to PCV in several ways.[154,155,156,157,158] In effect, there is selection bias in the control group. However, this approach to the counterfactual does partially control for numerous important variables, including the various national contexts, economic growth stages and rates, levels of donor support, and health system strengths.[159]

We mimicked Hib, rota, and HPV coverage data using the VIMC's 'Impact Extrapolation/Impact Ratio' approach. In effect, this ratio is an elasticity factor: change in deaths or DALYs avoided given change in coverage. This is the method the VIMC use to update the UNIVAC and LiST models when coverage data changes, in between re-runs of the full models.[160] To provide more detail, we:

- Compiled Hib, rota, and HPV coverage data for PCV AMC pilot eligible countries from 2000-2020.
- Based this all in the year 2010 (e.g., Year 1 for the PCV AMC is equivalent to Year 1 of Gavi support for Hib, rota or HPV.
- Multiply these country-year-coverage matrices through by the VIMC Impact Ratios to update the estimates of lives saved and DALYs averted by year and country if the coverage data had been different.

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[153] For example, one could consider the AMC under Covax/Cov-ACT, or similar market shaping tools like price-volume guarantees.
[154] The disease burden is different across the Gavi cohort, as well as the variance in disease burden between Gavi countries.
[155] The healthcare dimensions of the vaccines may be different: schedule, number of doses, cold chain requirements etc.
[156] Market factors may be different in terms of cost of production, number of suppliers, interchangeability/ease of switch, etc. The market dynamics outside of Gavi countries can also vary (e.g., HPV has seen high demand from China, which has constrained supply for the Gavi market).
[157] The relative multilateral and donor prioritization may – a driver of NVI - may vary.
[158] Time – Gavi and partners are learning organizations, and so it is assumed that NVIs and market shaping considerations improve over time. As such, there should be more coordination, better aligned supply and demand, and smoother introduction – all other things being equal – for more recent Gavi-supported vaccines.
[159] As described in the Section IV (ToC), these variables are thought be most closely linked to the mechanisms of interest at country level (price sensitivity, country level perception of security of supply, and Gavi 'push').
[160] The Impact Extrapolation approach is primarily a linear interpolation of current vaccine impact estimates with new coverage estimates assuming constant country and delivery strategy specific rates of mortality and morbidity averted per dose of vaccine. VIMC note "Overall, in our examples, we have shown that the IE works well and is an effective tool to update vaccine impacts. Notably, the activity stratification is accurate for static models with dose dependency but may overestimate the impact of coverage improvements when dynamic herd protection comes into play." Both the LiST and UNIVAC models are static models. See https://www.medrxiv.org/content/10.1101/2021.01.08.21249378v1 for further information.

This approach has many strengths. Using the LiST and UNIVAC PCV models controls for everything except for NVI/coverage (e.g., the approach would use the standard LiST/UNIVAC vaccine efficacy variables, the standard prevalence data per country and so on). The introduction/coverage would be the only variable that changes. A further positive is that it is a transparent comparator: there are no assumptions hidden in complex methods.

However, this approach does have downsides. For some antigens there will be limited years' worth of data to compare: HPV only received Gavi support in 2013 so there will only be 7 years of relevant comparator data. Secondly, the Impact Extrapolation approach is linear, so better suited to small changes in coverage data (e.g., 68-72%), rather than bigger changes like no introduction-introduction. This downside is mitigated somewhat by the models being both static for PCV. Thirdly, the counterfactual does not fully control for the factors like disease burden (e.g., countries may have chosen to introduce rota later than PCV because their burden of disease was lower). A further weakness is that it does not distinguish between the PCV AMC pilot vs the wider PCV program. This is extremely difficult to disentangle.

Country-based counterfactual

We proposed to not use the other shortlisted counterfactual – looking at countries outside of Gavi support. This approach was used in the Boston Consulting Group (BCG) evaluation, but we feel that the discontinuity is too high between the Gavi-73 countries, and wealthier countries (BCG called them the 'Threshold 50'), so as to limit our confidence in the potential insight this would yield. These middle-income countries, which are included in the VIMC's list of 112 countries, do pay more for PCV than the Gavi73, so this would be a way to understand the impact of prices on PCV uptake, but these countries are very different in terms of health system strength, government and donor health spending and other variables. In short, if the evaluation showed data saying that uptake of PCV was faster or slower in a group containing China, Peru, and Morocco, we feel it would be too easy to argue away the comparator.

Annex 9: Strength of Conclusions Rationale

The strength of conclusion revealed through the evaluation are determined using the rating system below:

Rating	Assessment of the findings by strength of evidence
Strong (1)	• The finding is supported by data and/or documentation which is categorized as being of good quality by the evaluators; and • The finding is supported by the majority of consultations, with relevant consultee base for specific issues at hand
Good (2)	• The finding is supported by majority of the data and/or documentation with a mix of good and poor quality; and/or • The finding is supported by the majority of the consultation responses
Limited (3)	• The finding is supported by some data and/or documentation which is categorized as being of poor quality; or • The finding is supported by some consultations as well as a few sources being used for comparison (i.e., documentation)
Poor (4)	• The finding is supported by various data and/or documents of poor quality; or • The finding is supported by some/few reports only and not by any of the data and/or documents being used for comparison; or • The finding is supported only by a few consultations or contradictory consultations

Annex 10: Interview List

Stakeholder Group	Name	Job Title	Organization
Gavi Secretariat	Anthony Brown	Senior Legal Counsel	Gavi Secretariat
	Edward Baker	Senior Manager, Strategy Development & Tenders	Gavi Secretariat
	Eric Godfrey	Senior Manager, Financial Forecasting & AMC	Gavi Secretariat
	Hamidreza Setayesh	Former SCM, Pakistan, and SCM, Nigeria	Gavi Secretariat
	Hope Johnson	Director, Monitoring & Evaluation	Gavi Secretariat
	Marie-Ange Saraka-Yao	Managing Director, Resource Mobilisation, Private Sector Partnerships and Innovative Finance	Gavi Secretariat
	Markus Beck	Senior Manager, Strategy Development & Tenders	Gavi Secretariat
	Matthew Blakley	Senior Manager	Gavi Secretariat
	Samuel Muller	SCM, Indonesia	Gavi Secretariat
	Sebastian Meaney	Head, UK Strategy	Gavi Secretariat
	Tanguy Flahault	Manager, Innovative Finance	Gavi Secretariat
	Veronica Denti	Senior Programme Manager, Vaccine Programmes	Gavi Secretariat
	Todi Mengistu	Senior Programme Officer, Monitoring and Evaluation	Gavi Secretariat
	Alexa Reynolds	SCM, Pakistan	Gavi Secretariat
	Dan Hogan	Head, Measurement and Strategic Information	Gavi Secretariat
	Danielle Rosset	Programme Officer, EMRO, PAHO and EURO Countries	Gavi Secretariat
	Komi Ahawo	SCM, Cameroon	Gavi Secretariat
	Homero Hernandez	Former SCM, Bolivia	Gavi Secretariat

	Maria-Jose Meza-Cuadra	Country Engagement Manager, Latin America and the Caribbean	Gavi Secretariat
	Nilgun Aydogan	SCM, Bangladesh	Gavi Secretariat
	Mihaela Minca	Programme Manager (formerly Programme Officer, Asia Pacific)	Gavi Secretariat
	Mario Jimenez	Programme Officer – Pakistan, Country Programmes	Gavi Secretariat
	Marguerite Cornu	Programme Manager, Country Support	Gavi Secretariat
	Alain McLaren	Senior Analyst, Immunisation Financing and Sustainability	Gavi Secretariat
Former Gavi Secretariat	Minzi Lam Meier	Former Head Financial Forecasting, Systems and AMC Finance	MM Global Health Consultants GmbH
Donors	Sophie Bracken	Vaccines Policy Adviser	FCDO
	Elizabeth Williams	ODA Programme Manager	FCDO
	Susan Elden	Senior Health Adviser, Global Funds Department	FCDO
	Francesca Manno	Director in the International Affairs Department, Ministero dell'Economia e delle Finanze	Government of Italy
	Gianmarco Cocozza	Associate Officer, Ministero dell'Economia e delle Finanze	Government of Italy
	Vittorio Sebastiani	Treasury Department Official, Ministero dell'Economia e delle Finanze	Government of Italy
	Andreas Karlberg Pettersen	Senior Advisor, Department of quality assurance and aid management section	NORAD
	Anja Sletten	Senior Advisor, Department of Education/Global Health	NORAD
	Lene Jeanette Lothe	Assistant Director, Department of Education/Global Health	NORAD

	Eduard Salakhov	Health Attaché, Counselor	Permanent Mission of the Russian Federation to the United Nations Office in Geneva
	Greg Widmyer	Director, Health Products, Programs, and Markets	Bill and Melinda Gates Foundation
	Nicolas Theopold	Senior Program Officer	Bill and Melinda Gates Foundation
	Danielle Hoegy	Senior International Development Officer	Global Affairs Canada
	Gillian Harris	International Development Officer	Global Affairs Canada
	Megan Cain	Director for the Global Health and Nutrition Platforms Division of the Health and Nutrition Bureau	Global Affairs Canada
	Tammy Bunbury	Deputy Director, Health and Nutrition Strategy and Partnerships Division	Global Affairs Canada
Manufacturers	Hyokyung Kim	Vice President	SK Chemicals
	An Vermeersch	Head of R&D Vaccines Global Health Department	GSK
	Ariane McCabe	Director of Global Health and Public Affairs	GSK
	Susan King	Director Public Market Development	GSK
	Aurore Maddison	Global Health Access Strategy Director	GSK
	Brad Thompson	Executive Director, Global Vaccines Marketing	Merck
	Diana Acosta	Director, Public Health Partnerships	Merck
	Hillary Mclaughlin	Associate Director, Quality	Merck

	Joan O. Benson	Executive Director, Public Health Partnerships, Global Vaccines Policy & Partnerships	Merck
	Harshet Jain	Head of BD for biologicals	Panacea Biotech
	Alvin Liu	Senior Director Vaccines Partnerships and Alliances	Pfizer
	Parag Deshmukh	Additional Director Global Strategic International Business Development	SII
	Suresh Jadhav	Executive Director	SII
	Rachel Park	Senior Business Development Manager	EU Biologics
In-country stakeholders	Yusuf Yusufari	Senior Program Officer, Vaccine Delivery, Nigeria	BMGF
	Soledad Urrutia	Specialist, Health Systems Development,	PAHO
	Cuauhtémoc Ruiz	Unit Chief, Comprehensive Family Immunization	PAHO
	Rosario Quiroga	Health Official	UNICEF Bolivia
	Naeem Asghar	formerly Deputy Director of Expanded Program for Immunization, Pakistan	WHO
	Rajendra Bohara	Immunization and Vaccine Development Team Leader, Bangladesh	WHO
	Jucy Merina Adhikari	Health Specialist (immunization), Bangladesh	UNICEF
	Balwinder Singh Chawla	Medical Officer, Immunization System Strengthening, Bangladesh	WHO
	Selina Ahmed	National Vaccine Safety and Policy	WHO
UNICEF	Abraham Kofi Ntow	Contracts Specialist	UNICEF
	David Mutuerandu	Procurement Manager	UNICEF
Modelers	Emily Carter	Assistant Scientist	JHU

	Yvonne Tam	Senior Research Associate	JHU
	Katy Gaythorpe	Research Lead of the Vaccine Impact Modelling Consortium	VIMC
	Andy Clark	Associate Professor	LSHTM
Civil Society	Rachel Silverman	Policy Fellow	CGD

Annex 11: OECD DAC definitions[161]

Topic	Definition (DAC)
Finding	A finding uses evidence from one or more evaluations to allow for a factual statement.
Conclusions	Conclusions point out the factors of success and failure of the evaluated intervention, with special attention paid to the intended and unintended results and impacts, and more generally to any other strength or weakness. A conclusion draws on data collection and analyses undertaken, through a transparent chain of arguments.
Lessons Learned	Generalizations based on evaluation experiences with projects, programs, or policies that abstract from the specific circumstances to broader situations. Frequently, lessons highlight strengths or weaknesses in preparation, design, and implementation that affect performance, outcome, and impact.
Recommendation	Proposals aimed at enhancing the effectiveness, quality, or efficiency of a development intervention; at redesigning the objectives; and/or at the reallocation of resources. Recommendations should be linked to conclusions.
Efficiency	A measure of how economically resources/inputs (funds, expertise, time, etc.) are converted to results.
Effectiveness	The extent to which the development intervention's objectives were achieved, or are expected to be achieved, taking into account their relative importance.

[161] OEDC, Glossary of Key Terms in Evaluation and Results Based Management

Annex 12: WUENIC 2020 data

The WUENIC database was updated with 2020 data after the draft report was published in July 2021. Dalberg re-ran the analysis for lives saved and DALYs averted using the new WUENIC data (Figures 21 and 22). This, in effect, converted the 2020 datapoint from a projected coverage estimate to an actual coverage estimate. The impact was not material given other sources of uncertainty in the modelled estimates. The table below shows a comparison between the 2019 and 2020 data.

Table 2: Comparison between 2019 and 2020 WUENIC data

Model/ touchpoint	Estimated cumulative lives saved in 2020		Difference
	2019 WUENIC data	2020 WUENIC data	
LiST - 2017	751,863.8	761,385.3	1.27 %
LiST - 2019	915,959.9	930,765.4	1.62 %
UNIVAC - 2017	514,096.4	518,743.8	0.90 %
UNIVAC - 2019	598,667.0	603,811.5	0.86 %

As a result, the vast majority of the findings and exhibits in the main report have not been changed from those reviewed by the Gavi Secretariat and expert committees involved in this evaluation. Figure 23 is the only one that has been updated in this final report – showing that PCV coverage hit 50% for the total Gavi-73 cohort in 2020, up from 49% in 2019.