March 2016

State of PCV Use and Impact Evaluations

A strategic gap analysis of the global evidence from published and ongoing impact studies evaluating routine PCV use.

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Executive Summary

SCOPE OF ANALYSIS: This report describes the state of pneumococcal conjugate vaccine (PCV) use and the availability of PCV impact evidence (as of March 10, 2016) in countries routinely using PCV10 or PCV13 and/or evaluating PCV's economic impact (projected or actual). Specifically, this report describes the ***amount of evidence*** that is published or actively being collected/analyzed on PCV10 and PCV13 impact and identifies key gaps. The analysis of the technical findings from these studies is ongoing and will help inform countries, donors, and key global and regional partners about areas of uncertainty, risk, and emerging technical or programmatic issues.

ANALYSIS FINDINGS:

OVERALL: As of March 2016, 135 countries have introduced PCV in their routine immunization program; 54 (40%) of which have a published or ongoing impact study, with at least one country in every WHO region conducting a PCV impact evaluation. In addition, 4 countries that are not yet using PCV in their national immunization program (NIP) are measuring the potential economic impact of the vaccine. In total, therefore, 58 countries are undertaking clinical or economic impact studies of PCV.

PRODUCT: Of the 135 countries that have introduced PCV, 69% (93 countries) are using PCV13, 22% (30 countries) are using PCV10, and 8% (11 countries: Austria, Canada, Colombia, Estonia, Germany, Korea, Philippines, Slovakia, Slovenia, Spain, and Sweden) are using both PCV10 and PCV13 in their NIP. A similar pattern of use is seen in Gavi countries, where 76% (41 countries) are using PCV13 and 24% (13 countries) are using PCV10. Globally, the number and proportion of countries using PCV and evaluating its impact are 31 (33%) among PCV13-using countries, 15 (50%) among PCV10-using countries, and 8 (73%) among countries using both products.

SCHEDULE: Most (n=108, 80%) of the 135 countries that have introduced PCV are using a 3-dose schedule; 37% (50 countries) are using a 2+1 schedule and 43% (58 countries) are using a 3+0 schedule. Only 19% (25 countries) are using a 3+1 schedule and 1% (1 country - Canada) is using both a 2+1 and 3+1 schedule. All Gavi countries are using a 3+0 schedule, except for Nepal, Moldova, and Georgia, who are using 2+1 schedules. Countries using a 3+0 schedule are less likely to have a PCV impact evaluation 16/58, 28%), than are countries with a 2+1 or 3+1 schedule (26/51, 51% and 13/26, 50%, respectively); this reflects also the lower proportion of PCV-using Gavi countries with impact evaluations than non-Gavi countries (16/54, 30% compared with 38/81, 47%)

OUTCOME: IPD (38/58 countries, 68%) and pneumonia (34/58 countries, 59%) are the most commonly measured disease outcomes in countries with PCV impact studies. Nasopharyngeal (NP) carriage is also being monitored in many studies (27/58 countries, 47%). Impact on mortality and economic outcomes are measured least by countries with PCV impact evaluation.

Introduction: PCV Impact Studies

Monitoring the health and economic impact of a vaccine in a routine use program is considered a core element of vaccine program management and disease control monitoring. Pneumococcal conjugate vaccine (PCV) impact studies are essential for understanding the effects of the global use of PCV over the past 15 years (and past 5 years in Gavi countries), particularly because the rapid pace of PCV introduction and progress toward universal vaccine coverage has surpassed that of any other vaccine, with the exception of the regional use of MenAfriVac. With this massive population-level change in immunity, it is important to monitor changes in the epidemiology of disease post-introduction, especially because the currently licensed PCV products target some, but not all, serotypes of the *Streptococcus pneumoniae* organism – leaving questions about the possibility of an increase in disease caused by serotypes not included in the vaccine and overall serotype distribution in the years following vaccine introduction.

PCV impact studies provide the ***evidence*** that will inform program optimization and drive the strategy on new and modified pneumococcal vaccines, treatment regimens, and other pneumococcal disease control strategies. These results can also influence policies in countries that have not yet made a decision on introduction, and in countries that will soon move toward self-financing (i.e., graduate from Gavi support). However, the capacity to undertake vaccine impact monitoring is absent in many countries and insufficient to monitor impact in others, leaving gaps in vaccine impact evidence.

This report aims to describe and evaluate the ***availability*** of evidence on PCV10 and PCV13 impact by reporting the number of impact studies per country and key information on PCV products, schedules, and outcomes assessed in the evaluations. Our analyses were performed using data contained within the VIEW-hub database, from which select impact study data are made available on the online VIEW-hub interactive data visualization platform, accessible at www.VIEW-hub.org. We begin this report by providing background information about global PCV introductions to date and products and schedules in current use. Then, we present information on published and ongoing PCV impact studies by region, product, dosing schedule, and outcome measured.

Methods

The methods for compiling the data included in this analysis are described in **Table 1**.

Table 1: Inclusion and exclusion criteria for PCV impact studies described in this report, by product and income group

	High-income countries	Low- and middle-income countries
PCV10 or PCV13	**Included**: Impact studies from HICs with routine PCV use • Published: extensive search (2009-3/10/2016) • Unpublished: o Opportunistically identified and included o Published PCV7 surveillance that extends to the PCV10/13 use period	**Included**: Impact studies from LMICs with routine PCV use • Published: extensive search (2009-3/10/2016) • Unpublished: systematically identified through* o Gavi-funded studies list o BMGF-funded studies list o CDC collaborations list o GREEN (Latin America Collaboration) o Communications with other partners
	Excluded: Research studies outside context of routine use	**Excluded**: Research studies outside context of routine use
PCV7 or unlicensed products	**Excluded all PCV7-only information from this impact gap analysis** • PCV7 information was systematically abstracted for the Dosing Landscape Project (papers published between 1990-2010† for IPD, pneumonia, NP, mortality, indirect effects). These are available, as needed, for any strategic questions/issues. **Included PCV7 impact studies only if the study also evaluated PCV10 or PCV13**	

Published and ongoing PCV impact studies were included in the VIEW-hub database (and thus in this analysis) if they met one of the following inclusion criteria:

- Country where the study has taken place must be using PCV in its national immunization program (NIP), either nationally or sub-nationally
- Study is evaluating the economic impact of PCV (regardless of the country's introduction status). This includes predictive/modeled economic studies published prior to vaccine introduction, as well as empirical economic studies conducted post-PCV introduction into routine immunization programs.

Ongoing studies designed to measure PCV impact in settings where the vaccine has not yet been introduced into the NIP were excluded from this report (with the exception of economic impact studies, as previously described). However, these studies will be included in future reports once the vaccine has been officially introduced. Such studies collecting pre-intro data that we are aware of include Mongolia and Viet Nam.

Although WHO-coordinated invasive bacterial disease (IBD) surveillance is performed in many countries that have introduced PCV, these data are not necessarily being used to assess impact of PCV. We briefly describe the available WHO surveillance data that could be used to monitor impact; however, these data were only included in our analyses if they

*Ongoing studies in EMR, SEAR, and AFR were included to a high a degree of certainty. Ongoing studies in the PAHO region are included, but verification of the data from these studies is ongoing through collaboration between the PCV Technical Coordination Project and the study teams in the region.

† Systematic review conducted by IVAC/CDC for Dosing Landscape Project (2010) was leveraged.

were published in the peer-reviewed literature or are part of an ongoing study specifically designed to evaluate PCV impact.

Terms and Definitions

Analysis

In IVAC's VIEW-hub impact study database (with select data viewable at www.VIEW-hub.org), each impact study publication or ongoing (unpublished) impact evaluation was considered an ***analysis***. For ongoing impact assessments, each *analysis* is bound by the same protocol (in terms of study design, data source, and set of outcomes evaluated), within a defined geographic setting (country).

Study

Since a single study may result in multiple analyses that are presented in separate publications, we needed a method to avoid double or triple counting studies. We grouped analyses into study families, which we will henceforth refer to simply as ***studies***. In order to determine which study an analysis belongs to (whether it belongs to an existing study or if it represents a new/unique study), we carefully considered their relatedness in terms of study subjects (namely cases). We made such determinations on a case-by-case basis, but analyses were generally considered to be part of the same study if:

- They shared the same data source or catchment area
- They were analyses of different study outcomes, but on the same cases (patients/children)
- The study population of one analysis is a complete subset of that of another larger analysis

PCV Introductions

Key Messages

- 135 (70%) of 194 countries have introduced PCV into routine immunization programs.
- 54 (74%) of the 73 Gavi countries have introduced PCV and 4 more are approved for Gavi support to introduce PCV.
    - Among the 19 Gavi countries that have not yet introduced, 11 (58%) countries have announced plans to introduce PCV into their NIP, leaving only 8 (42%) that have yet to make a decision on PCV introduction.
- Introduction of PCV in low- and middle-income countries (largely driven by Gavi support) has advanced more quickly in the Africa region than in the Asia region.
    - PCV has been introduced in 37 (79%) of the 47 AFR countries, compared to 18 (47%) of the 38 WPR & SEAR countries.
- Although PCV introduction in Gavi countries initially lagged behind that of high-income countries, the rate of uptake improved significantly since Gavi began supporting PCV introduction.
    - On average, the rate of universal PCV introduction in Gavi countries increased 12% each year (between 2009 and 2015), compared to an annual increase of 3% in high-income countries during the same time period.
- 49% (66.6 million) of the world's infants are not yet receiving PCV because their country has not yet introduced the vaccine.
    - Most of these infants (59%, 39.6 million) are living in Gavi countries.
- An additional 7% (9.7 million) of the world's infants, living in countries that have introduced PCV, are unlikely to be fully immunized with PCV because they are not being reached by routine immunization programs (as indicated by DTP3 coverage).
    - Most of these infants (77%, 7.5 million) are also living in Gavi countries.

PCV Introductions: The Global Picture

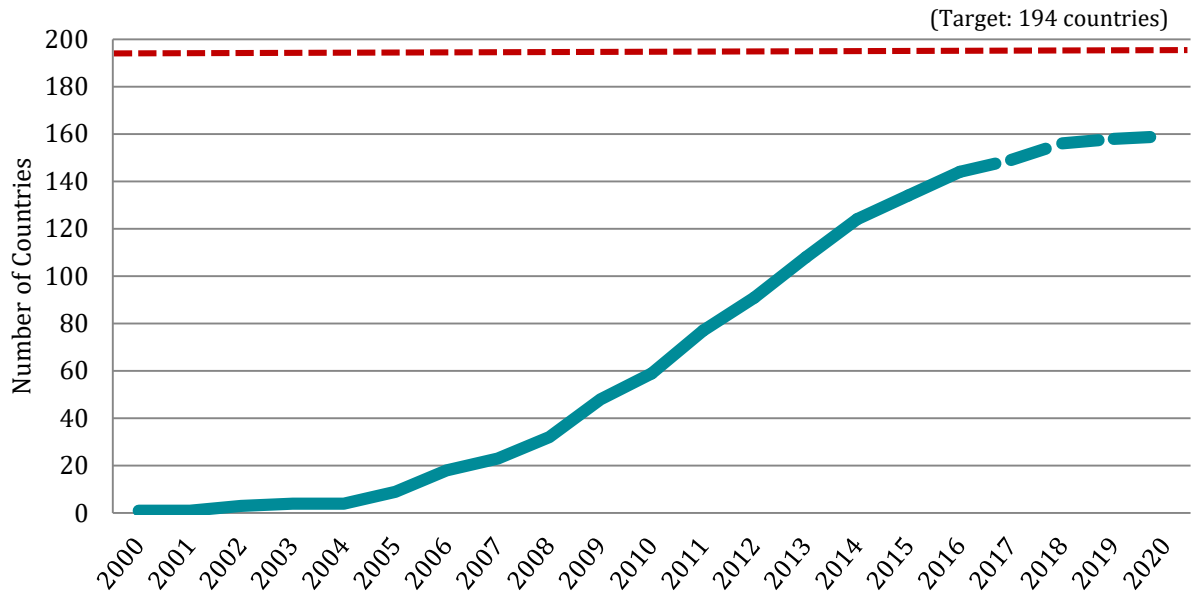
The global introduction of PCVs into national routine immunization programs started after initial licensure in 2000 and uptake of the vaccines has continued since then (**Figure 1**). To date, 135 countries have introduced PCV into their NIP (**Figure 2** displays global introductions by program type.) **Table 2** summarizes the number of countries that have introduced PCV, both globally and in Gavi countries.

Table 2: Number of countries that have introduced PCV among 194 nations

Countries (#)	Global Introductions (135 Countries)			
	Program Type			Total Introductions
	Universal Use	At-Risk Populations	Subnational Use	
Gavi (73)	53	-	1	54
Non-Gavi (121)	73	6	2	81
All Countries (194)	126	6	3	135

Note: See Appendix A for the complete list of countries that have introduced PCV, by region.

Figure 1: Number of countries introducing PCV globally, over time



Note: Dashed lines represent projected introductions in the future.
Source: IVAC, VIMS Global Vaccine Introduction Report, Dec 2015

Figure 2: Global introductions of PCV

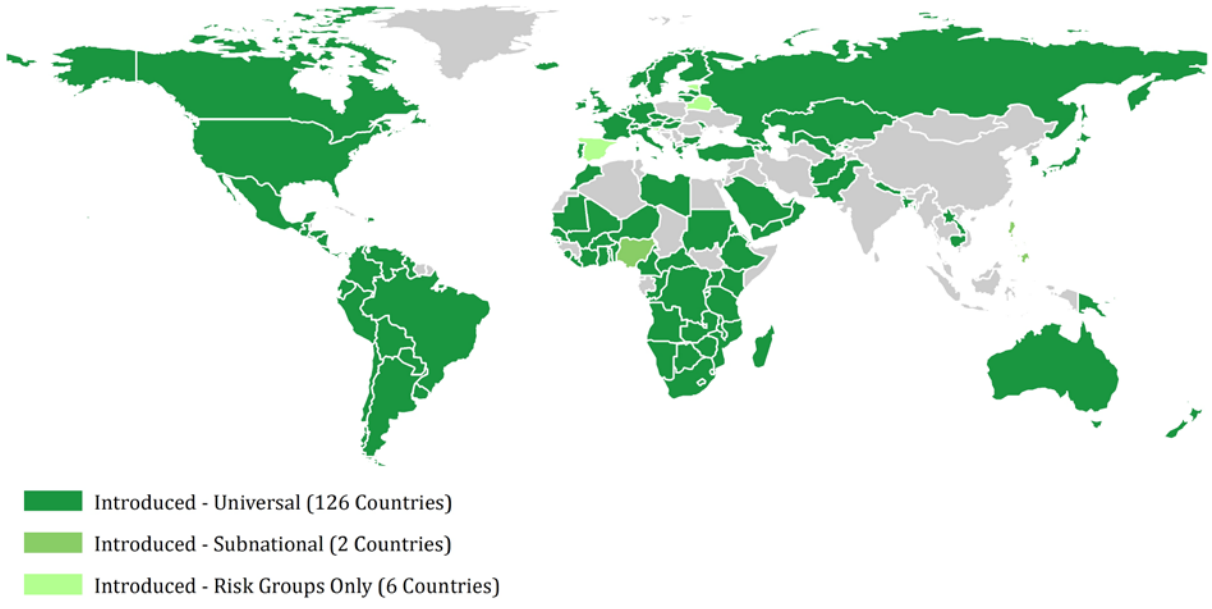
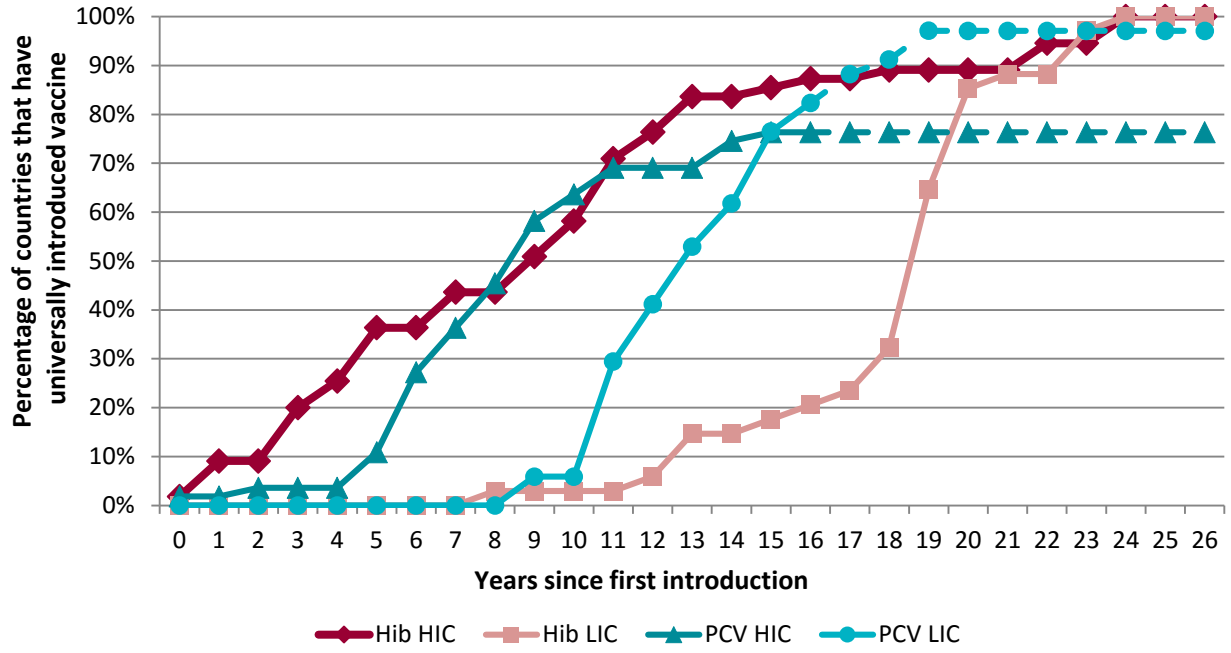


Figure 3 illustrates the pace of PCV introduction by country income strata, compared to Hib vaccine, which was first introduced in 1989. While it took 11 year for Hib vaccine to be introduced in 70% of high-income countries (HIC), it took 9 additional years (20 years from first licensure) for 70% of low-income countries (LIC) to introduce the vaccine. By contrast, the pace of PCV rollout in LICs, while initially slow, quickly accelerated to over 70% uptake within 15 years of PCV's first introduction, and just 1 year after HICs reached that same level. Thus, not only has the gap between country introduction shrunk comparing HIC and LIC progress from 9 years to 1 year, the number of years since first use of vaccine and 70% uptake has shrunk by 5 years.

Figure 3: PCV and Hib vaccine introductions, by income group



HIC: high-income country; LIC: low-income country
Note: Dashed lines represent projected introductions in the future. Projections are limited for HICs.
Source: IVAC, VIMS Global Vaccine Introduction Report, Dec 2015

Although rapid progress for PCV introduction is shown by counting the number of countries with PCV in their routine schedule, more relevant is an analysis of the children who have access to these vaccines. Forty-nine percent (66.6 million) of the world's 135.3 million infants currently live in countries that have not yet introduced PCV into their national immunization programs (NIPs), and therefore do not have access to the vaccine. An additional 7% of the world's infant cohort live in countries with PCV but are unlikely to be immunized as evidenced by incomplete DTP3 coverage.

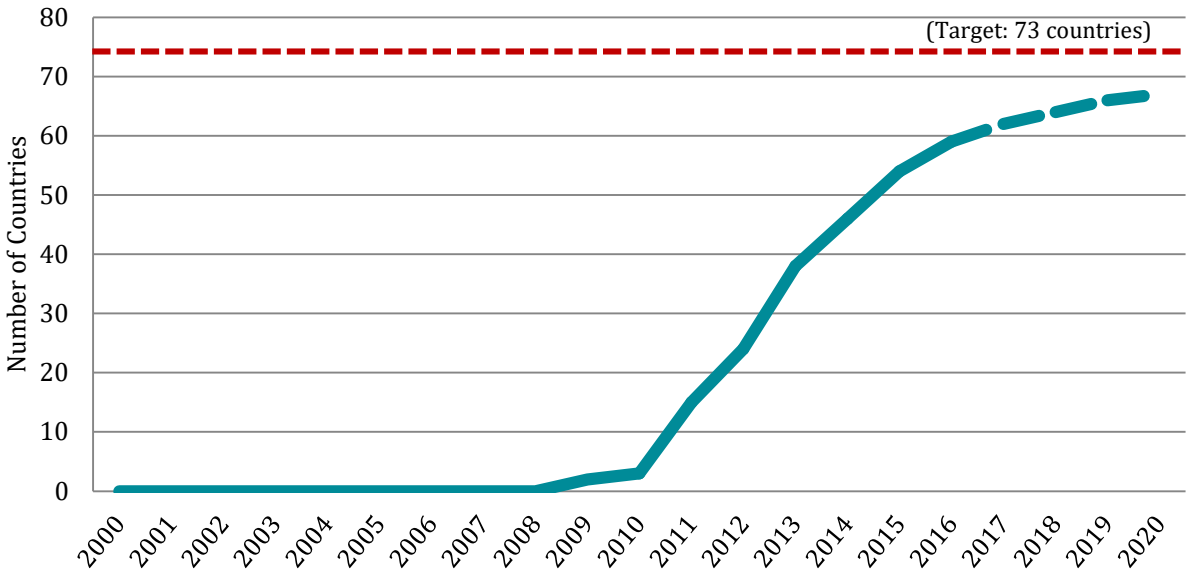
Globally, 20 countries have announced plans to introduce PCV into their NIPs in the next three years, of which 11 are Gavi countries. Thirty-nine countries have not yet made a decision about introducing the vaccine (within this 3-year time frame), including 8 Gavi countries (Chad, Korea DPR, Somalia, Sri Lanka, South Sudan, Timor-Leste, Ukraine, and Viet Nam).

PCV Introductions: Focus on Gavi Countries

Gavi PCV support began in 2009. Currently, countries are eligible for Gavi support if their average gross national income (GNI) over the past three years is equal to or below the eligibility threshold amount (USD 1,580). Such countries are eligible to apply for New Vaccine Support (NVS) and/or Health Systems Strengthening (HSS) support.

Over the past five years, the number of Gavi countries introducing PCV has increased, on average 10% per year. Currently, 54 (74%) of the 73 Gavi countries have introduced PCV. (**Figure 5**). An additional 11 Gavi countries are planning to introduce PCV, four of which have already received approval (with/without clarification) for Gavi support (Haiti, Kyrgyzstan, Mongolia, and Myanmar).

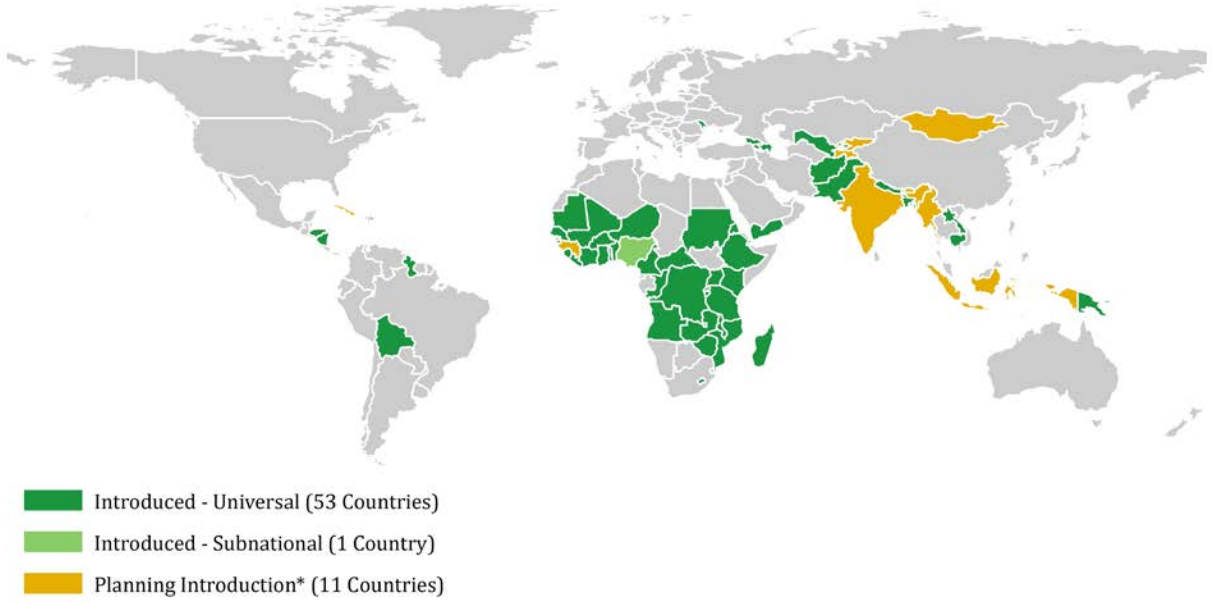
Figure 4: Number of Gavi countries introducing PCV over time



Note: Dashed lines represent projected introductions in the future.
Source: IVAC, VIMS Global Vaccine Introduction Report, Dec 2015

Figure 5 displays PCV introduction in Gavi countries, by program type.

Figure 5: PCV introduction in Gavi countries

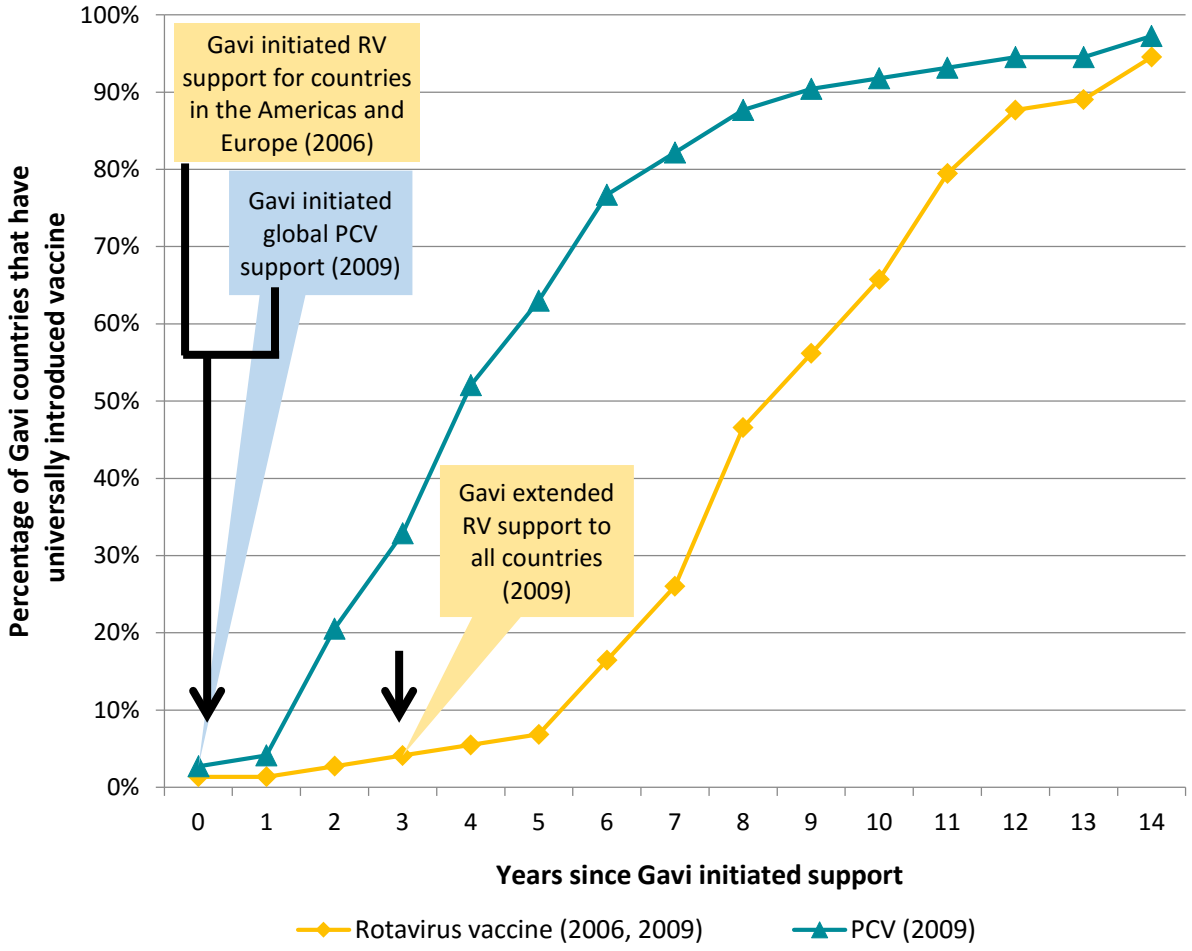


**Includes Gavi countries that have Gavi approval, approval with clarification, or conditional approval to introduce; are planning to apply for Gavi support; or planning introduction without Gavi support within the next 3 years.*

Presently, 49% (39.6 million) of the 80.3 infants living in Gavi countries lack access to PCV (i.e. country has not introduced PCV). Many of these countries have large birth cohorts (e.g. India, Indonesia) and contribute substantially to the total number of infants eligible for vaccination. India has committed to beginning PCV introduction in the coming year with Gavi support for 20% of the birth cohort. The decisions on product, schedule and timing are underway. Beyond the countries that are yet to introduce PCV are an additional 10% (7.5 million) of the Gavi infant cohort who are unlikely to be receiving PCV, due to low coverage of routine immunizations (using DTP3 coverage as a proxy).

Figure 6 compares the rates of introduction for RV vaccine and PCV, two new vaccines licensed in the same era and eligible for Gavi support. Gavi did not begin supporting PCV until nine years after its initial licensure and introduction; conversely, Gavi support for RV vaccine was initiated shortly after vaccine licensure (the same year for countries in Europe and the Americas, and within three years for all other countries). However, since Gavi's initiation of support for PCV, PCV uptake in Gavi countries occurred more rapidly than it did for rotavirus vaccine. Three years after Gavi support was made available to all countries, PCV introductions reached 33% of Gavi countries, compared to just 16% for rotavirus vaccine.

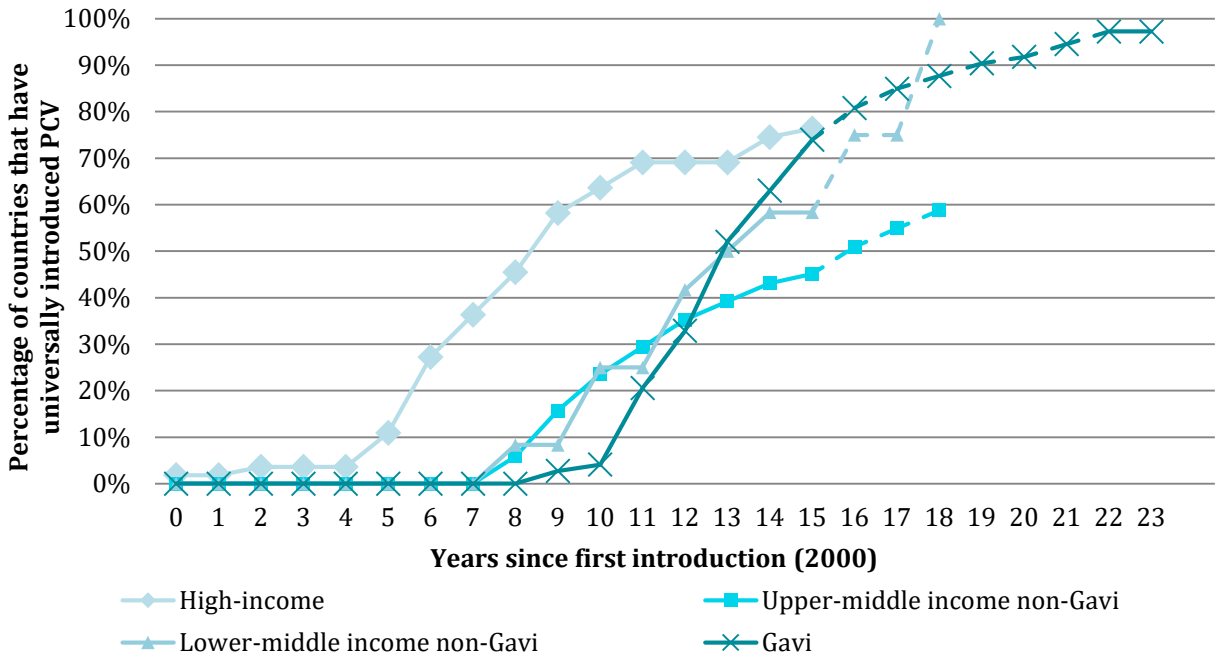
Figure 6: Percentage of Gavi countries introducing PCV and rotavirus vaccine over time



Note: Dashed lines represent projected introductions in the future.
Source: IVAC, VIMS Global Vaccine Introduction Report, Dec 2015

Notably, the rate of PCV uptake in Gavi countries has reached nearly that of high-income countries (HIC) by the end of 2015 (74% of Gavi countries vs. 76% of HICs) (**Figure 7**). On average, the proportion of Gavi countries universally introducing PCV rose approximately 12% each year since Gavi began support for PCV (2009-2015). In HICs, the increase in introductions was only 3% each year in the analogous six-year period.

Figure 7: PCV introductions, by Gavi and income status



Uptake of PCV into country vaccine programs is heterogeneous across regions, even when only the Gavi countries are considered. The speed of introduction of PCV in LICs eligible for Gavi support has been driven largely by countries in AFR, with 37 (79%) of the 47 AFR countries now using PCV in their NIPs, 33 (89%) of which are Gavi countries. This compares to just 18 (47%) of the 38 SEAR/WPR countries, 7 (39%) of which are Gavi countries. Furthermore, PCV was first introduced in a Gavi country in SEAR/WPR in 2013, four years after the first Gavi country in AFR introduced in 2009.

Products & Schedules in Use Globally

Key Messages

- PCV product use is unequal; 68% (93 countries) are using PCV13 and 22% (30 countries) are using PCV10; 8% (11 countries) use both.
  - 41 (76%) Gavi-eligible countries using PCV have implemented PCV13.
- Product-specific supply constraints in past years have influenced country product choice and product allocation by Gavi.
- 108 (80%) of the 135 of countries using PCV are using 3-dose schedules (either 2+1 or 3+0), including all Gavi countries that have introduced PCV.
- Gavi countries use a 3+0 schedule for PCV, with the exception of Georgia, Moldova and Nepal (which use a 2+1 schedule).
- With the introduction of IPV, alternate interval PCV dosing schedules are being used and evaluated.
  - Nepal (2+1) and Bangladesh (3+0) are the two countries currently using alternate interval dosing schedules.

Countries are responsible for choosing the PCV product and dosing schedule they will use in routine immunization programs. However, methods for decision-making and guidance on product choice for countries are not well defined, and assumptions of effectiveness, budget, and/or supply constraints may influence such decisions. Schedule choice is usually made in the context of a country's routine immunization schedule to optimize the visits already made for infants.

Global PCV Use by Product

Two PCV products are currently licensed for use, 10-valent and 13-valent PCV. **Table 3** illustrates the serotypes included in each formulation.

Table 3: Serotypes included in PCV10 and PCV13 product formulations

Formulation	Serotype												
	1	3	4	5	6A	6B	7F	9V	14	18C	19A	19F	23F
PCV10	■		■	■		■	■	■	■	■		■	■
PCV13	■	■	■	■	■	■	■	■	■	■	■	■	■

■ Serotype included in the vaccine

The distribution of products currently in use in NIPs is displayed in **Figure 8**, and is summarized in **Table 4**.

Figure 8: Countries using PCV, by product currently in use

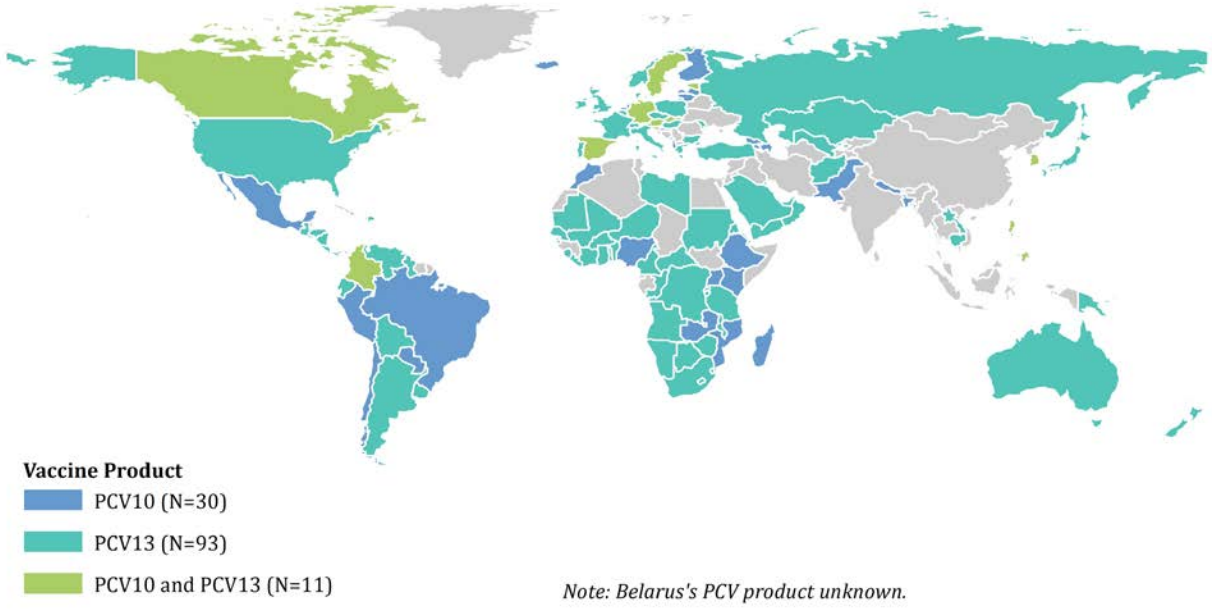


Table 4: PCV products used globally and in Gavi countries

	Product(s) currently used in NIP			
	PCV10	**PCV13**	**Both**	***Unknown***
Gavi Countries	13	41	-	-
Non-Gavi Countries	17	52	11	1
All Countries	30	93	11	1

Global PCV Use by Schedule

WHO/SAGE recommendations for PCV use include three dosing schedule options: 3+1, 3+0 or 2+1 (for either PCV10 or PCV13 product). The distribution of country dosing schedules is shown in **Figure 9, Table 5,** and **Table 6,** while that of Gavi countries alone is shown in **Figure 10**.

Figure 9: Countries using PCV, by dosing schedule currently in use

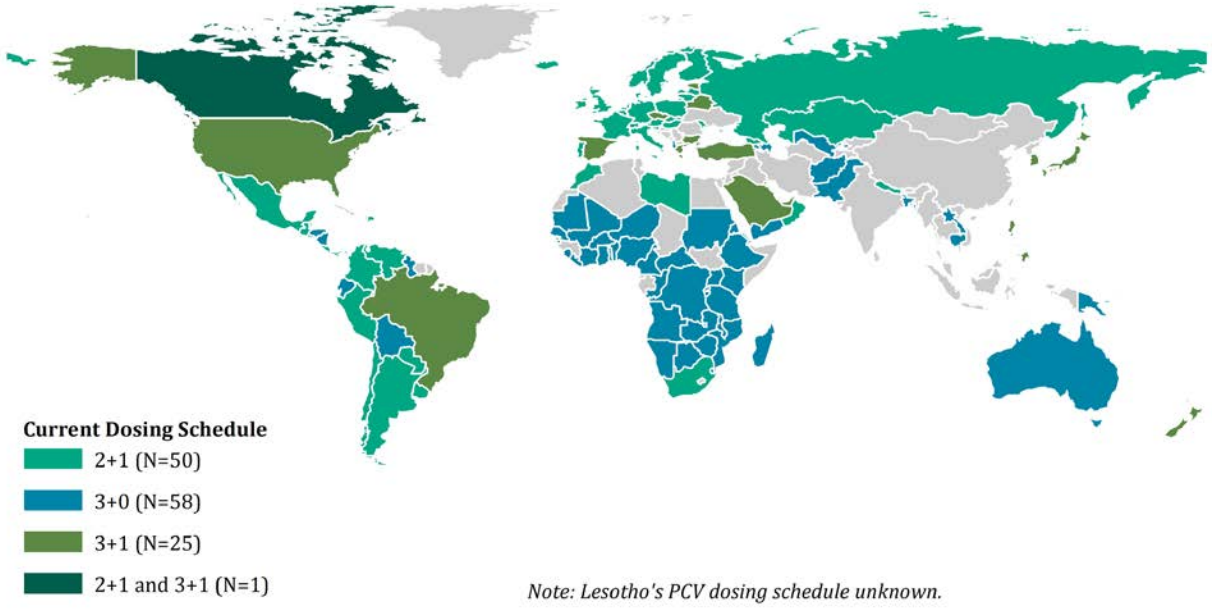


Table 5: PCV dosing schedules used globally and in Gavi countries

	Current dosing schedule used in NIP				
	2+1	**3+0**	**3+1**	**2+1 and 3+1**	***Unknown***
Gavi Countries	3	50	-	-	*1*
Non-Gavi Countries	47	8	25	1	-
All Countries	50	58	25	1	*1*

Figure 10: Gavi countries that have introduced PCV, by dosing schedule

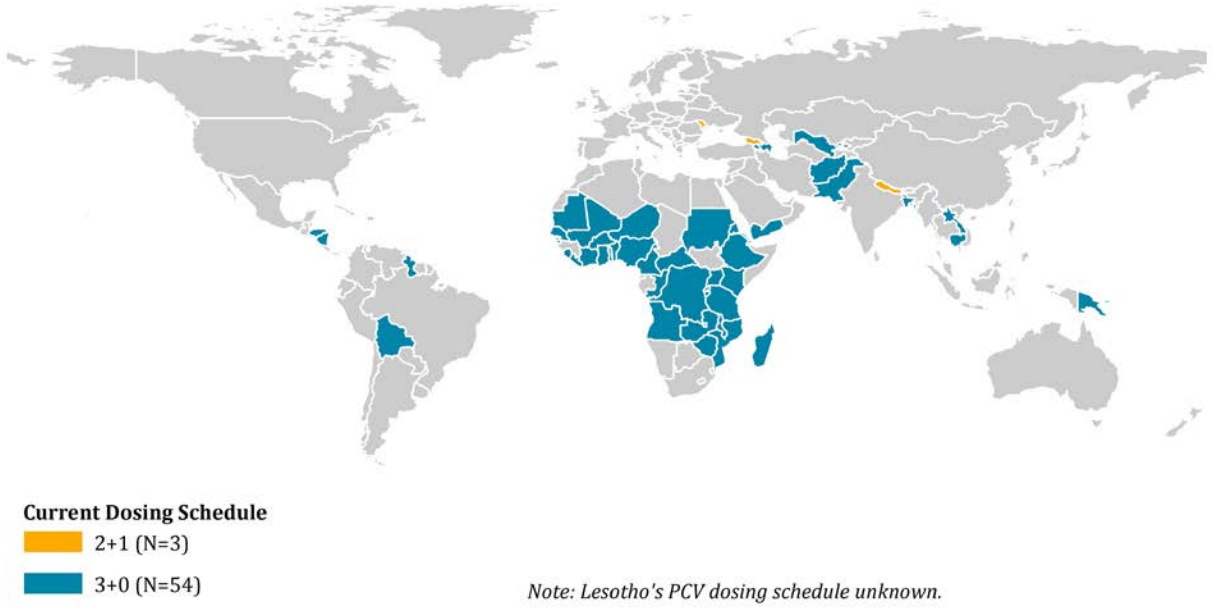


Table 6: Countries using PCV10 or PCV13 in NIP, by dosing schedule (Gavi countries highlighted in gold)

WHO Region	Dosing Schedule		
	2+1	3+0	3+1
AFR	SOUTH AFRICA	ANGOLA	
		BENIN	
		BOTSWANA	
		BURKINA FASO	
		BURUNDI	
		CAMEROON	
		CENTRAL AFRICAN REPUBLIC	
		CONGO	
		CONGO, DR	
		CÔTE D'IVOIRE	
		ERITREA	
		ETHIOPIA	
		GAMBIA	
		GHANA	
		GUINEA-BISSAU	
		KENYA	
		LIBERIA	
		MADAGASCAR	
		MALAWI	
		MALI	
		MAURITANIA	
		MOZAMBIQUE	
		NAMIBIA	
		NIGER	
		NIGERIA	
		RWANDA	
		SAO TOME AND PRINCIPE	
		SENEGAL	
		SIERRA LEONE	
		SWAZILAND	
		TANZANIA	
		TOGO	
		UGANDA	
		ZAMBIA	
		ZIMBABWE	
AMR	ARGENTINA	BARBADOS	BAHAMAS
	CHILE	BOLIVIA	BRAZIL
	CANADA*	ECUADOR	CANADA*
	COLOMBIA	GUYANA	JAMAICA
	COSTA RICA	HONDURAS	TRINIDAD AND TOBAGO
	DOMINICAN REPUBLIC	NICARAGUA	UNITED STATES
	EL SALVADOR		
	GUATEMALA		
	MEXICO		
	PANAMA		
	PARAGUAY		

	PERU		
	URUGUAY		
	VENEZUELA		
EMR	LEBANON	AFGHANISTAN	BAHRAIN
	LIBYAN ARAB JAMAHIRIYA	DJIBOUTI	KUWAIT
	MOROCCO	PAKISTAN	QATAR
	OMAN	SUDAN	SAUDI ARABIA
		YEMEN	UNITED ARAB EMIRATES
EUR	ANDORRA	ALBANIA	BELARUS
	AUSTRIA	ARMENIA	BULGARIA
	BELGIUM	AZERBAIJAN	CZECH REPUBLIC
	CYPRUS	UZBEKISTAN	ESTONIA
	DENMARK		GREECE
	FINLAND		SPAIN
	FRANCE		TURKEY
	GEORGIA		
	GERMANY		
	HUNGARY		
	ICELAND		
	IRELAND		
	ISRAEL		
	ITALY		
	KAZAKHSTAN		
	LATVIA		
	LITHUANIA		
	LUXEMBOURG		
	MOLDOVA, REPUBLIC OF		
	MONACO		
	NETHERLANDS		
	NORWAY		
	POLAND		
	PORTUGAL		
	RUSSIAN FEDERATION		
	SLOVAKIA		
	SLOVENIA		
	SWEDEN		
	SWITZERLAND		
	UNITED KINGDOM		
SEAR	NEPAL	BANGLADESH	
WPR	SINGAPORE	AUSTRALIA	JAPAN
		CAMBODIA	KOREA, REPUBLIC OF
		FIJI	MARSHALL ISLANDS
		KIRIBATI	MICRONESIA,
		LAO, PDR	NEW ZEALAND
		PAPUA NEW GUINEA	NIUE
		SOLOMON ISLANDS	PALAU
			PHILIPPINES

**Canada uses both 2+1 and 3+1 dosing schedule for PCV; schedule varies by province.*
Note: Lesotho's PCV dosing schedule is unknown.

With the exception of Georgia, Moldova, and Nepal (who are using a 2+1 schedule), all Gavi countries that have introduced PCV are using a 3+0 schedule for PCV.

Nine non-Gavi countries are currently using a 3+0 schedule (Albania, Australia, Barbados, Botswana, Ecuador, Fiji, Namibia, Swaziland, and Uzbekistan), while the remaining non-Gavi countries maintain a 2+1 or 3+1 schedule.

The 2+1 schedule was first used at the provincial level by Quebec, Canada in 2004 (de Wals, 2014). The schedule was first used nationally by the UK in 2006 following an immunogenicity study of various schedules, motivated by the reduction in the number of injections to allow room in the schedule for other vaccines and reduction in PCV program costs without compromising impact. Careful post-introduction studies have shown the schedule to be highly effective, particularly for suppression of nasopharyngeal (NP) carriage of pneumococcus and herd effects of PCV. Many non-Gavi countries have likewise introduced this schedule.

PCV Impact Studies

WHO Invasive Bacterial Disease (IBD) Surveillance

In addition to published literature and ongoing research studies of PCV impact, global surveillance of invasive bacterial disease is coordinated by the World Health Organization (WHO) in every WHO region. As many of these data could contribute to assessments of PCV impact, we briefly describe the surveillance network here. However, the remaining analyses covered in this report will include data from WHO IBD surveillance sites only if they were used in a published PCV impact study or are a part of an ongoing study designed specifically to assess vaccine impact.

The most recent WHO Vaccine Preventable Diseases Surveillance Bulletin reports that there are 128 sites in 56 countries reporting IPD surveillance data to the WHO program; 57 sites in 41 countries meet the following criteria for consistent performance:

(1) Enrolled cases in all 12 months of the year AND
(2) (a) Enrolled ≥100 meningitis cases or ≥500 cases with suspected pneumococcal disease (meningitis, sepsis or pneumonia),
OR
(b) Enrolled ≥50 meningitis cases or ≥250 cases with suspected pneumococcal disease (meningitis, sepsis or pneumonia), AND collected blood or cerebrospinal fluid (CSF) specimens on >90% of enrolled cases.

Of these 57 consistently performing sites, 45 are in Gavi countries that are currently receiving financial support from WHO. These data may in the future be used to measure impact of PCV in those countries that have introduced. This analysis includes data from WHO Invasive Bacterial Surveillance Sites only if they have published them as evidence of PCV impact in a peer-reviewed journal.

We have included a summary table from the WHO Bulletin (**Table 7**) on the amount of data that is available from this surveillance system; further details can be found on the WHO surveillance website.‡

Table 7: Number of reporting countries and sites that met criteria for consistent surveillance performance and number of children <5 years of age hospitalized for the treatment of suspected meningitis, pneumonia, or sepsis in consistently performing and targeted sites, WHO Invasive Bacterial Vaccine Preventable Disease Network, July 2013-June 2014

Region	Sites reporting data to WHO	Member States with site(s) meeting criteria	Sites meeting criteria	Sites receiving targeted* support from WHO meeting criteria for consistent performance	Of sites receiving WHO targeted support and meeting criteria for consistent performance		
					Number of children <5 years of age enrolled with suspected meningitis (% of total global cases)	Number of children <5 years of age enrolled with suspected pneumonia or sepsis (% of total global cases)	Total number of suspected meningitis, pneumonia or sepsis cases enrolled
AFR	49	20	26	22	6964 (38)	11 (<1)	6975
AMR	18	7	9	3	1499 (8)	4073 (32)	1499
EMR	20	4	8	8	3547 (20)	810 (6)	4357
EUR	14	4	5	4	427 (2)	N/A	427
SEAR*	6	3	5	5	5127 (28)	5857 (46)	10,984
WPR	21	3	4	3	625 (3)	1891 (15)	2516
Total	**128**	**41**	**57**	**45**	**18,189 (100)**	**12,642 (100)**	**26,758**

**Targeted defined as a consistently performing site in a Gavi-eligible country that receives financial support from WHO.*
Source: Vaccine Preventable Diseases Surveillance, Global Invasive Bacterial and Rotavirus Surveillance Bulletin. Volume 11: Data Period 2013-2014. July 2015.

‡ http://www.who.int/immunization/monitoring_surveillance/burden/VPDs/en/

PCV Impact Studies: The Global Picture

Key Messages

- Currently, there are 58 countries evaluating the impact of PCV10/13 use in routine immunization programs or evaluating the vaccine's economic impact; 4 of these are countries that have not yet introduced PCV, but are evaluating economic impact.
- **Of the 135 countries that have introduced PCV globally, 54 (40%) have conducted or are conducting a PCV impact evaluation, 16 of which are Gavi countries.**
- Among Gavi countries using PCV, 30% (16/54 countries) have PCV impact evaluations that are completed or ongoing.

From a global or regional perspective, not every country needs to have an impact study in order for the technical community to have credible insights into the impact of PCV on individuals and communities. However, there need to be studies in countries representing different epidemiological and geographic settings to inform global and regional policies and allow countries with similar epidemiological settings to infer their own PCV impact. There remains a misalignment between the aspiration for optimal public health program monitoring at the country level and the availability of human and financial resources to conduct these evaluations. **Table 8** enumerates the number of countries with PCV impact studies by Gavi country status. **Figure 11** overlays PCV country use and countries with at least one impact study.

Nevertheless, availability of PCV impact studies in the published literature has increased and is expected to increase more rapidly as more countries will soon have sufficient number of years of post-PCV introduction observation to begin analyzing the impact.

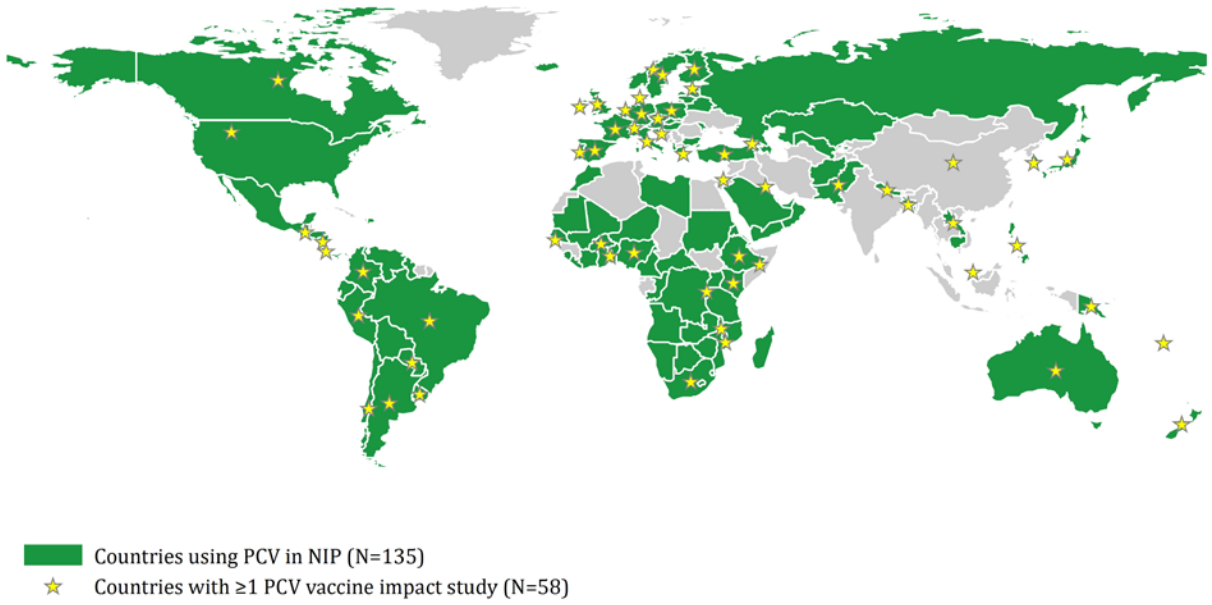
Table 8: Number of countries with ≥1 PCV10 or PCV13 impact study, globally and in Gavi countries

	# Countries with ≥1 PCV10 or PCV13 Impact Study
Gavi Countries*	17**
Non-Gavi Countries	41
All Countries	58**

**Mongolia and Viet Nam have studies designed to measure PCV impact, but have not introduced the vaccine into their NIP; therefore, they are not counted here.*

***4 of the 58 countries with PCV impact studies are countries evaluating economic impact of PCV (pre-introduction): China, Croatia, Malaysia, and Somalia. Somalia is a Gavi country.*

Figure 11: Countries using PCV in their NIP and evaluating PCV impact



Note: There may be other ongoing PCV impact studies (not included here) in countries that have not yet introduced PCV, but are planning to, that are currently collecting pre-introduction baseline data (such as Mongolia and Viet Nam). These studies will be added to our database once the country has introduced the vaccine.

PCV Impact Study Gaps by Region

Key Messages

- Although at least one country is conducting a PCV impact evaluation in each WHO region, the quantity of studies varies substantially by region.
- Availability of PCV impact data is dependent on the timing of vaccine introduction; therefore evidence of PCV impact in Africa, where introduction started earlier, is more mature than that in Asia.
- Of all the WHO regions, PCV impact evaluations are most common in EUR and AMR and least common in EMR and SEAR.

Table 9: Availability of PCV studies evaluating both health and economic impact, by WHO region and Gavi status

WHO Region	# Countries in Region		# Countries (%) in Region with Routine PCV Use		# Countries (% of PCV-using countries) in Region with ≥1 PCV10 or PCV13 Impact Study		# PCV10 or PCV13 Impact Studies	
	Gavi	Total	Gavi	Total	Gavi	Total	Gavi	Total
AFR	37	47	33 (89%)	37 (79%)	9 (27%)	10 (27%)	14	19
AMR	6	35	4 (67%)	25 (71%)	1 (25%)	12 (48%)	1	32
EMR	6	21	5 (83%)	14 (67%)	1 (20%)	2 (14%)	1	2
EUR	8	53	5 (63%)	41 (77%)	1 (20%)	20 (49%)	1	39
SEAR*	9	11	2 (22%)	2 (18%)	2 (100%)	2 (100%)	3	3
WPR*	7	27	5 (71%)	16 (59%)	2 (40%)	8 (50%)	2	9
Global	**73**	**194**	**54 (74%)**	**135 (70%)**	**16 (30%)**	**54 (40%)**	**22**	**104**

Note: The impact studies reported in this table exclude economic studies modeling/projecting the impact of rotavirus vaccine in countries that have not yet introduced the vaccine.
**Mongolia (in WPR) and Viet Nam (in SEAR) have studies designed to measure PCV impact, but have not introduced the vaccine into their NIP; therefore, they are not counted here.*

Table 10: Availability of PCV studies evaluating health impacts, by WHO region and Gavi status

WHO Region	# Countries in Region		# Countries (% in Region) with Routine PCV Use		# Countries (% of PCV-using countries) in Region with ≥1 PCV10 or PCV13 Impact Study		# PCV Impact Studies	
	Gavi	Total	Gavi	Total	Gavi	Total	Gavi	Total
AFR	37	47	33 (89%)	37 (79%)	8 (24%)	9 (24%)	14	19
AMR	6	35	4 (67%)	25 (71%)	1 (25%)	10 (40%)	1	25
EMR	6	21	5 (83%)	14 (67%)	1 (20%)	2 (14%)	1	2
EUR	8	53	5 (63%)	41 (77%)	0 (0%)	18 (44%)	0	32
SEAR*	9	11	2 (22%)	2 (18%)	2 (100%)	2 (100%)	3	3
WPR*	7	27	5 (71%)	16 (59%)	2 (40%)	6 (38%)	2	7
Global	**73**	**194**	**54 (74%)**	**135 (70%)**	**14 (26%)**	**47 (35%)**	**21**	**87**

Note: The impact studies reported in this table exclude economic studies modeling/projecting the impact of rotavirus vaccine in countries that have not yet introduced the vaccine, as well as studies only evaluating vaccine economic impact.
**Mongolia (in WPR) and Viet Nam (in SEAR) have studies designed to measure PCV impact, but have not introduced the vaccine into their NIP; therefore, they are not counted here.*

The regions with the least data are the South-East Asia Region (SEAR), where only two countries have introduced PCV, both of which have ongoing PCV impact evaluations (Nepal and Bangladesh), and the Eastern Mediterranean Region (EMR), where we are aware of

three countries that have an impact evaluation (Pakistan, Kuwait, and Somalia[§]) among the 14 countries using PCV.

Availability of data on impact of PCV in routine use is dependent on vaccine introduction and rollout. In general, introductions occurred first in high-income countries primarily in the European and North American regions, followed by Gavi-supported countries in the Africa region. Low- and middle-income countries (both Gavi and non-Gavi) in the Asia region began introducing later; therefore, a lag in the availability of PCV impact evidence from this area is expected. Furthermore, because there are so few Gavi countries in Asia, the opportunities for PCV impact is more limited than in Africa, enhancing the importance of assuring that PCV impact studies are well planned and coordinated, and emphasizing the importance of a PCV impact plan for India, which will be introducing PCV in the near term.

PCV impact studies from low- and middle-income countries, especially those with high pneumococcal disease burden, are important because they will expand the evidence base for sustaining PCV immunization in the highest disease burden settings.

Importantly, the WHO regions, by which countries were stratified in this gap analysis, are often epidemiologically heterogeneous. Further scrutiny of such differences in disease burden is important to strategically assess epidemiologic gaps in PCV impact studies.

PCV Impact Study Gaps by Product

Key Messages

- PCV13 is more commonly evaluated than PCV10 both in absolute and relative measures.
    - Among the 54 countries with a PCV impact evaluation, 15 (28%) use PCV10, 31 (57%) use PCV13, and 8 (15%) are use both products.
- A greater fraction of the PCV10-using countries have an impact evaluation than PCV13 or dual-use countries.
    - 50% of PCV10-using countries have an impact evaluation; 33% of PCV13-using countries have an impact evaluation, and 73% of dual-product use countries have an impact evaluation.
- Among Gavi countries, there are an equal number of countries (8 each) evaluating PCV10 and PCV13; however, this represents a smaller fraction of PCV13-using countries (20%) than PCV10-using countries (62%).

Analysis of PCV impact studies by the product (PCV10 or PCV13) (**Table 11 and 12**), and national dosing schedule (2+1, 3+0, or 3+1) (**Table 13**) is important as it could potentially influence global and regional policy recommendations and decisions in the future, or underscore the need for further evidence surrounding PCV impact.

[§] Somalia has a modeled economic PCV impact study only (it hasn't introduced PCV yet).

Table 10: Number of countries using and evaluating PCV, by current product in NIP, globally and in Gavi countries

	Current product in NIP*			
	PCV10	PCV13	PCV10 and PCV13	Total
Gavi Countries	8	8	0	16
Non-Gavi Countries	7	23	8	38
All Countries	15	31	8	54

Table 11: Percent of PCV-10 and PCV-13 using countries that are evaluating impact, globally and in Gavi countries

	Current product in NIP*		
	PCV10	PCV13	PCV10 and PCV13
Gavi Countries	62%	20%	-
Non-Gavi Countries	41%	44%	73%
All Countries	50%	33%	73%

**Tables 11 and 12 stratify countries using and evaluating PCV impact by the current product in their NIP, not by the product(s) evaluated in the impact studies. The product(s) currently used in the NIP are often the same as the product(s) evaluated, but that is not always true (as some countries have switched products and may or may not have evaluated all products currently and previously used).*

Table 13 lists countries that have at least one PCV10 or PCV13 impact study, by the vaccine product currently used in the national immunization program (NIP), with Gavi countries highlighted in gold. The year of introduction is included in the table, which can provide perspective on the amount of post-PCV introduction data that is potentially available, but does not necessarily reflect the actual amount of post-introduction data reported in the PCV impact studies.

Table 12: Countries with ≥1 PCV impact study, by current product in NIP and product ever introduced

WHO Region	Country	Intro Year	Current Product	PCV-10 Introduced	PCV-13 Introduced
AFR	Burkina Faso	2013	PCV13		
	Ethiopia	2011	PCV10		
	Gambia	2009	PCV13		
	Kenya	2011	PCV10		
	Malawi	2011	PCV13		
	Mozambique	2013	PCV10		
	Nigeria	2014	PCV10		
	Rwanda	2009	PCV13		
	South Africa	2009	PCV13		
	Togo	2014	PCV13		
AMR	Argentina	2012	PCV13		
	Brazil	2010	PCV10		

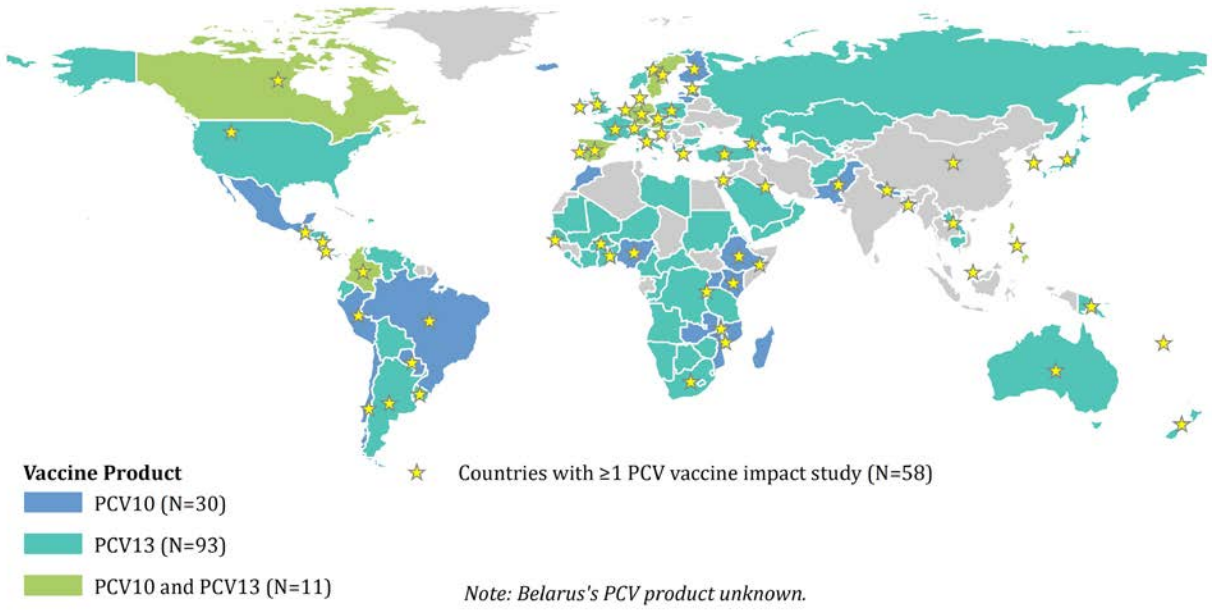
	Canada	2002	PCV10 & PCV13		
	Chile	2011	PCV10		
	Colombia	2011	PCV10 & PCV13		
	Costa Rica	2008	PCV13	Not currently in use**	
	Guatemala	2012	PCV13		
	Nicaragua	2010	PCV13		
	Paraguay	2012	PCV10		
	Peru	2009	PCV10		
	United States	2000	PCV13		
	Uruguay	2008	PCV13		
EMR	Kuwait	2007	PCV13		
	Pakistan	2012	PCV10		
	Somalia*	-	-		
EUR	Croatia*	-	-		
	Czech Republic	2010	PCV13		
	Denmark	2007	PCV13		
	Estonia	2014	PCV10 & PCV13		
	Finland	2010	PCV10		
	France	2006	PCV13		
	Georgia	2014	PCV10		
	Germany	2006	PCV10 & PCV13		
	Greece	2006	PCV13		
	Ireland	2008	PCV13		
	Israel	2009	PCV13		
	Italy	2005	PCV13		
	Netherlands	2006	PCV10		
	Norway	2006	PCV13		
	Poland	2006	PCV13		
	Portugal	2015	PCV13		
	Spain	2001	PCV10 & PCV13		
	Sweden	2009	PCV10 & PCV13		
	Switzerland	2006	PCV13		
	Turkey	2008	PCV13		
	United Kingdom	2006	PCV13		
SEAR❖	Bangladesh	2015	PCV10		
	Nepal	2015	PCV10		
WPR❖	Australia	2005	PCV13		
	China*	-	-		
	Fiji	2012	PCV10		
	Japan	2011	PCV13		
	Korea, Republic of	2014	PCV10 & PCV13		
	Lao PDR	2013	PCV13		
	Malaysia*	-	-		
	New Zealand	2008	PCV13	Not currently in use**	
	Papua New Guinea	2013	PCV13		
	Philippines	2013	PCV10 & PCV13		

**Somalia, Croatia, China, and Malaysia have yet to introduce PCV into their NIP; however, there have been (modeled) studies assessing the economic impact of PCV in those countries.*
***Costa Rica and New Zealand previously used PCV10, but have since switched to PCV13.*
❖Mongolia and Viet Nam have studies designed to measure PCV impact, but have not introduced the vaccine into their NIP; therefore, they are not listed here.
Note: Gavi countries are highlighted in gold.

Figure 12 maps the countries with impact studies, according to the product in their NIP, illustrating that both PCV10 and PCV13 are used in every region of the globe and with the exception of SEAR, all regions have an impact evaluation completed or ongoing of both PCV10 and PCV13.

SEAR has no impact evaluation of PCV13; 2 ongoing impact studies (Bangladesh and Nepal) are being conducted in the region, but both are evaluating PCV10. EMR has 3 impact studies (PCV10 study in Pakistan, PCV13 study in Kuwait, and pre-PCV economic impact study in Somalia[**]). WPR has 10 countries with impact studies, 2 evaluating PCV10, 2 evaluating PCV13, and 6 evaluating both PCV10 and PCV13 (independently). AFR, AMR, and EUR have at least one impact study evaluating each product independently (i.e., not a head-to-head evaluation of the impact of both products, but simultaneous and separate studies).

Figure 12: Countries evaluating PCV10 or PCV13 impact, by product currently in use



Thirty countries (22%) of the 135 countries that have introduced PCV are using PCV10, and 15 of those (50%) have ongoing or published impact studies. Ninety-three (69%) of the

[**] Somalia has only a modeled economic impact study for PCV10.

135 countries that have introduced PCV are using PCV13 and 31 of these (33%) have ongoing or published impact studies.

- Eight (62%) of the 13 Gavi countries using PCV10 are evaluating impact.
- Eight (20%) of the 41 Gavi countries using PCV13 are evaluating impact.

There are no PCV13 impact studies ongoing in SEAR, as both countries that have introduced PCV in the region are using PCV10.

PCV Impact Study Gaps by Dosing Schedule

Key Messages

- Among the 54 countries that have introduced PCV into its NIP and are conducting PCV impact evaluation, 25 countries (46%) are currently using a 2+1 schedule, 16 countries (30%) are using a 3+0 schedule, and 13 countries (24%) are using a 3+1 schedule.
    - **Sixteen of the 54 countries using and evaluating PCV are Gavi countries, 2 of which are using a 2+1 dosing schedule for PCV and 14 are using a 3+0 schedule.**
- Of the countries that are using a 2+1 and 3+1 schedule, 50% of each are evaluating PCV impact, whereas only 28% of countries using a 3+0 schedule are evaluating impact.
    - **Most Gavi countries that have introduced PCV are using a 3+0 dosing schedule; thus, PCV impact evaluations in Gavi countries are predominantly happening in countries using a 3+0 schedule.**

Two countries, Nepal and Bangladesh (both Gavi countries), are evaluating PCV schedules that are modifications of the standard EPI 6, 10, 14 week schedule; this change was motivated by wanting to avoid giving 3 injections at the 14-week visit, required by the inclusion of IPV. Nepal's schedule (6w, 10w, 9m) is not in accordance with the recommended minimum 8-week interval between the two primary doses in a 2+1 schedule. Bangladesh's schedule (6w, 10w, 18w) is aligned with the WHO recommendation for a minimum 4-week interval between doses in a 3+0 schedule. **Table 13** provides the categorization of countries where impact studies have been done or are ongoing by dosing schedule, product and Gavi status. A summary evaluation is provided in **Table 14**. A global map (**Figure 13**) provides a visual display of the distribution of impact studies by dosing schedule.

Table 13: Countries with ≥1 PCV10 or PCV13 impact study, by current product and dosing schedule

WHO Region	Dosing Schedule								
	2+1			3+0			3+1		
AFR			PCV13 South Africa	PCV10 Ethiopia Kenya Mozambique Nigeria	PCV13 Burkina Faso Gambia Malawi Rwanda Togo				
AMR	PCV10 Chile Paraguay Peru	PCV10 & PCV13 Canada* Colombia	PCV13 Argentina Costa Rica Guatemala Uruguay		PCV13 Nicaragua		PCV10 Brazil	PCV10 & PCV13 Canada*	PCV13 United States
EMR				PCV10 Pakistan					PCV13 Kuwait
EUR	PCV10 Finland Georgia Netherlands**	PCV10 & PCV13 Germany Sweden	PCV13 Denmark France Ireland Israel Italy Norway Poland Portugal Switzerland United Kingdom				PCV10 & PCV13 Estonia Spain		PCV13 Czech Republic Greece Turkey
SEAR❖	PCV10 Nepal			PCV10 Bangladesh	PCV13 Australia				
WPR❖				PCV10 Fiji	PCV13 Lao, PDR Papua New Guinea		PCV10 & PCV13 Korea, Republic of Philippines		PCV13 Japan New Zealand***

**Canada's PCV dosing schedule varies by province/territory; some use a 2+1, while others use a 3+1 dosing schedule.*
***The Netherlands switched from a 3+1 dosing schedule to a 2+1 schedule in Nov 2014.*
****New Zealand has conducted impact evaluation of PCV10, but PCV10 is no longer in use in the country.*
❖Mongolia and Viet Nam have studies designed to measure PCV impact, but have not introduced the vaccine into their NIP; therefore, they are not listed here.
Note: Somalia, Croatia, China, and Malaysia are not listed above, as they have yet to introduce PCV into the NIP.
Gavi countries are highlighted in gold.

Table 14: Number of countries using and evaluating PCV (and percent of all countries using that schedule, with an impact study), by current dosing schedule in NIP, globally and in Gavi countries.

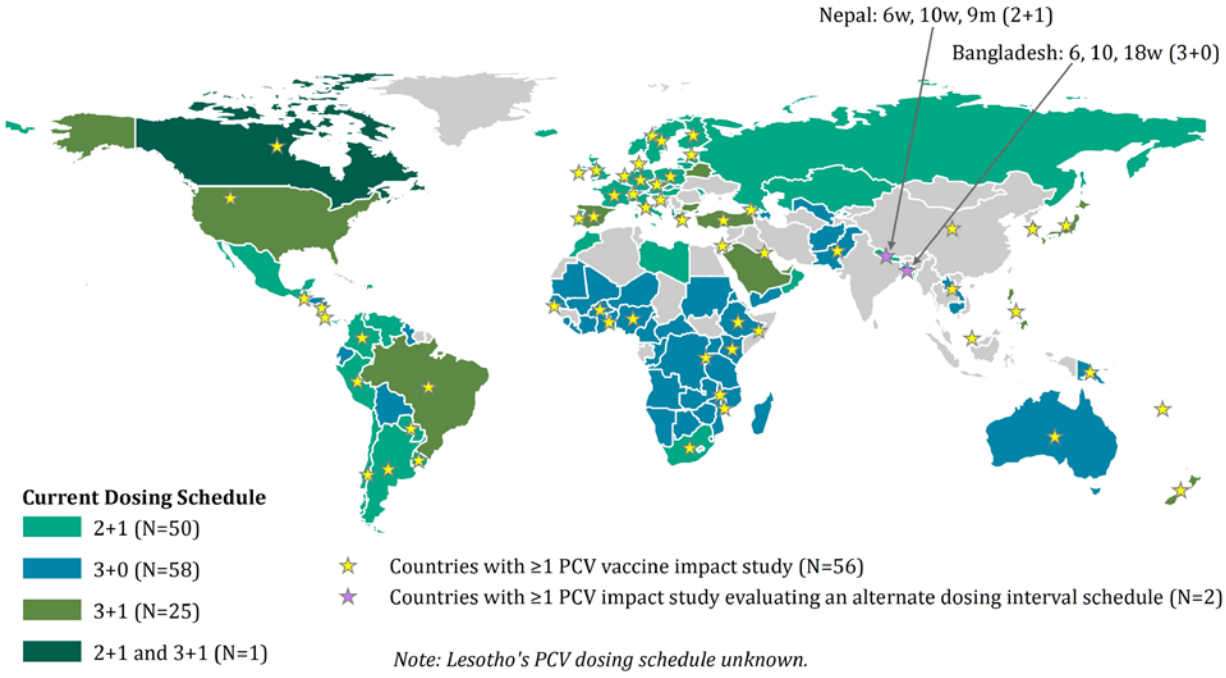
	Current PCV dosing schedule in NIP			
	2+1	**3+0**	**3+1**	**2+1 and 3+1**
Gavi Countries*	2 (67%)	14 (28%)	-	-
Non-Gavi Countries	23 (49%)	2 (25%)	12 (48%)	1 (100%)
All Countries	25 (50%)	16 (28%)	12 (48%)	1 (100%)

**Mongolia and Viet Nam have studies designed to measure PCV impact, but have not introduced the vaccine into their NIP; therefore, they are not counted here.*

Twenty-five (50%) of the 50 countries using a 2+1 schedule, 16 (28%) of the 58 countries using a 3+0 schedule, 12 (48%) of the 25 countries using a 3+1 schedule, and 1 (100%) of the 1 country using both a 2+1 and 3+1 schedule for their PCV program are evaluating PCV impact.

- Two (67%) of the 3 Gavi countries using a 2+1 schedule and 14 (28%) of the 50 Gavi countries using a 3+0 schedule are evaluating PCV impact. No Gavi country is using or evaluating the 3+1 PCV dosing schedule.

Figure 13: Countries evaluating PCV10 or PCV13 impact, by dosing schedule currently in use



Of particular interest are countries evaluating alternate interval dosing schedules due to logistics or programmatic issues that interfere with the recommended dosing timing of 3+1, 3+0, or 2+1 schedules. Both Nepal and Bangladesh are evaluating unique schedules, which change the timing of a PCV dose because of concerns with giving 3 injections at the 14-week routine immunization visit (i.e., IPV will be introduced at 14w).

- Bangladesh is evaluating a 6w, 10w, 18w schedule (3+0), lengthening the window between the 2nd and 3rd doses of PCV.
- Nepal is evaluating a 6w, 10w, 9m, schedule (2+1), shortening the recommended window between the 2 primary doses from 8 to 4 weeks. The results of impact studies in these countries could have implications for the dosing schedule (and timing of doses) chosen for PCV programs in other countries (if they are shown to be non-inferior).

Impact Study Gaps: By Outcome(s) Measured

Key Messages

- Invasive pneumococcal disease (IPD) and pneumonia are the most commonly evaluated outcomes in countries conducting PCV evaluations.
    - Of the countries with PCV impact studies, 68% and 59% are evaluating PCV impact on IPD and pneumonia, respectively.
- Other commonly measured outcomes are nasopharyngeal (NP) carriage and economic outcomes, which are respectively evaluated in 47% and 41% of countries with PCV impact studies.
- Impact of PCV on mortality is being measured in 24% of countries with PCV impact studies.
    - Data on PCV impact on mortality are being collected in studies in AFR, AMR, EUR, SEAR, and WPR; however, no data on this outcome is being collected in EMR.
    - PCV10 or PCV13 impact on mortality has been published in three regions: AMR (Brazil, Canada, Nicaragua, and the United States); EUR (Denmark, Spain, and Sweden); and WPR (New Zealand). None of these are high mortality sites.
- Herd effects (also termed indirect impact) is being evaluated in 55% (n=32) of countries evaluating PCV impact. In every region, there is at least 1 country measuring herd effect of PCV.
- Every WHO region has countries contributing evidence of PCV impact on IPD, pneumonia, and NP carriage, as outcomes.

Table 16 lists the countries with published and ongoing PCV10 and PCV13 impact studies, by outcome(s) assessed, and **Table 17** tabulates the number of countries reporting on each outcome. *This gap analysis does not evaluate the quality or quantity of data from each country for each outcome.* Similarly, the availability of data does not exactly correlate with the ability to determine PCV impact from such data; some studies may be underpowered to provide robust analyses for only one or another outcome.

The amount of available evidence on PCV10 and PCV13 impact varies by outcome across the globe. In general, the most common outcomes evaluated in PCV impact studies are IPD and pneumonia.

IPD is the most commonly assessed outcome, and is measured in 38 (68%) countries evaluating PCV impact.

Pneumonia is also commonly being assessed, and is measured in 34 (59%) countries evaluating PCV impact.

NP carriage was measured in 27 (47%) countries evaluating PCV impact.
Future analyses will assess whether NP studies are measuring direct or indirect effects of PCV and the degree to which these studies are concomitant with disease outcome evaluations.

Mortality is being assessed in 14 (24%) countries evaluating PCV impact; many are unpublished because the analysis or data collection is still ongoing. It is unclear how many of these studies will have a sufficient amount of data for a valid assessment of this outcome. Gavi countries with a mortality outcome include, in Africa: Burkina Faso, Gambia, Kenya, and Malawi; in Central America: Nicaragua; and in Asia: Bangladesh.

Health economic data are being collected in 24 (41%) countries evaluating PCV impact.

Studies measuring multiple outcomes allow for triangulation of impact and an assessment of relationships between changes in NP colonization and the disease impacts, and analysis of data from such studies is a part of ongoing work.

Future analyses may assess the availability of studies measuring multiple outcomes in a single population; such data may allow for triangulation of impact and assessment of the relationships between changes in NP colonization and disease outcomes.

Table 15: PCV10 and PCV13 impact studies, by outcome(s) measured

WHO Region (# Countries with PCV impact evaluation)	Gavi Status (# Countries with PCV impact evaluation)	Country (# Studies)	IPD	Pneumonia	NP carriage	Herd effect	Mortality	Economic	Other❖
AFR (10)	Gavi (9)	Burkina Faso (2)	✓	✓	✓	✓	✓	✓	✓
		Ethiopia (1)						✓	
		Gambia (1)	✓	✓	✓	✓	✓	✓	
		Kenya (2)	✓	✓	✓	✓	✓	✓	✓
		Malawi (4)	✓	✓	✓	✓	✓		
		Mozambique (1)	✓	✓	✓				
		Nigeria (1)	✓	✓					✓
		Rwanda (1)	✓	✓					
		Togo (1)	✓	✓	✓	✓			
	Non-Gavi (1)	South Africa (5)	✓	✓	✓	✓			✓
AMR (12)	Gavi (1)	Nicaragua (1)		✓		✓	✓		
	Non-Gavi (11)	Argentina* (3)	✓	✓			✓	✓	✓
		Brazil (3)	✓	✓	✓	✓	✓		✓
		Canada (3)	✓	✓	✓	✓	✓	✓	✓
		Chile (1)	✓						
		Colombia (1)	✓					✓	
		Costa Rica (1)	✓	✓					
		Guatemala (1)		✓					
		Paraguay (2)			✓			✓	
		Peru (2)			✓			✓	
		United States (12)	✓	✓	✓	✓	✓	✓	✓
		Uruguay (1)	✓	✓	✓	✓			
EMR (3)	Gavi (2)	Pakistan (1)	✓	✓	✓			✓	
		Somalia (1)						✓	
	Non-Gavi (1)	Kuwait (1)	✓			✓			
EUR (21)	Gavi (1)	Georgia (1)						✓	
	Non-Gavi (20)	Croatia (1)						✓	
		Czech Republic (1)	✓	✓	✓	✓			

		Denmark (2)	✓	✓	✓	✓	✓		
		Estonia (1)						✓	
		Finland (2)	✓	✓	✓	✓			✓
		France* (5)	✓	✓	✓	✓			✓
		Germany (4)	✓	✓	✓	✓		✓	✓
		Greece* (3)	✓	✓		✓		✓	✓
		Ireland (1)		✓	✓	✓			✓
		Israel (1)	✓	✓	✓	✓			✓
		Italy (1)			✓				
		Netherlands (2)	✓	✓	✓	✓		✓	
		Norway (1)	✓	✓	✓	✓			
		Poland (1)		✓		✓			
		Portugal (1)	✓			✓			
		Spain (2)	✓	✓		✓	✓		
		Sweden* (2)	✓		✓	✓	✓		
		Switzerland (1)	✓	✓	✓	✓			
		Turkey (1)	✓						
		United Kingdom (6)	✓	✓	✓	✓		✓	✓
SEAR (2)**	Gavi (2)**	Bangladesh (2)	✓	✓	✓	✓	✓		
		Nepal (1)	✓	✓	✓			✓	✓
WPR (10)**	Gavi (2)**	Lao PDR (1)		✓	✓	✓			
		Papua New Guinea (1)	✓	✓	✓				
	Non-Gavi (8)	Australia (2)	✓	✓	✓	✓			✓
		China (1)						✓	
		Fiji (1)	✓	✓	✓	✓			
		Japan (1)						✓	
		Korea, Republic of (1)			✓				
		Malaysia (1)						✓	
		New Zealand (1)	✓	✓	✓	✓	✓		✓
		Philippines (1)						✓	

❖Other outcomes not specifically listed here, such as acute otitis media (AOM), mastoiditis, empyema, antibiotic non-susceptibility, etc.
✓Based on expert(s) and lead staff knowledge of ongoing studies or that the outcome was published for PCV7 impact, but has not yet been reported for PCV10 or PCV13 impact. These data will be verified for the future gap analyses and reports.
Note: Outcome measured means that a study explicitly states that the outcome was measured in the study population and/or data was reported for the outcome.
*Argentina, France, Greece, and Sweden also have PCV impact studies which collect data on non-pneumonia non-meningitis outcomes (e.g., sepsis, bacteremia).
**Mongolia and Viet Nam (both Gavi countries) have studies designed to measure PCV impact, but have not introduced the vaccine into their NIP; therefore, they are not included here.*

Table 16: Number of countries with PCV impact evaluation for various outcomes

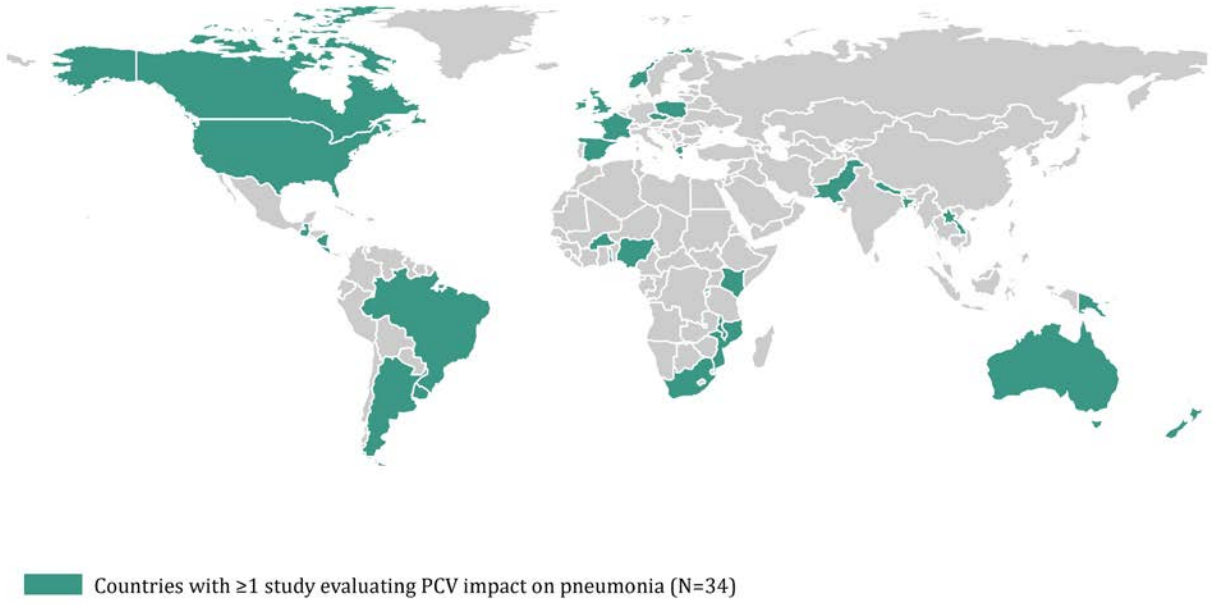
	Outcome Measured in PCV Impact Study						
	IPD	**Pneumonia**	**NP carriage**	**Herd effect**	**Mortality**	**Economic**	**Other**
# Countries	38	34	27	32	14	24	18

Measuring PCV Impact on Pneumonia

Thirty-four (59%) of the 58 countries with PCV impact evaluation are measuring pneumonia, 14 (41%) of which are Gavi countries. Along with IPD, pneumonia is one of the most commonly measured outcomes in countries evaluating PCV impact. It is evaluated in 9 (90%) of AFR countries, 8 (67%) of AMR countries, 1 (33%) of EMR countries, 9 (43%) of EUR countries, 2 (100%) of SEAR countries and 5 (50%) of WPR countries with PCV impact evaluation.

- Fourteen (82%) of the 17 Gavi countries evaluating PCV impact are collecting data on pneumonia. Pneumonia data are available from Gavi countries in all regions, except EUR.

Figure 14: Countries with ≥1 PCV10 or PCV13 study evaluating impact on pneumonia



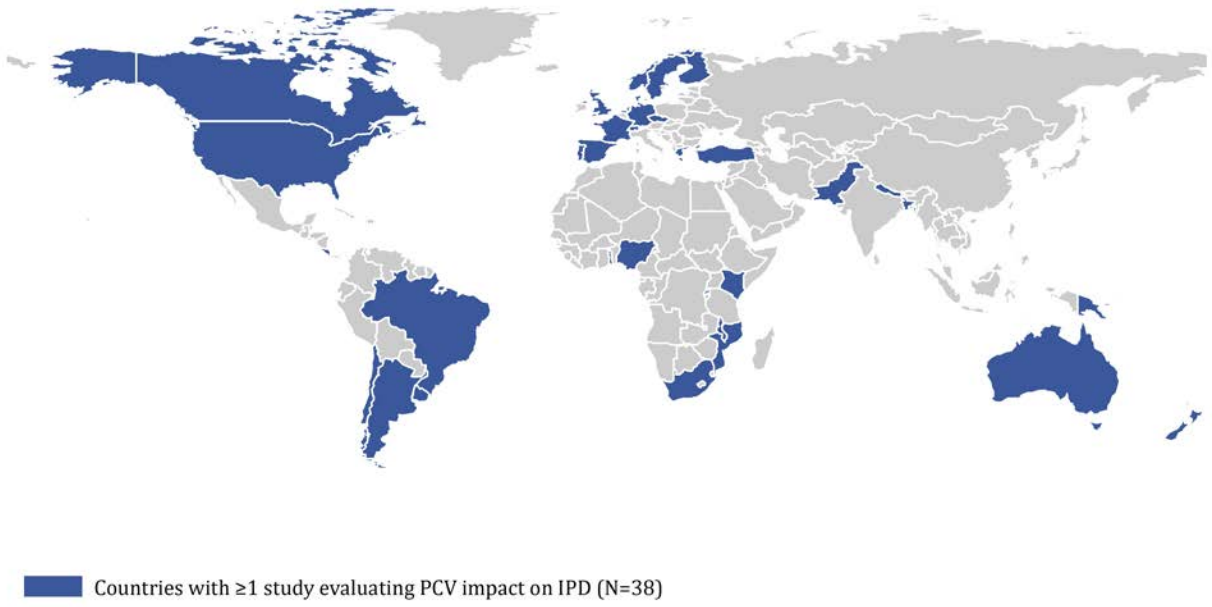
Note: Mongolia also has an ongoing PCV study designed and prepared to measure impact on pneumonia, but is not shown here because it has not introduced PCV into its NIP.

Measuring PCV Impact on IPD

Thirty-eight (68%) of the 58 countries with PCV impact studies are measuring impact on IPD, 10 (27%) of which are Gavi countries. This includes 8 (80%) of AFR countries, 7 (58%) of AMR countries, 2 (67%) of EMR countries, 15 (71%) of EUR countries, 2 (100%) of SEAR countries and 4 (40%) of WPR countries with PCV impact evaluation.

- Eleven (65%) of the 17 Gavi countries evaluating PCV impact are collecting data on IPD. IPD data are available from Gavi countries in all regions, except AMR and EUR.

Figure 15: Countries with ≥1 PCV10 or PCV13 study evaluating impact on IPD



Note: Mongolia also has an ongoing PCV study designed and prepared to measure impact on IPD, but is not shown here because it has not introduced PCV into its NIP.

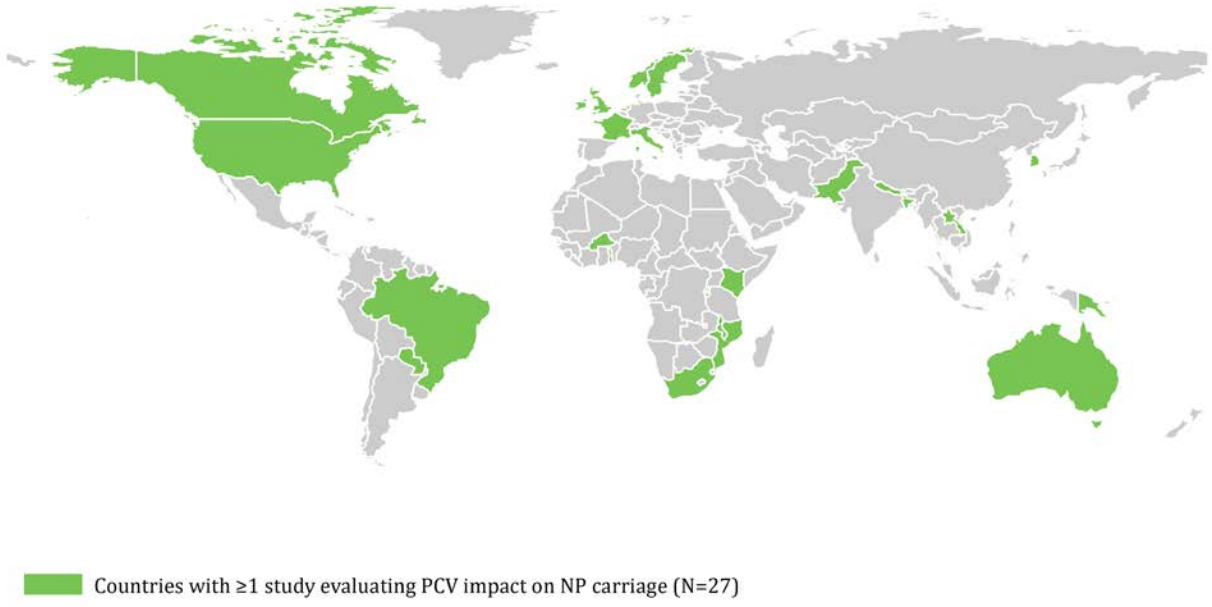
Measuring PCV Impact on Nasopharyngeal Carriage

Twenty-seven (47%) of the 58 countries with PCV impact studies are measuring pneumococcal nasopharyngeal (NP) carriage, 11 (41%) of which are Gavi countries. This includes 7 (70%) of AFR countries, 4 (33%) of AMR countries, 1 (33%) of EMR countries, 7 (33%) of EUR countries, 2 (100%) of SEAR countries, and 5 (50%) of WPR countries with PCV impact evaluation.

- Eleven (65%) of the 17 Gavi countries evaluating PCV impact are collecting data on NP carriage. NP carriage data are available from Gavi countries in all regions, except AMR and EUR.

Of particular interest are studies that contemporaneously measure NP carriage and a disease outcome since these improve our understanding of the relationship between carriage and disease, as well as the impact of vaccination on this relationship. *Such sites and studies will be identified in future gap analyses and reports.*

Figure 16: Countries with ≥1 PCV10 or PCV13 study evaluating impact on NP carriage



Note: Mongolia and Viet Nam also have ongoing PCV studies designed and prepared to measure impact on NP carriage, but are not shown here because they have not introduced PCV into its NIP.

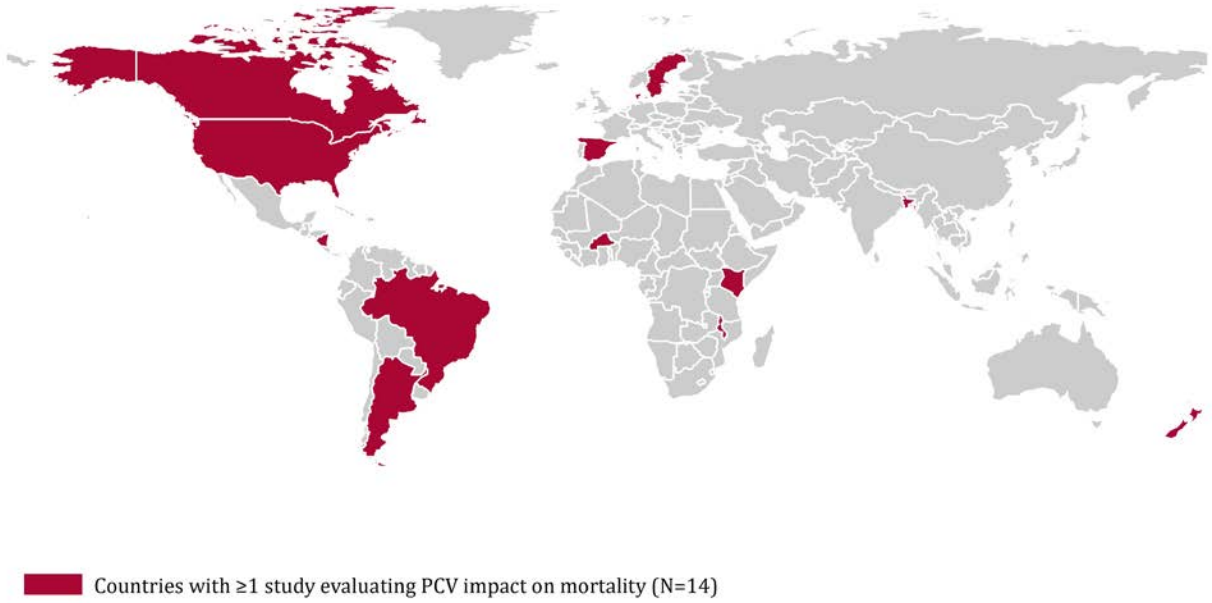
Measuring PCV Impact on Mortality

Fourteen (24%) of the 58 countries with PCV impact studies measure mortality as an outcome, 6 (43%) of which are Gavi countries. The 14 mortality studies includes 4 (40%) of AFR countries, 5 (42%) of AMR countries, 0 of the EMR countries, 3 (14%) of EUR countries, 1 (50%) of SEAR countries and 1 (10%) of the WPR countries with PCV impact evaluation.

- Six (35%) of the 17 Gavi countries evaluating PCV impact are collecting data on mortality. Mortality data are available from Gavi countries in AFR, AMR, and SEAR, but not in EMR, EUR, and WPR.

No studies on mortality from a Gavi country, except Nicaragua have been published. Studies evaluating PCV10 or PCV13 impact on mortality have been published in three regions: AMR (Brazil, Canada, Nicaragua, and the United States); EUR (Denmark, Spain, and Sweden); and WPR (New Zealand).††

Figure 17: Countries with ≥1 PCV10 or PCV13 study evaluating impact on mortality



†† Note: Data on impact of PCV9 on mortality in Gambia was published, however this study did not meet our criteria for inclusion in this analysis (i.e., results reported from impact of an unlicensed product and not routine use study).

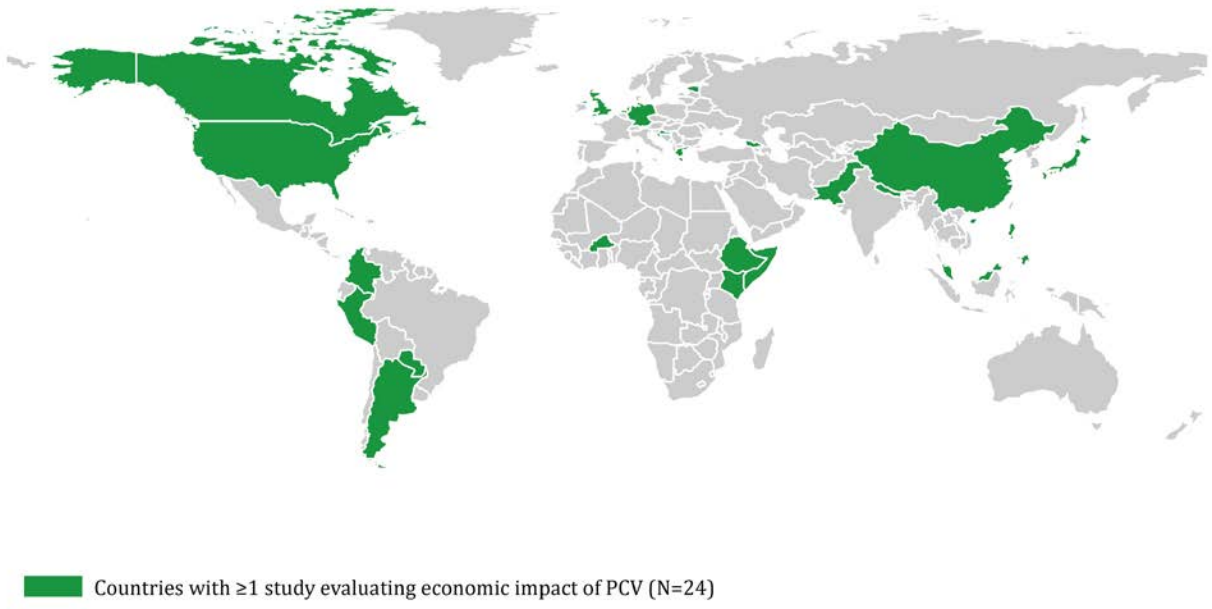
Measuring Economic Impact

Twenty-four (41%) of the 58 countries with PCV impact studies assess economic outcomes (e.g., cost of illness, cost-effectiveness, return on investment), 8 (33%) of which are Gavi countries. This includes 4 (40%) of AFR countries, 6 (50%) of AMR countries, 2 (67%) of the EMR countries, 7 (33%) of EUR countries, 1 (50%) of SEAR countries, and 4 (40%) of the WPR countries with PCV impact evaluation.

- Eight (47%) of the 17 Gavi countries evaluating PCV impact are measuring the economic impact of the vaccine. Economic impact data are available from Gavi countries in all regions, except AMR and WPR.

Note: These figures include published and ongoing studies conducted in the context of routine PCV use, as well as studies estimating the potential economic impact of PCV where it has not yet been introduced. The majority of these studies are from modeled economic (or cost-effectiveness) studies. Thus, the availability of data on the actual (observed) economic impact of PCV use is very limited.

Figure 18: Countries with ≥1 PCV10 or PCV13 study measuring economic impact

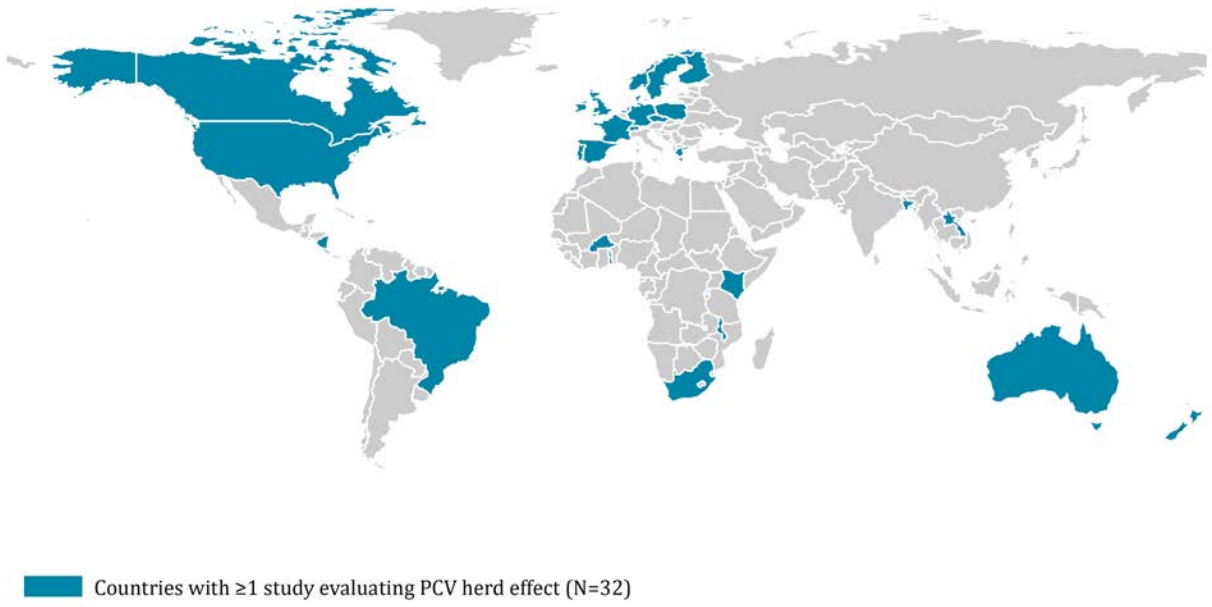


Measuring PCV Herd Effects on Disease and NP Colonization

Thirty-two (55%) of the 58 countries with PCV impact studies are measuring herd effects of PCV (i.e., reductions in disease or colonization in unvaccinated portions of the population, including unvaccinated children and non-age-eligible older individuals), 8 (25%) of which are Gavi countries. This includes 7 (70%) of AFR countries, 4 (33%) of AMR countries, 1 (33%) of the EMR countries, 8 (38%) of EUR countries, 2 (100%) of SEAR countries and 5 (50%) of WPR countries with PCV impact evaluation.

- Eight (47%) of the 17 Gavi countries evaluating PCV impact are collecting data on herd effects of PCV vaccination. PCV herd effects data are available from Gavi countries in all regions, except EMR and EUR.

Figure 19: Countries with ≥1 PCV10 or PCV13 impact study measuring herd effects



Note: Mongolia also has an ongoing PCV study designed and prepared to measure herd effects, but is not shown here because it has not introduced PCV into its NIP.

Measuring Other Outcomes

In addition to the outcomes mapped above, 18 (31%) of the 58 countries with PCV impact studies measure outcomes not listed here (e.g., acute otitis media, mastoiditis, empyema, antibiotic non-susceptibility, etc.), 4 (22%) of which are Gavi countries. This includes 4 (40%) of AFR countries, 4 (33%) of AMR countries, 0 of the EMR countries, 7 (33%) of EUR countries, 1 (50%) of SEAR countries, and 1 (10%) of WPR countries with PCV impact evaluation.

- Four (24%) of the 17 Gavi countries evaluating PCV impact are collecting data on other outcomes not already specifically listed. These data are available from Gavi countries only in AFR and SEAR.

Conclusions

One hundred and thirty-five countries in the world are currently using PCV and 58 countries have either a published or ongoing study documenting the impact of PCV10 and/or PCV13, on health or economic outcomes. Collectively, these studies have documented impact on both PCV10 and PCV13, used in various dosing schedules. Given that less than half of PCV-using countries have any evaluation going on, and that only 30% (16/54) of Gavi countries have evaluations, there are substantial gaps, when assessed by outcome. The maps provide a visual display of the paucity of data, when all countries are considered.

While there are published/ongoing studies in all WHO regions, there are important gaps.

- **West Africa**: There is a very limited number of evaluations going on outside of eastern and southern Africa in spite of the huge populations in some of these countries.
- **Large Countries:** The countries with the greatest number of pneumococcal deaths, and highest pneumococcal rates are poorly represented. Among India, Pakistan, Indonesia, Nigeria and Ethiopia, only Pakistan has an ongoing study that is likely to produce high quality impact data.
- **Regional Limitations:**
    - We identified very few countries in EMR and SEAR that have introduced PCV and are conducting PCV impact evaluation. For example, Pakistan (which is using PCV10) and Kuwait (which is using PCV13) are the only PCV-using countries in EMR that are contributing to the impact evidence base in their region. Other countries in the region may have differing levels of child mortality and morbidity than these two countries and therefore, the evidence generated from these countries may not be perceived as regionally representative.
    - In addition, there are gaps in PCV impact evidence from sub-regions within Europe as well, such as Eastern Europe. Although the majority of PCV impact evidence to date are originating from European countries, the proportion of PCV-using countries in Eastern Europe that are conducting impact evaluations is relatively low (28%).
    - Meanwhile, even though few south-east Asian countries have introduced PCV, the two countries that have introduced are actively monitoring PCV impact (Nepal and Bangladesh).
    - For Gavi countries, PCV impact data are still heavily concentrated in AFR and AMR, largely due to the higher rate of PCV introduction in those regions, compared to EMR, SEAR, and WPR.
- **Mortality**: The most compelling outcome of PCV is a reduction in mortality. Although a surprising number of countries are aiming to evaluate this impact, only a very small number are Gavi countries, and among these are not countries with the greatest mortality.

- **Economic Outcomes**: This is among the least measured outcomes with major gaps in Africa and south Asia. Especially among Gavi countries in transition, data on the health economic benefits are likely to play a substantial role is sustaining the PCV investment.
- **Herd Effects**: Very limited data on impact beyond the targeted age group, which especially for Gavi countries in transition, may be a critical driving force for sustaining the program.
- **Studies with multiple outcomes:** PCV impact on pneumonia and IPD are the most commonly evaluated outcomes in countries with PCV impact studies. NP carriage is another outcome that is being monitored in several countries but almost not at all in western Africa. The studies that monitor both disease and carriage may provide further insights on whether and how NP carriage may be used as a surrogate for disease outcomes.

Next Steps

This gap analysis of PCV impact studies aims to describe the ***availability of evidence*** that has been or is being collected globally, with focus on product, schedule, and outcomes by country, as of March 10, 2016. This analysis provides the first view of potential gaps within the objectives of the PCV Technical Coordination Project and the Reduced Dose Policy Analysis funded by the Bill & Melinda Gates Foundation.

Ongoing work includes systematically identifying and evaluating evidence from published and ongoing work to review and summarize the impact of each vaccine, by outcome, schedule, and setting. Topics of interest for such ongoing activities are listed below. *(Note: the topics listed here are in no particular order, and may be edited and reordered based on Foundation priorities, Gavi priorities, relevance to WHO and NITAGs, or other considerations.)*

As results from studies on PCV10 and PCV13 become available, summary analyses will be conducted to assess many of the technical questions about quantitative impact observed (rather than gaps in availability of PCV impact data). This work is ongoing in the context of the PCV Technical Coordination grant from the BMGF and the PCV product assessment grant from Gavi.

Future analyses

1. Assess the availability of PCV impact evaluations across the WHO regions by income strata of countries.
    - Due to Gavi support for introduction and impact evaluation for PCV, it is likely that a higher proportion of Gavi countries have ongoing or published PCV impact studies than non-Gavi middle-income countries. In particular, the middle-income countries outside of the PAHO region are predicted to have a fewer PCV introductions and PCV impact studies compared to other income strata countries.

2. Assess the availability of PCV impact evaluations specifically among countries that are on the path toward graduation to assess the strength of evidence to sustain the PCV program.

3. Future analyses may stratify by geographic region, rather than WHO region, to better understand gaps in sub-regions of interest: Eastern Europe and the Middle East.

4. The use of PCV catch-up schedules in various countries is being mapped; this has become of interest to Gavi for potential support in the countries that have not yet introduced PCV.

5. Further disaggregate the analysis of PCV impact studies by outcome to assess those using different approaches to measure pneumonia impact (e.g., use of administrative data, chest radiographs, NP carriage, and urine antigen testing), which can inform future assessments of pneumonia.

6. Analysis of age groups evaluated in NP carriage studies to determine the direct and indirect effects of PCV on this outcome, important to understanding differences in schedules on indirect effects of PCV; and possibly to assess the methods used in such studies to evaluate the relative merits of each approach.

7. Assess the 2015 pneumococcal disease burden estimates in relation to PCV use, by region. Compare the regional disease burden estimates and location of PCV impact studies for future MCEE estimates and updating of assumptions used in models. (The 2015 pneumococcal disease burden estimates from the MCEE project are finalized and are expected to be published in 2016 after country review).
    - To inform MCEE investigators of any assessment of the MCEE burden estimates as it related to the location and available results of PCV impact studies.

8. Assess the generalizability of the PCV health economic impact studies since it is likely that the methods and outcomes are not well harmonized across these studies. Given their paucity they could provide strong evidence to improve sustainability of PCV programs as countries graduate from Gavi support or for countries whom have not yet introduced PCV.

9. Data from studies with multiple outcomes may be triangulated to understand relationships between the impact on different outcomes; this will inform whether conducting less resource intensive assessments is feasible for inferring impact (e.g., using NP carriage studies in countries with limited resources).

10. Compare the availability of data on serotype-specific effects of PCV10 and PCV13 (direct and indirect), specifically for serotypes 3, 19A, 7F, that are in PCV13, but not in PCV10 to understand product differences and better inform product choice. This is also relevant for impact of serotypes 1 and 5, serotypes important for Gavi countries.

11. Assess which studies intend to (or are able to) monitor serotype replacement to better understand what data will be available for a global re-analysis of serotype replacement.

12. Evaluation of vaccine effectiveness from sites using alternate dosing schedules (such as Nepal and Bangladesh with off-label studies, or reduced-dose schedules) to address emerging concerns for crowded immunization schedules and other programmatic considerations that may alter current dosing schedules.

Several topics have become of particular interest to the PCV Partners and others in the pneumococcal field.

- Serotype specific data from Mozambique and Kenya, both PCV10 using countries, will may critical evidence from high-burden LMIC settings (e.g. provide evidence on impact against 19A in PCV10 using country).

- Data from Finland on the impact of PCV10, providing further evidence on protection of PCV10 against VT-related serotypes such as 19A.

- GSK applying for a serotype 19A label within their PCV10 product label, which has now been approved in Europe (by the EMA) and evidence used to support such decision-making.

- Data and coordination among Latin Americas sites regarding evidence on the use and impact of PCVs in the region (through the GREEN research group). The region includes countries using both PCV10 and PCV13 in a variety of dosing schedules.

Strategic gap analyses are to be conducted on the amount of evidence and the technical content of such evidence to address arising issues surrounding PCV use via systematic and comprehensive evaluations. Those analyses will continue to inform national and global immunization programs and inform country-level decision makers on the potential impact of PCV use in their own national immunization programs.

Acknowledgements and Notes

This report was prepared by Linh Nguyen, Olivia Cohen, and Kate O'Brien as part of the Targeted Assessment Study Coordination (TASC) project, funded by Gavi, the Vaccine Alliance. The report leverages the VIEW-hub database and online platform (www.VIEW-hub.org), which is supported through multiple grants funded by Gavi and the Bill & Melinda Gates Foundation.

Vaccine introduction dates and proposed impact studies do not imply an obligation by any funding organization. Such information reported here reflects documentation or communication that we have received from our partners (e.g. Gavi, the Bill & Melinda Gates Foundation, the Centers for Disease Control & Prevention, the World Health Organization, and others).

Various data sources and information were used to generate this report, and are maintained at the Johns Hopkins Bloomberg School of Public Health for use by the International Vaccine Access Center (IVAC) and its affiliated partners.

For any inquiries or feedback on this gap analysis report or VIEW-hub (regarding global vaccine use or PCV impact studies), please contact Linh Nguyen at linh.nguyen@jhu.edu or Olivia Cohen at ocohen3@jhu.edu.

Appendix A. Global PCV Introductions, by Region

WHO Region	Country		
AFR	ANGOLA	GHANA	RWANDA
	BENIN	GUINEA-BISSAU	SAO TOME AND PRINCIPE
	BOTSWANA	KENYA	SENEGAL
	BURKINA FASO	LESOTHO	SIERRA LEONE
	BURUNDI	LIBERIA	SOUTH AFRICA
	CAMEROON	MADAGASCAR	SWAZILAND
	CENTRAL AFRICAN REPUBLIC	MALAWI	TANZANIA
	CONGO	MALI	TOGO
	CONGO, DR	MAURITANIA	UGANDA
	CÔTE D'IVOIRE	MOZAMBIQUE	ZAMBIA
	ERITREA	NAMIBIA	ZIMBABWE
	ETHIOPIA	NIGER	
	GAMBIA	NIGERIA	
AMR	ARGENTINA	DOMINICAN REPUBLIC	PANAMA
	BAHAMAS	ECUADOR	PARAGUAY
	BARBADOS	EL SALVADOR	PERU
	BOLIVIA	GUATEMALA	TRINIDAD AND TOBAGO
	BRAZIL	GUYANA	UNITED STATES
	CANADA	HONDURAS	URUGUAY
	CHILE	JAMAICA	VENEZUELA
	COLOMBIA	MEXICO	
	COSTA RICA	NICARAGUA	
EMR	AFGHANISTAN	LIBYAN ARAB JAMAHIRIYA	SAUDI ARABIA
	BAHRAIN	MOROCCO	SUDAN
	DJIBOUTI	OMAN	UNITED ARAB EMIRATES
	KUWAIT	PAKISTAN	YEMEN
	LEBANON	QATAR	
EUR	ALBANIA	GEORGIA	NETHERLANDS
	ANDORRA	GERMANY	NORWAY
	ARMENIA	GREECE	POLAND
	AUSTRIA	HUNGARY	PORTUGAL
	AZERBAIJAN	ICELAND	RUSSIAN FEDERATION
	BELARUS	IRELAND	SLOVAKIA
	BELGIUM	ISRAEL	SLOVENIA
	BULGARIA	ITALY	SPAIN
	CYPRUS	KAZAKHSTAN	SWEDEN
	CZECH REPUBLIC	LATVIA	SWITZERLAND

	DENMARK	LITHUANIA	TURKEY
	ESTONIA	LUXEMBOURG	UNITED KINGDOM
	FINLAND	MOLDOVA, REPUBLIC OF	UZBEKISTAN
	FRANCE	MONACO	
SEAR	BANGLADESH	NEPAL	
WPR	AUSTRALIA	LAO PEOPLE'S DEMOCRATIC REPUBLIC	PAPUA NEW GUINEA
	CAMBODIA	MARSHALL ISLANDS	PHILIPPINES
	FIJI	MICRONESIA, FEDERATED STATES OF	SINGAPORE
	JAPAN	NEW ZEALAND	SOLOMON ISLANDS
	KIRIBATI	NIUE	
	KOREA, REPUBLIC OF	PALAU	

Gavi countries are highlighted in gold.

Appendix B. Contact Information & Corresponding Authors for PCV Impact Studies

A 'general pneumococcal point person' as well as the available contact information for corresponding author(s) of publications included in the VIEW-hub database and gap analysis to date are included below. The 'general point person(s)' for each country is not necessarily a study-specific PI, but rather an initial point of contact for ongoing PCV impact work in the particular country. Ongoing work for the PCV Technical Coordination Secretariat includes communication with these individuals to identify specific-study PIs and improve our list of contacts for future gap analyses and related PCV projects.

WHO Region	**Country**	**General Pneumococcal Point Person For Country**	**Corresponding Author Information** (Abstracted from PubMed)	**PubMed Abstract Links** **Note: Not a Systematically Inclusive List; Consists of First Deep Dive Into the Literature*
AFRO	Burkina Faso	Bradford Gessner <bgessner@aamp.org> Jennifer Moisi <jmoisi@aamp.org> Cynthia Whitney <cgw@cdc.gov> Chris Van Beneden <cav7@cdc.gov>		
	Gambia	Grant Mackenzie <gmackenzie@mrc.gm>	- E Usuf <effuau@gmail.com>	1. http://www.ncbi.nlm.nih.gov/pubmed/24503271
	Haiti	Umesh Parashar uap2@cdc.gov		
	Kenya	Laura Hammitt <lhammitt@jhu.edu> Anthony Scott < ascott@kemri-wellcome.org>	- Anthony Scott <ascott@kemri-wellcome.org> - Philip Ayieko <payieko@nairobi.kemi-wellcome.org> - Laura Hammitt <lhammitt@jhu.edu>	1. http://www.kemri-wellcome.org/index.php/en/studies_inner/75 2. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3691111/ 3. http://www.ncbi.nlm.nih.gov/pubmed/25103393 4. http://www.sciencedirect.com/science/article/pii/S2214109X14702244 5. http://www.ncbi.nlm.nih.gov/pubmed/24465570 6. http://www.ncbi.nlm.nih.gov/pubmed/22403235
	Malawi	Neil French <N.French@liverpool.ac.uk> Malcolm Molyneux <mmolyneux999@gmail.com>		
	Mozambique	Betuel Sigauque <Betuel.Sigauque@manhica.net> Cynthia Whitney <cgw@cdc.gov>		
	Nigeria	Stephen Obaro <Stephen.obaro@unmc.edu>		
	Rwanda	Bradford Gessner <bgessner@aamp.org> Jennifer Moisi <jmoisi@aamp.org>		
	South Africa	Shabir Madhi <shabirm@nicd.ac.za>	- Shabir Madhi <shabirm@nicd.ac.za>	1. http://www.ncbi.nlm.nih.gov/pubmed/25784729 2. http://thorax.bmj.com/content/early/2015/06/19/thoraxjnl-2014-206593.short?rss=1
	Tanzania	Robert Booy <RobertB2@chw.edu.au>		

	Togo	Bradford Gessner <bgessner@aamp.org> Jennifer Moisi <jmoisi@aamp.org>		
	Zambia	Don Thea < dthea@bu.edu > ***(Note: no ongoing evaluations of PCV in Zambia)***		
AMRO	Argentina	Maria Luisa Avila <avilaaguero@gmail.com> Lucia Helena de Oliviera <oliveiral@who.int>	- Tregnaghi MW (CEDEPAP, Córdoba, Argentina) - A. Urueña <anauru@yahoo.com>	1. http://www.ncbi.nlm.nih.gov/pubmed/24892763 2. http://www.ncbi.nlm.nih.gov/pubmed/21621575
	Brazil	Carla Domingues <carla.domingues@saude.gov.br> Maria Luisa Avila <avilaaguero@gmail.com> Lucia Helena de Oliviera <oliveiral@who.int>	- Carla Domingues <Carla.domingues@saude.gov.br> - Ana Lucia Andrade <ana@iptsp.ufg.br> - G. Vespa (Escola Paulista de Medicina, Universidade Federal de São Paulo)	1. http://www.ncbi.nlm.nih.gov/pubmed/24726406 2. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3647414/ 3. http://www.ncbi.nlm.nih.gov/pubmed/24892409 4. http://www.ncbi.nlm.nih.gov/pubmed/25760162 5. http://www.ncbi.nlm.nih.gov/pubmed/20107706
	Canada	Jim Kellner <jim.kellner@calgaryhealthregion.ca>	- Philippe De Wals <Philippe.De.Wals@ssss.gouv.qc.ca> - Gillian Lim <Gillian.lim@oahpp.ca> - Stephanie Earnshaw <searnshaw@rti.org>	1. http://www.ncbi.nlm.nih.gov/pubmed/18845982 2. http://www.ncbi.nlm.nih.gov/pubmed/20125062 3. http://www.ncbi.nlm.nih.gov/pubmed/22921290 4. http://www.ncbi.nlm.nih.gov/pubmed/24486346 5. http://www.ncbi.nlm.nih.gov/pubmed/25887086 6. http://www.ncbi.nlm.nih.gov/pubmed/24313450 7. http://www.ncbi.nlm.nih.gov/pubmed/23597716 8. http://www.ncbi.nlm.nih.gov/pubmed/22530841
	Chile	Rosana Lagos <rosanna.lagos@adsl.tie.cl> Maria Luisa Avila <avilaaguero@gmail.com> Lucia Helena de Oliviera <oliveiral@who.int>	- Rosana Lagos < rosanna.lagos@adsl.tie.cl>	1. http://www.ncbi.nlm.nih.gov/pubmed/18959497 2. http://www.ncbi.nlm.nih.gov/pubmed/25679919
	Colombia	Maria Luisa Avila <avilaaguero@gmail.com> Lucia Helena de Oliviera <oliveiral@who.int>	- MW Tregnaghi - GSK Vaccines (Panama City & Bueños Aires Teams)	1. http://www.ncbi.nlm.nih.gov/pubmed/24892763
	Costa Rica	Maria Luisa Avila <avilaaguero@gmail.com> Lucia Helena de Oliviera <oliveiral@who.int>	- A. Arguedas <aarguedas@iped.net>	1. http://www.ncbi.nlm.nih.gov/pubmed/22300725
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	Nicaragua	Maria Luisa Avila <avilaaguero@gmail.com> Lucia Helena de Oliviera <oliveiral@who.int>	- S. Becker-Dreps <sbd@unc.edu>	1. http://www.ncbi.nlm.nih.gov/pubmed/24445827 2. http://www.ncbi.nlm.nih.gov/pubmed/25444795
	Panama	Maria Luisa Avila <avilaaguero@gmail.com> Lucia Helena de Oliviera <oliveiral@who.int>	- M.W. Tregnaghi	1. http://www.ncbi.nlm.nih.gov/pubmed/24892763
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	Peru	Maria Luisa Avila <avilaaguero@gmail.com> Lucia Helena de Oliviera <oliveiral@who.int>	- M.W. Tregnaghi	1. http://www.ncbi.nlm.nih.gov/pubmed/24171921
	United States	Cyndy Whitney <cgw3@cdc.gov> Farrar, Jennifer Loo <ihi4@cdc.gov>	- Sandra Richter (Cleveland Clinic) - R. Singleton <Ris2@cdc.gov> - P.P. Gounder (CDC) - L. Simonson <lone@gwu.edu> - Matt Moore <matt.moore@cdc.hhs.gov> - C. Stoecker <cfstoecker@tulane.edu> - Jaime Rubin <jaime.rubin@i3innovus.com>	1. http://wwwnc.cdc.gov/eid/article/19/7/12-1830_article 2. http://www.ncbi.nlm.nih.gov/pubmed/23001026 3. http://www.ncbi.nlm.nih.gov/pubmed/24273178 4. http://www.ncbi.nlm.nih.gov/pubmed/21264063 5. http://www.ncbi.nlm.nih.gov/pubmed/24815804 6. http://www.thelancet.com/journals/laninf/article/PIIS1473-3099(14)71081-3/fulltext?rss=yes 7. http://www.ncbi.nlm.nih.gov/pubmed/23821695

				8. http://www.ncbi.nlm.nih.gov/pubmed/20883739
	Uruguay	Maria Luisa Avila <avilaaguero@gmail.com> Lucia Helena de Oliviera <oliveiral@who.int>	- García Gabarrot G: Departamento de Laboratorios, Ministerio de Salud Pública, Montevideo, Uruguay. - Maria Hortal: <marujahortal@gmail.com> - Maria Pirez <mcpirez@yahoo.com> - Teresa Camou <tcamou@msp.gub.uy>	1. http://www.ncbi.nlm.nih.gov/pubmed/25375647 2. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4048159/ 3. http://www.ncbi.nlm.nih.gov/pubmed/22664222 4. http://www.ncbi.nlm.nih.gov/pubmed/24492286 5. http://www.ncbi.nlm.nih.gov/pubmed/25375647
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	Denmark	Ziita Harboe <ZIT@ssi.dk>	- Helene Ingels (Statens Serum Institut) <HIG@ssi.dk>, <helene ingels@yahoo.dk>	1. http://www.ncbi.nlm.nih.gov/pubmed/22504662 2. http://www.ncbi.nlm.nih.gov/pubmed/25034421
	Finland	Jukka Jokinen <jukka.jokinen@thl.fi>	- Arto Palmu <arto.palmu@thl.fi> - Jukka Jokinen <jukka.jokinen@thl.fi>	1. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4364013/ 2. http://www.ncbi.nlm.nih.gov/pubmed/23158882
	France	Robert Cohen < robert.cohen@wanadoo.fr>	- Robert Cohen <robert.cohen@wanadoo.fr> - F. Angoulvant (Groupe de Pathologie Infectieuse Pédiatrique, Société Francaise de Pédiatrie) - C. Alexandre (Department of Paediatrics, Paediatric Emergency Unit and Infectious Diseases, Université Lille Nord-de-France, Lille, France)	1. http://www.ncbi.nlm.nih.gov/pubmed/22330166 2. http://www.ncbi.nlm.nih.gov/pubmed/24532543 3. http://www.ncbi.nlm.nih.gov/pubmed/20626365
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	Israel	Ron Dagan <rdagan@bgu.ac.il>	- G. Regev <gregev@hsph.harvard.edu> - S. Ben-Shimol (University of Negev)	1. http://www.ncbi.nlm.nih.gov/pubmed/23518404 2. http://www.ncbi.nlm.nih.gov/pubmed/24516649 3. http://www.ncbi.nlm.nih.gov/pubmed/25159581 4. http://www.ncbi.nlm.nih.gov/pubmed/25764098
	Italy	F. D'Ancona V. Alfonsi M. Caporali	- R. Camilli (Dipartimento di Malattie Infettive, Parassitarie ed Immunomediate, Istituto Superiore di Sanità)	1. http://www.ncbi.nlm.nih.gov/pubmed/24124543
	Netherlands	Lieke Sanders <L.Sanders@umcutrecht.nl>	- Marie-Josée J <m.j.j.mangen@umcutrecht.n> - Gerwin Rodenburg <g.d.rodenburg@umcutrecht.nl>	1. http://erj.ersjournals.com/content/early/2015/07/09/13993003.00325-2015.full 2. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2953990/
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	Mongolia	Kim Mulholland Kim.Mulholland@lshtm.ac.uk		
	New Zealand	David Goldblatt <d.goldblatt@ucl.ac.uk>	- E. Lim, H. Heffernan - Adrian Trenholme <Adrian.Trenholme@middlemore.co.nz>	1. https://surv.esr.cri.nz/PDF_surveillance/IPD/2012/2012AnnualIPDRpt.pdf 2. http://www-ncbi-nlm-nih-gov.ezp.welch.jhmi.edu/pubmed/24045313
	Papua New Guinea	Kim Mulholland <Kim.Mulholland@lshtm.ac.uk>		

Note: Table excludes publications reporting ONLY on PCV7 and those reporting on any experimental PCV product that did not move forward for licensure (e.g. PCV9).
*Table has not systematically included publications after 2010 (date of Landscape Dosing review); publications from 2010-2015 have been included based on extensive literature reviews of PubMed and other databases, but should not be considered 100% comprehensive. An update of the systematic review to identify and include all publications in future gap analyses is ongoing.