

GLOBAL SEROTYPE DISTRIBUTION OF INVASIVE PNEUMOCOCCAL DISEASE IN OLDER CHILDREN AND ADULTS: AGEDD STUDY

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INTRODUCTION

- Global serotype distribution of IPD in adults and children ≥5 years of age pre-pneumococcal conjugate vaccine (PCV) introduction has not been described.
- These data are essential to project the potential impact of PCV through direct & indirect effects of vaccination.
- The objective of the Adult Global Estimation of Disease Burden and Distribution of Serotypes of Serious Pneumococcal and Meningococcal disease (AGEDD) project is to estimate the global & regional morbidity, mortality, and serotype/serogroup distribution of invasive pneumococcal disease (IPD) in older children and adults (and of meningococcal disease in all ages) through a systematic review of published and unpublished data.
- Here we estimate the proportion of IPD due to PCV serotypes prior to PCV introduction into national immunization programs by geographic region and age group ≥5 years.**

METHODS

- Systematic literature review of 16 databases identified studies conducted 1980-2010 reporting IPD cases ≥ 5 years of age with IPD serotype/serogroup.
- Additionally, we abstracted data from national surveillance reports from Australia, Canada, New Zealand, South Africa, United States, and several European countries not identified in the literature search.
- Exclusion criteria:**
 - <20 serotyped pneumococcal isolates
 - >10% of pneumococcal isolates from sputum samples
 - Data were from Post PCV introduction
- Isolates reporting serogroups only (e.g., SG 6) were apportioned into serotypes (e.g., ST 6A, 6B, 6C) using ratios from studies in the same region/age stratum
- Analysis was stratified by age in years: 5-17, 18-64, 65+
- Random-effects meta-analysis was used to estimate the average serotype proportion within region/age group, normalizing across all serotypes to 100%.
- Proportion of PCV-types² was estimated by summing individual serotype proportion meta-estimates. PCV7 & PCV10 assume cross-protection against 6A.

RESULTS

- 69,897 isolates (>2400 in each region) were available from IPD cases ≥5 years from 74 studies in 54 countries.
- Age-group specific serotype data were sparse in Africa and Asia, especially from adults over age 20 years (TABLE 1)
- Top 10 serotypes accounted for 55-85% of all IPD in each region/age strata.
- Rank order of top serotypes in each region varied by age (TABLE 2).
 - STs 1 & 5 were less important in adults 65+ than in younger age groups.
 - STs 3, 4, 14, and 23F were most prominent among 65+ in all regions.
 - STs 1, 5, 14, 18C and 23F were most prominent among 5-17 year olds.
 - STs were diverse across regions in 18-64 yo: Top 2 STs include 1, 4, 5, 8, 9V & 14.
- Africa and Asia had same top 5 STs in 5-17 year age group but were more diverse in 18-64 year age group (shared only 2 STs in top 5).
- PCV10/13/15 serotypes² accounted for ≥50% of IPD in all regions in all age groups (FIGURE 1).
- PCV13 included ~8-12% more IPD serotypes than PCV10 in age/region strata, with ST3 more important than ST19A in older age groups. (FIGURES 1 & 2)

CONCLUSIONS

- IPD serotype data in older children and adults were available in all regions but the amount of data was limited in Africa and Asia, particularly for those >65 years, and for non-PCV serotypes in Africa and LAC in all ≥5 age strata.
- While there was diversity in the rank order of serotypes by both age and region, serotypes included in PCV10 and PCV13 accounted for a substantial proportion (>50%) of IPD in all age strata ≥5 years in every region.
- Serotype 1 was less important in adults >65 years and ST3 was relatively more important compared to younger ages. ST14, a common pediatric serotype in all regions, was more prominent in adults >65 years than in younger adults.
- If current and future PCV products induce indirect effects for IPD among adults as has been observed for PCV7, we expect there to be no more than a 50% reduction in IPD rates among those ≥5 years in all regions of the world. Substantially more impact will necessitate additional strategies to reduce the IPD burden in those ≥5 years.

Table 1. Data availability of invasive pneumococcal STs

Region	5 – 17 year olds		18 – 64 year olds		≥ 65 year olds		≥ 5 years old	
	Studies (Countries ¹)	Isolates (Serotypes)	Studies (Countries)	Isolates (Serotypes)	Studies (Countries)	Isolates (Serotypes)	Studies (Countries)	Isolates (Serotypes)
AFRICA	1 (1)	63 (10)	1 (1)	72 (14)	---	---	6 (4)	4,591 (30)
ASIA	4 (4)	625 (50)	1 (1)	57 (24)	1 (1)	85 (10)	21 (12)	2,369 (62)
EUROPE	5 (4)	1,006 (30)	2 (2)	7,362 (46)	4 (4)	14,355 (45)	20 (15)	38,618 (69)
LAC	14 (14)	2,949 (13)	13 (13)	6,114 (15)	11 (11)	3,013 (13)	19 (18)	14,161 (29)
N. AMERICA*	1 (1)	109 (26)	2 (2)	910 (43)	2 (2)	693 (43)	4 (2)	2,401 (60)
OCEANIA*	1 (1)	408 (19)	1 (1)	2,677 (23)	2 (2)	3,244 (20)	4 (3)	7,757 (27)

*Includes national surveillance database

Table 2. Top 10 serotypes by region and age

Rank	Age 5-17 years						Age 18 ≥ -64 years						Age >65 years					
	Africa	Asia	Europe	N. Amer.	LAC*	Oceania	Africa	Asia	Europe	N. Amer.	LAC*	Oceania	Africa	Asia	Europe	N. Amer.	LAC*	Oceania
1	1	1	1	14	1	18C	1	1	4	9V	14	4	No data	23F**	14	14	14	14
2	5	5	18C	18C	14	14	5	4	8	4	1	14		3	4	3	3	4
3	23F	23F	23F	23F	5	4	6B	23F	14	23F	8	9V		14	3	23F	1	9V
4	14	19F	19F	19F	19F	19F	9V	3	3	14	3	6B		4	9V	4	6B	23F
5	19F	14	7F	4	6B	9V	23F	19A	19F	3	7F	23F		6A	23F	22F	19F	6B
6	6A	18C	6A	19A	18C	19A	4	12F	1	6B	5	19F		6B	1	9V	7F	19F
7	19A	6B	3	6B	23F	23F	19A	19F	6A	19F	23F	3		19A	6B	6A	5	3
8	4	7F	8	9V	19A	1	19F	46	9V	22F	19F	22F		19F	9N	6B	23F	22F
9	18A	9A	14	12F	6A	6B	14	18C	7F	12F	6B	18C		22F**	8	12F	6A	19A
10	18C	19A	9V	3	3	22F	9A	5	23F	6A	6A	19A		9V**	22F	19F	9V	18C
Top 10 (%)	84.7	69.8	56.7	71.3	73.2	64.8	66.6	65.8	63.9	65.9	54.8	67.1	82.3	58.1	69.3	60.0	71.6	

*Most LAC data available only for PCV-15 STs. **Serogroup was not subtyped but other subtypes observed were <1% in this region for other age groups and in other regions for this age group.

1 Countries with age-stratified serotype data

5-17 Years

Africa* – Gambia;
 Asia – China, Israel, Taiwan, and Turkey;
 Europe – Croatia, France, Slovenia, United Kingdom;
 Latin American and the Caribbean (LAC) – Argentina, Bolivia, Brazil, Chile, Colombia, Cuba, Ecuador, Mexico, Panama, Paraguay, Peru, Dominican Republic, Uruguay, Venezuela;
 North America – United States;
 Oceania – Australia

18-64 Years

Africa* – Gambia;
 Asia – Thailand;
 Europe – Czech Republic and United Kingdom;
 LAC – Argentina, Bolivia, Brazil, Chile, Colombia, Cuba, Ecuador, Mexico, Panama, Paraguay, Dominican Republic, Uruguay, Venezuela;
 North America – Canada and United States;
 Oceania – Australia and New Zealand

65+ Years

Africa*
 Asia – Taiwan;
 Europe – Czech Republic, Denmark, Norway, and United Kingdom;
 LAC – Argentina, Bolivia, Brazil, Chile, Colombia, Cuba, Mexico, Panama, Paraguay, Uruguay, Venezuela;
 North America – Canada and United States;
 Oceania – Australia, New Zealand, Papua New Guinea

*Note: age-stratified adult data exist for South Africa and Kenya but were not available at the time of this analysis.

2 PCV serotypes:

PCV7 = 4, 6B, 9V, 14, 18C, 19F, 23F (+6A cross-protection)
 PCV10 = PCV7 + 1, 5, 7F
 PCV13 = PCV10 + 3, 6A, 19A
 PCV15 = PCV15 + 22F, 33F

Figure 1. Proportion of serotypes included in pneumococcal conjugate vaccines by region and age

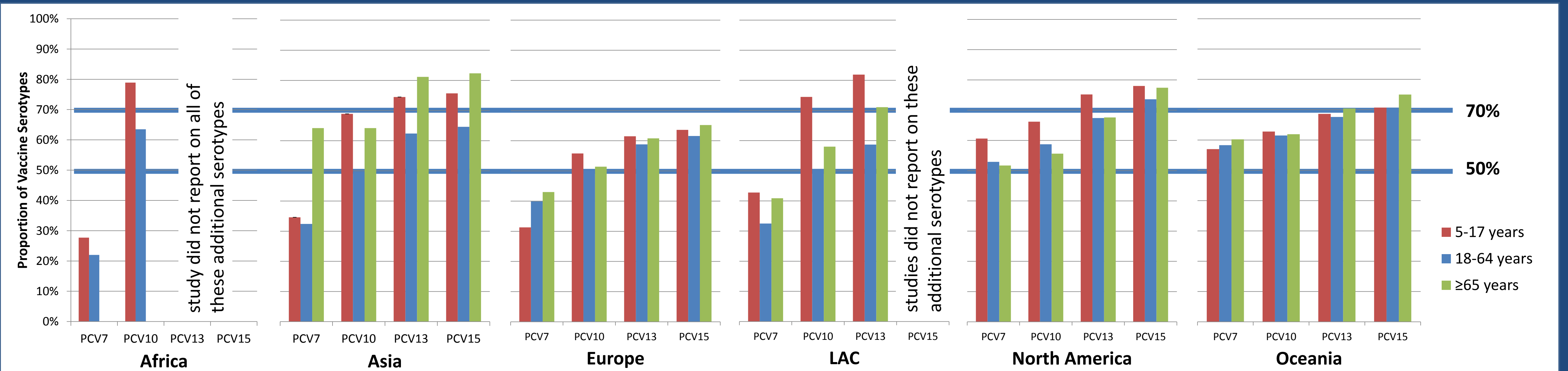


Figure 2. Proportion of select PCV serotypes by region and age

