

GPS

Global Pneumococcal Sequencing Project

Continued surveillance of invasive pneumococcal disease in African countries is needed to guide optimal vaccine design

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Background

Despite the success of Pneumococcal Conjugate Vaccines (PCVs), invasive pneumococcal disease (IPD) remains an important health priority with an increasing proportion of IPD caused by non-vaccine serotypes (NVTs). We investigated the changes in prevalent serotypes causing IPD and identified underlying lineages among children ≤ 2yr surrounding PCV introductions in South Africa, Malawi and The Gambia, drawing comparisons with the USA.

Methods

- Bacterial collection:** Randomly selected IPD isolates were collected at least 2 years before and after the introduction of PCV13 from South Africa, Malawi, The Gambia, and the USA (Table 1).
- Processing of data:** Serotype was inferred from genome sequences using SeroBA and **pneumococcal lineage** was designated as per abstract ISPPD-0286 described.

Results

1. The most common cause of IPD in children ≤ 2 years old were NVT pneumococci 2-5 years after PCV13 introduction (Table 1)

Table 1. The prevalent serotypes causing IPD in children ≤ 2 years old from the USA, South Africa, Malawi, and The Gambia

Country	USA	South Africa	Malawi	The Gambia
n	674	1351	226	172
Source				
Blood	626	916	118	117
CSF	31	394	108	27
Other sites	17	42	0	28
Vaccine period				
Pre-PCV	1998-1999	2005-2009	1997-2011	1996-2009
PCV7	2001-2009	2010-2011	-	2010-2011
PCV13	2012	2013-2014	2014-2015	2013-2014
Five most prevalent serotypes^a				
Pre-PCV	14, 18C, 19F ⁴ , 6A/6B/9V	14, 23F, 6B, 19F	5' 23F, 6B' 6A, 1	1, 5, 14' 23F, 6B
PCV7	19A, 7F, 22F , 33F , 15B/C	19A, 6A, 14, 19F, 23F	-	1, 5, 12F, 6B
PCV13	15B/C, 22F , 19A 33F, 12F	8, 12F, 15B/C , 35B, 16F	35B	12F, 1, 24, 11B, 15B/C

^aThe non-vaccine serotypes are written in red.
Serotypes with < 2 isolates are not listed.

Conclusions

We show differences in serotypes and lineages between countries. Compared to the pre-PCV periods when only a few VTs were predominant, increasing serotype diversity suggests a larger number of serotypes circulating with relatively even distribution post-PCV13. Continued surveillance is needed to help guide future vaccine formulation.

2. Comparison of top five serotypes and their associated lineages following PCV13 introduction (Figure 1)

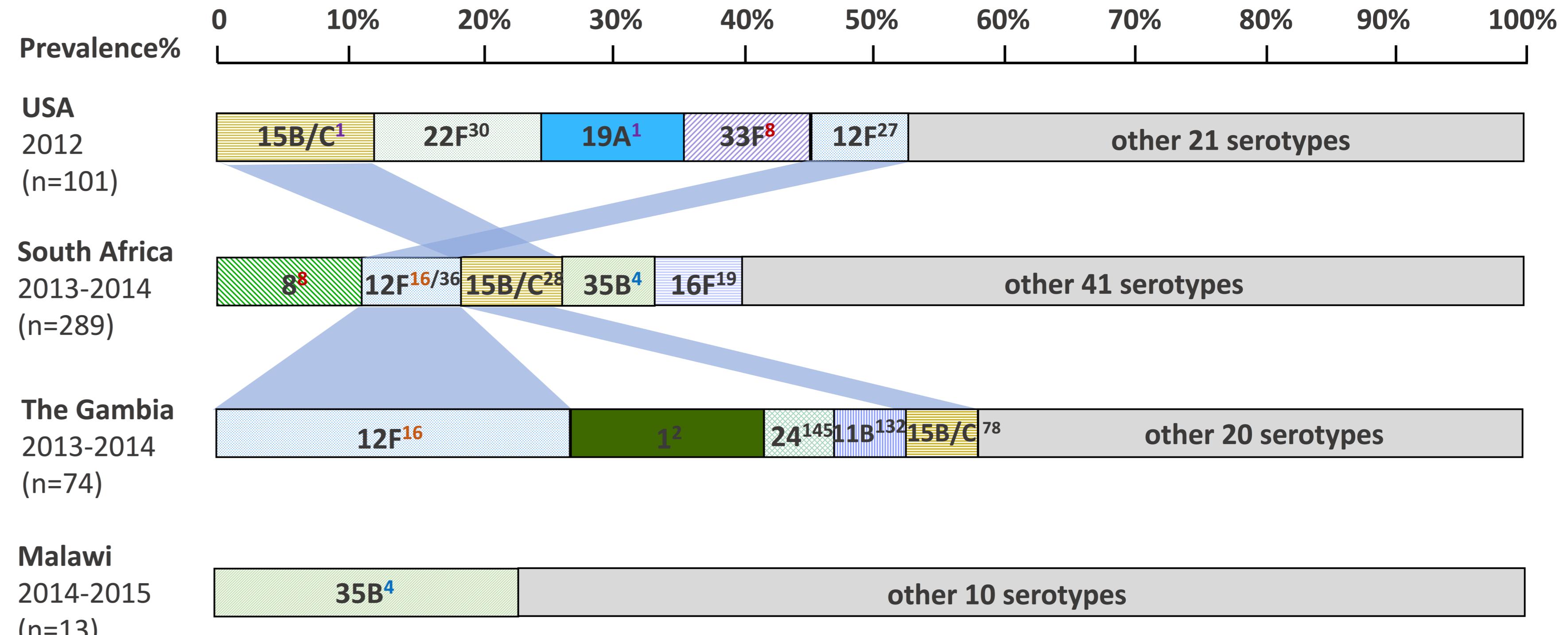


Figure 1. The top five serotypes are indicated in boxes in proportion to their prevalence and their mainly associated lineages are written superscript. GPSCs shared between countries are written in same colour. Serotypes with < 2 isolates are not listed.

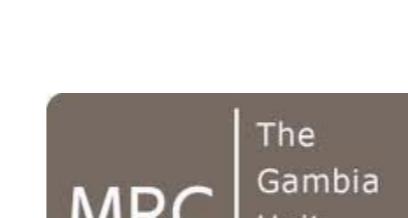
- The top five serotypes varied between countries, with only serotypes 12F and 15B/15C common to South Africa (2013-2014), The Gambia (2013-2014), and the USA (2012).
- The lineages associated with the top five serotypes also differed between the USA and African countries, except for lineage GPSC8, which accounted for all serotype 8 (ranked 1st) in South Africa; and 96% (54/56) of serotype 33F (ranked 4th) in the USA.
- Lineage GPSC16 which mainly expressed serotype 12F was found in South Africa (n=10), The Gambia (n=20), and Malawi (n=1).
- The serotype 35B isolates from South Africa and Malawi mainly belonged to same lineage, GPSC4.

3. Serotype diversity showed an increasing trend in African countries over the collection periods (Table 2)

Table 2. Serotype diversity in the last year of each vaccine period by country

Country	USA	South Africa	Malawi	The Gambia
Last year of pre-PCV (baseline)	0.87 (0.83 to 0.91)	0.91 (0.89 to 0.92)	0.84 (0.73 to 0.94)	0.80 (0.64 to 0.96)
Last year of PCV7	0.80* (0.73 to 0.82)	0.93* (0.91 to 0.95)	-	0.92 (0.84 to 0.98)
Last year of post-PCV13	0.93* (0.92 to 0.95)	0.95* (0.94 to 0.96)	0.95* (0.85 to 1)	0.93 (0.89 to 0.97)

Serotype diversity was measured by Simpson's index of diversity. The index ranges between 0 and 1 with greater the value indicating greater sample diversity. To test whether estimates of D were significantly different between pre-PCV and post-PCV7/PCV13 period, p values were calculated using two-tailed Welch's t-test. Values $P < 0.05$ are statistically significant and indicated by an asterisk in the table.



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