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Invasive Pneumococcal Disease Due to Serotypes in Pneumococcal Conjugate Vaccines in Children of High-Income Countries

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BACKGROUND

- The serotype distribution of invasive pneumococcal disease (IPD) often drives the decision of which pneumococcal conjugate vaccine (PCV) a country will include in the national immunization program (NIP).
- The objective of this analysis is to estimate the percentage of IPD due to serotypes in the available 10-valent PCV (PCV10) and 13-valent PCV (PCV13) and in the investigational 15-valent PCV (PCV15) and 20-valent PCV (PCV20).

METHODS

- We analyzed IPD cases by serotype from children ≤5 years old from high-income countries. Country-specific IPD data were obtained from national, regional, or sentinel surveillance systems or from hospital networks. Up to the 3 most recent years of publicly reported data from peer-reviewed publications, online reports, and databases were included in the analysis. More than one source of data could be included for each country. Excluded countries reported <20 cases overall or only reported data prior to pediatric PCV introduction into the NIP **(Figure 1)**.
- The percent of IPD due to vaccine serotypes was calculated for PCV10 (serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, and 23F); PCV13 (PCV10-types and serotypes 3, 6A, and 19A), plus 6C, which is structurally highly related to 6A; PCV15 (PCV13-types and serotypes 22F and 33F) plus 6C; and PCV20 (PCV15-types and serotypes 8, 10A, 11A, 12F, and 15B), plus 6C and 15C, which is structurally highly related to 15B.
- Cases of IPD with missing serotype information or those non-typeable were excluded from the total count of IPD cases. If more than 1 year of data were reported, the percentage of IPD due to PCV serotypes was simply averaged over the total number of years reported. The percentage of IPD was reported for countries grouped by PCV use in the pediatric NIP.

Figure 1. Country inclusion flow diagram

Inclusion criteria	Number of countries meeting criteria
High-income country based on World Bank definitions	n=80
IPD surveillance system or hospital network identifying cases of IPD[a]	n=42
Publicly available data[b]	n=40
If PCV in NIP, data reported after PCV introduction[c]	n=38
>20 cases identified, and serotype data reported[d]	n=27

[a] n=38 excluded due to no surveillance system or hospital network reporting IPD cases.
[b] n=2 excluded (Israel and Taiwan).
[c] n=2 excluded (Portugal and Croatia).
[d] n=7 excluded (Cyprus, Greece, Luxembourg, Malta, Switzerland, Belgium, and Panama).

RESULTS

Country and case inclusion

- The 27 high-income countries that met the criteria for inclusion reported approximately 8,500 cases of IPD with a serotype identified in children ≤5 years old.
- The majority of countries introduced PCV10 or PCV13 into the country NIP >5 years prior to the beginning of the data reporting period included in this analysis. PCV10 was used in 7 (25.9%) countries, PCV13 in 17 (63.0%) countries, and both PCV10 and PCV13 in 3 (11.1%) countries. Most countries (74.1%) used a 2+1 schedule **(Table 1)**.

Percentage of IPD due to vaccine serotypes by country pediatric NIP PCV use

- The percentage of IPD due to vaccine serotypes varied substantially across countries regardless of the PCV used and the number of years between the start of pediatric NIP PCV use and the beginning of the data-reporting period that was included in the analysis **(Table 2)**.
  - Countries with PCV10 only in the pediatric NIP: the percentage of IPD due to serotypes in PCV10, PCV13, PCV15, and PCV20 ranged from 0% to 56.1%, 24.3% to 77.8%, 28.0% to 79.9%, and 43.9% to 93.3%, respectively.
  - Countries with PCV13 only in the pediatric NIP: the percentage of IPD due to serotypes in PCV10, PCV13, PCV15, and PCV20 ranged from 0% to 33.3%, 3.9% to 72.4%, 8.1% to 72.4%, and 39.4% to 93.1%, respectively.
  - Countries with PCV10 and PCV13 in the pediatric NIP: the percentage of IPD due to serotypes in PCV10, PCV13, PCV15, and PCV20 ranged from 0% to 31.5%, 17.4% to 77.4%, 23.9% to 82.1%, and 71.7% to 91.1%, respectively.

Prevalent vaccine serotypes

- Serotype 3 ranked among the top 3 PCV serotypes in most countries.
- Serotype 19A ranked among the top 3 PCV serotypes in countries using PCV10 regardless of region, schedule, or the number of years between PCV introduction and the beginning of the time period of data included in the analysis.
- In countries with PCV13 only in the NIP, serotypes 8, 10A, 12F, 15B/C, and 22F were commonly identified regardless of schedule or the number of years between PCV introduction and the beginning of the time period of the data included in the analysis.

RESULTS (continued)

Table 1. Country characteristics and pneumococcal vaccine use

Country	WHO region	Surveillance system (type) or hospital network (n hospitals)	NIP pediatric schedule[a]	Year PCV introduced into pediatric NIP	PCV used during years of data reported in the analysis	Year PCV use began relevant to years of data reported in the analysis
Australia	WPRO	National, passive, mandatory	3+0[b]	2005	PCV13	2011
Austria	EURO	National, passive, mandatory	2+1	2002	PCV10	2012[c]
Belgium	EURO	Sentinel, passive, voluntary	2+1	2007	PCV10	2015 (Flanders region), 2016 (Wallonia region)[d]
Canada	AMRO	Multi-provincial, passive, voluntary	2+1	2002–2006 depending upon province	PCV13	2010[e]
Chile	AMRO	Laboratory based	2+1	2011	PCV10	2011[f]
Czech Republic	EURO	National, active, mandatory	3+1[g]	2005	PCV10, PCV13	2009 (PCV10), 2010 (PCV13)
Denmark	EURO	National, passive, mandatory	2+1	2007	PCV13	2010
England & Wales	EURO	National, passive, mandatory	2+1[h]	2006	PCV13	2010
Finland	EURO	National, passive, mandatory	2+1	2010	PCV10	2010
France	EURO	National, active, voluntary	2+1	2006	PCV13	2010
Germany	EURO	National, active, mandatory	2+1[i]	2006	PCV10, PCV13	2009, 2010
Hong Kong	WPRO	National, passive, mandatory	3+1[j]	2010	PCV13	2011
Ireland	EURO	National, passive, mandatory	2+1	2008	PCV13	2010
Italy	EURO	National, passive, voluntary	2+1	2005	PCV13[k]	2010
Japan	WPRO	Hospital network (n=341)	3+1	2011	PCV13	2013
Netherlands	EURO	Sentinel, passive, voluntary	2+1	2006	PCV10	2011
New Zealand	WPRO	National, passive, mandatory	3+1	2008	PCV13	2014[l]
Norway	EURO	National, passive, mandatory	2+1	2006	PCV13	2011
Panama	AMRO	Laboratory based	2+1	2010	PCV13	2011
Poland	EURO	National, passive, mandatory	2+1	2017	PCV10	2017[m]
Singapore	WPRO	National, passive, mandatory	2+1	2009	PCV13	2011
Slovakia	EURO	National, active, mandatory	2+1	2009	PCV10, PCV13	2010
Slovenia	EURO	National, passive, mandatory	2+1	2005	PCV10[n]	2015
South Korea	WPRO	Hospital network (n=44)	3+1	2014	PCV10, PCV13	2014
Spain	EURO	Regional, passive, mandatory	2+1	2001	PCV13	2015
Sweden	EURO	National, passive, mandatory	2+1	2009	PCV10, PCV13[o]	2010
United States	AMRO	Sentinel, passive, mandatory	3+1	2001	PCV13	2010

AMRO: Americas Region; EURO: European Region; NIP: national immunization program; PCV: pneumococcal conjugate vaccine; PCV10: 10-valent pneumococcal conjugate vaccine; PCV13: 13-valent pneumococcal conjugate vaccine; WHO: World Health Organization; WPRO: Western Pacific Region.
[a] PCV schedule information accessed on International Vaccine Access Center ViewHub (https://view-hub.org/).
[b] In Australia, a 3+0 schedule was used during the years of data included in this analysis (2016–2018). In 2018, Australia switched from a 3+0 to a 2+1 schedule.
[c] In Austria, PCV10 was used during the years of data included in this analysis (2016–2018). Austria switched to PCV13 in 2020.
[d] In Belgium, PCV10 was used in both the Flanders and Wallonia regions during the years of data included in this analysis (2016–2018). The Flanders region switched from PCV13 to PCV10 in July 2015, and the Wallonia region (includes Brussels) switched from PCV13 to PCV10 in May 2016. Both regions switched back from PCV10 to PCV13, Wallonia in late 2018 and Flanders in July 2019.
[e] In Canada, PCV10 was used from 2009 to 2010 in 2 provinces.
[f] In Chile, PCV10 was used during the years of data included in this analysis (2014–2015). Chile switched from PCV10 to PCV13 in 2017.
[g] In the Czech Republic, a 3+1 schedule was used during the years of data included in this analysis (2016–2018). In 2018, they switched to a 2+1 schedule. Both PCV10 and PCV13 are recommended and estimates of PCV coverage do not differentiate between use of PCV10 and PCV13.
[h] England and Wales switched to a 1+1 schedule in 2020.
[i] In Germany, PCV13 is used primarily. In 2015, Germany switched from a 3+1 to a 2+1 schedule.
[j] In Hong Kong, a 3+1 schedule was used during the year of data included in this analysis (2018). They switched from a 3+1 to a 2+1 schedule in July 2019.
[k] The Piemonte region of Italy switched from PCV13 to PCV10 in 2018. The other regions continue to use PCV13.
[l] New Zealand switched from PCV7 to PCV10 in 2011, to PCV13 in 2014 (the year marking the beginning of data included in this analysis), and to PCV10 in 2017.
[m] In Poland, serotype data were available from 2016–2017; however, these years of data were excluded from the analysis because they were prior to introduction of PCV10 in the NIP.
[n] Slovenia switched from PCV10 to PCV13 in 2019.
[o] In Sweden, both PCV10 and PCV13 are recommended; however, PCV10 is primarily used.

Table 2: Percentage of IPD due to vaccine serotypes among children

Country	Age group	Data reporting period[a]	Years between start of PCV use and beginning of data reporting period	Total IPD cases with a serotype identified[b]	Percentage of IPD serotypes due to vaccine serotypes				Top 3 vaccine serotypes	Data source
					PCV10	PCV13	PCV15	PCV20		
Countries with pediatric NIP use of PCV10										
Austria	<1 y	2016–2018	4	26	9.5%	70.7%	75.5%	93.3%	19A; 3; 10A	3
Austria	1–4 y	2016–2018	4	59	14.4%	35.1%	37.2%	43.9%	3; 19A; 1, 4, 7F, 23F, 15B	3
Austria	<5 y	2017–2018	4	76	14.5%	53.9%	57.9%	72.4%	3, 19A; 6C; 10A	17
Belgium	<2 y	2016–2018	1 (PCV10), 0 (PCV13)	534	3.7%	30.0%	38.8%	61.6%	19A, 12F, 33F	1
Chile	<5 y	2014–2015	3	281	20.3%	62.6%	66.2%	73.0%	19A; 3; 1, 14	2
Finland	<1 y	2016–2018	6	23	15.0%	57.5%	61.7%	83.3%	19A; 15B; 3	3
Finland	1–4 y	2016–2018	6	75	0.0%	74.3%	79.9%	86.6%	19A; 3; 6C	3
Finland	<5 y	2017–2019	7	86	1.2%	72.1%	75.6%	82.6%	19A; 3; 6C	4
Netherlands	<1 y	2016–2018	5	21	10.3%	51.8%	66.3%	86.9%	19A; 33F; 8	3
Netherlands	1–4 y	2016–2018	5	22	24.9%	35.7%	42.4%	58.6%	1; 19A, 23F, 33F; 6C, 18C, 8, 11A, 15C	3
Slovenia	1–4 y	2016–2018	1	88	56.1%	77.8%	78.8%	87.0%	14; 19A; 1	3
Sweden	<1 y	2016–2018	6	27	7.4%	24.3%	28.0%	63.5%	10A; 8; 19A	3
Sweden	1–4 y	2016–2018	6	75	6.5%	38.7%	46.0%	63.7%	19A; 6C; 22F	3
Countries with pediatric NIP use of PCV13										
Australia	<5 y	2016–2018	5	1112	9.4%	46.9%	55.7%	71.3%	3; 19A; 19F	5
Canada	<5 y	2015–2017	5	641	4.4%	19.5%	39.3%	63.5%	15B; 22F; 33F	6
Denmark	<1 y	2016–2018	6	28	6.7%	18.9%	24.4%	81.1%	8; 12F; 10A	3
Denmark	1–4 y	2016–2018	6	38	0.0%	6.7%	12.0%	39.4%	12F; 15C; 33F	3
England and Wales	<1 y	2016–2018	6	435	2.7%	16.6%	26.8%	68.7%	8; 10A; 3	3
England and Wales	1–4 y	2016–2018	6	521	2.4%	14.0%	25.4%	68.3%	12F; 10A; 15BC	3
England and Wales	<5 y	July 2016–June 2017	6	527	1.9%	15.2%	24.1%	74.8%	12F; 8; 10A	8
France	<1 y	2016–2018	6	351	7.6%	17.0%	25.0%	53.6%	8; 10A; 3	3
France	1–4 y	2016–2018	6	464	2.3%	12.0%	19.8%	45.5%	12F; 10A; 3	3
France	<5 y	2013, 2015, 2017	3	568	7.2%	18.1%	26.9%	55.8%	15BC; 12F; 19A	9
Germany	<2 y	July 2015–June 2018	5	310	5.2%	16.8%	25.5%	53.5%	10A; 3; 12F	18
Hong Kong	<5 y	2018	7	29	13.8%	72.4%	72.4%	93.1%	3; 15C; 15B, 19A	10
Ireland	<1 y	2016–2018	3	43	8.1%	24.0%	35.1%	55.3%	19A; 10A; 33F	3
Ireland	1–4 y	2016–2018	3	88	2.1%	15.7%	26.5%	51.0%	12F; 19A; 22F	3
Italy	<1 y	2016–2018	6	74	3.9%	3.9%	8.1%	39.9%	8; 10A, 11A, 15B; 19F	3
Italy	1–4 y	2016–2018	6	136	9.6%	18.4%	25.1%	63.2%	12F; 10A; 3	3
Italy	<5 y	2015–2017	5	133	7.5%	15.8%	23.3%	64.7%	12F; 15B; 22F	11
Japan	<5 y	April 2014–March 2016	1	348	7.8%	20.4%	30.7%	58.6%	19A; 12F; 22F	12
New Zealand	<5 y	2014–2016	0	108	6.5%	37.0%	52.8%	72.2%	19A; 3; 33F	13
Norway	<1 y	2016–2018	5	20	13.1%	28.2%	48.0%	66.7%	3; 22F; 33F	3
Norway	1–4 y	2016–2018	5	41	6.6%	27.9%	36.8%	54.2%	19A; 15B; 22F	3
Panama	<5 y	2014–2015	3	26	7.7%	30.8%	30.8%	42.3%	19A; 3; 19F, 23F, 8, 15B, 15C	2
Poland	<5 y	2018	1	75	33.3%	66.7%	68.0%	84.0%	3; 14; 19A	14
Singapore	<5 y	2015–2017	4	27	18.5%	70.4%	70.4%	70.4%	19A; 3; 6B, 14	15
Spain	<1 y	2016–2018	1	198	11.4%	29.0%	34.8%	62.9%	8; 3; 19A	3
Spain	1–4 y	2016–2018	1	367	11.1%	29.2%	36.5%	62.7%	3; 12F; 8	3
United States	<5 y	2015–2016	5	298	6.7%	19.5%	36.2%	58.7%	22F, 33F; 15C; 3	16
Countries with pediatric NIP use of PCV10 and PCV13										
Czech Republic	1–4 y	2016–2018	7 (PCV10), 8 (PCV13)	37	3.7%	58.1%	60.6%	66.9%	3; 19A; 6A, 15C	3
Czech Republic	<5 y	2016–2018	7 (PCV10), 8 (PCV13)	62	1.6%	45.2%	46.8%	56.5%	3; 19A; 6A, 8, 15C	7
Slovakia	1–4 y	2016–2018	6	22	31.5%	77.4%	82.1%	91.1%	19A; 1; 8	3
South Korea	≤5 y	May 2014–May 2016	0	46	0.0%	17.4%	23.9%	71.7%	10A; 15B; 19A	19

IPD: invasive pneumococcal disease; PCV: pneumococcal conjugate vaccine; PCV10: 10-valent pneumococcal conjugate vaccine; PCV13: 13-valent pneumococcal conjugate vaccine; PCV15: 15-valent pneumococcal conjugate vaccine; PCV20: 20-valent pneumococcal conjugate vaccine.
[a] Reported as calendar years unless otherwise specified.
[b] Excludes cases with a missing or non-typeable isolate serotype result.

CONCLUSIONS

- **Compared with the available PCVs (PCV10 and PCV13), the percentage of IPD due to PCV15 and PCV20 serotypes was higher, with PCV20 serotypes accounting for the highest percentage of IPD among children in high-income countries.**

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DATA SOURCE

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