

Genomic epidemiology and antimicrobial resistance of invasive pneumococcal serotype 8 in the pre- and post-PCV13 eras in South Africa, 2005–2020



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Background

- Non-vaccine pneumococcal serotype 8 (st8) is the most common cause of invasive pneumococcal disease (IPD) in South Africa after the introduction of pneumococcal conjugate vaccines (PCVs)
- Incidence increases in IPD due to st8 sequence type (ST) 53 have been reported worldwide
- We describe the genomic epidemiology of st8 before (2005-2011) and after (2012-2020) the introduction of PCV13, as well as antimicrobial resistance patterns in South Africa

Methods

- St8 isolates were randomly selected from our national, active, laboratory-based surveillance for IPD (GERMS-SA) for the period 2005-2020
- Percentage change in rates (per 100,000 population) for age groups <5 and ≥5 years, comparing pre-PCV13 (2005-2011) and post-PCV13 (2012-2020) periods were determined
- Whole-genome sequencing was performed on Illumina platform as part of the Global Pneumococcal Sequencing project (GPS)
- Global Pneumococcal Sequencing Clusters (GPSCs) were derived from the genome using Pop-PUNK
- St8 phylogeny was created using BWA for reference-based alignment; the resulting pseudo-genome alignment was used as an input to Gubbins to create recombination free phylogenies with RAXML
- Antimicrobial resistance was determined by broth microdilution as part of our surveillance using CLSI guidelines

Results

- From 2005 through 2020, 53,993 IPD cases were reported of which 2,466 (6.3%) were st8; 2,208/2,466 (89.5%) had viable isolates; genomic data were available for 399 isolates (18%)
- St8 post-PCV13 rates increased by 95% (95% CI:12% to 251%; rate: 0.4-0.8) in the <5 years and 51% (95% CI:14% to 99%; rate: 0.2-0.3) in the ≥5 years
- We identified fifteen sequence types (STs) and 1 novel ST, all of which clustered into 5 GPSC lineages (Figure 1)
- GPSC3 was the most common lineage accounting for 95.2% (380/399) of the isolates; comprised predominantly ST53 (88.9%, 337/380) followed by ST3847 (7.6%, 29/380), a single-locus variant (SLV) of ST53, both of which were the most common genotypes before and after PCV13 introduction (Figure 2)
- GPSC98 was the second most common lineage (2.5%, 10/399); followed by GPSC224 (1.8%, 7/399) (Figure 1)
- GPSCs 22 and 277 were rare lineages, both accounting for 0.5% (2/399) and were only observed in the post-PCV13 period in this collection
- St8 genotypes assumed a clonal genetic structure with GPSC3 (ST53) being the established clone spanning across the pre- and post-PCV13 periods (Figure 3)
- non-GPSC3 lineages formed distinct sub-clusters, more noticeably in the post-PCV13 period
- MIC₅₀ and MIC₉₀ for penicillin and ceftriaxone were 0.015 and 0.03; 0.03 and 0.5 µg/ml, respectively. MIC₉₀ for erythromycin was 0.06 µg/ml

Discussion and conclusion

- Significant increases in st8 IPD were observed from the pre- to the post-PCV13 periods in children and adults in South Africa, and appears to be driven by the expansion of GPSC3 lineage, more importantly the ST53 genotype as reported in other countries
- Although largely susceptible to commonly used antimicrobials, st8 is an important cause of IPD and continued monitoring is pivotal

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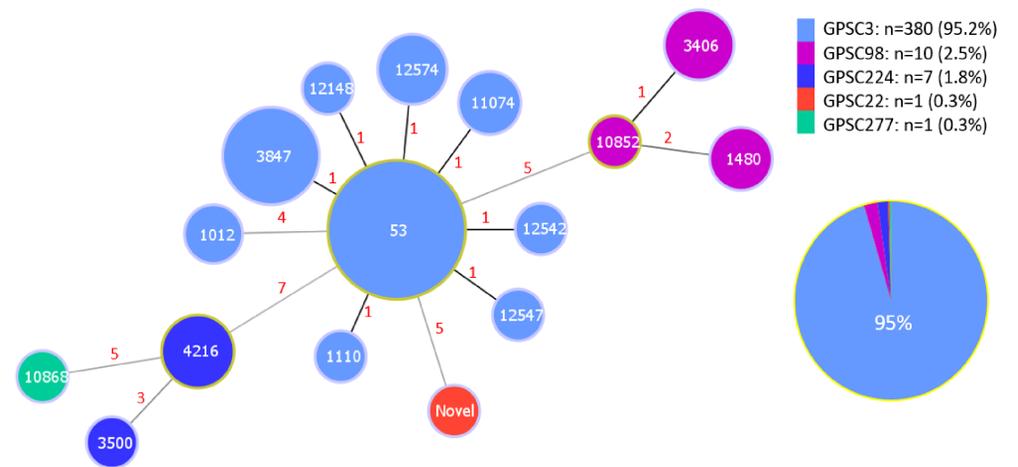


Figure 1: Pneumococcal serotype 8 sequence types (STs) [n=399] grouped by Global Pneumococcal Sequencing Clusters (GPSCs) among persons of all age groups in South Africa between 2005-2020. Differences in the number of loci among the seven house-keeping genes are written in red. GPSC distribution is shown by the pie chart

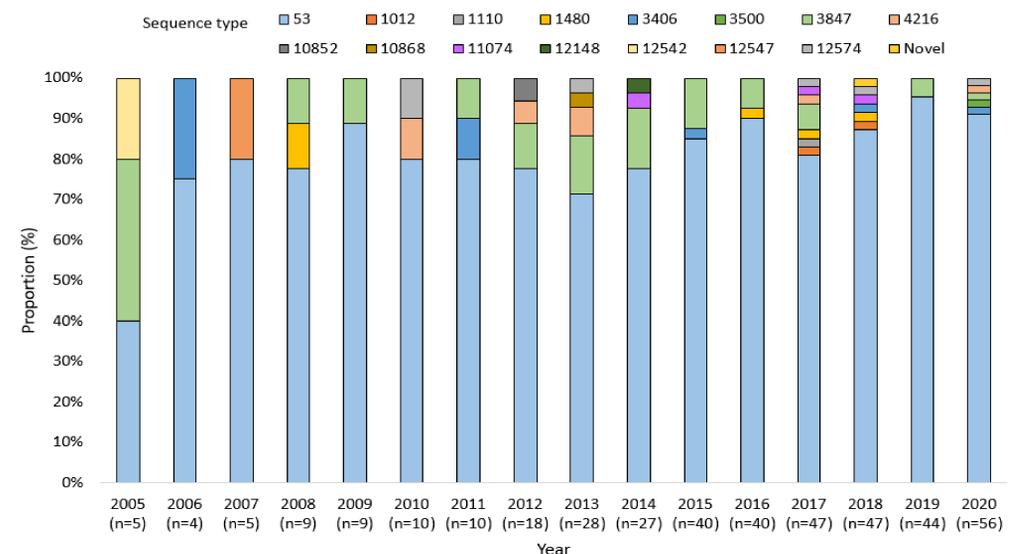


Figure 2: Distribution of pneumococcal serotype 8 sequence types (STs) [n=399] by year (2005-2020) among persons of all age groups in South Africa

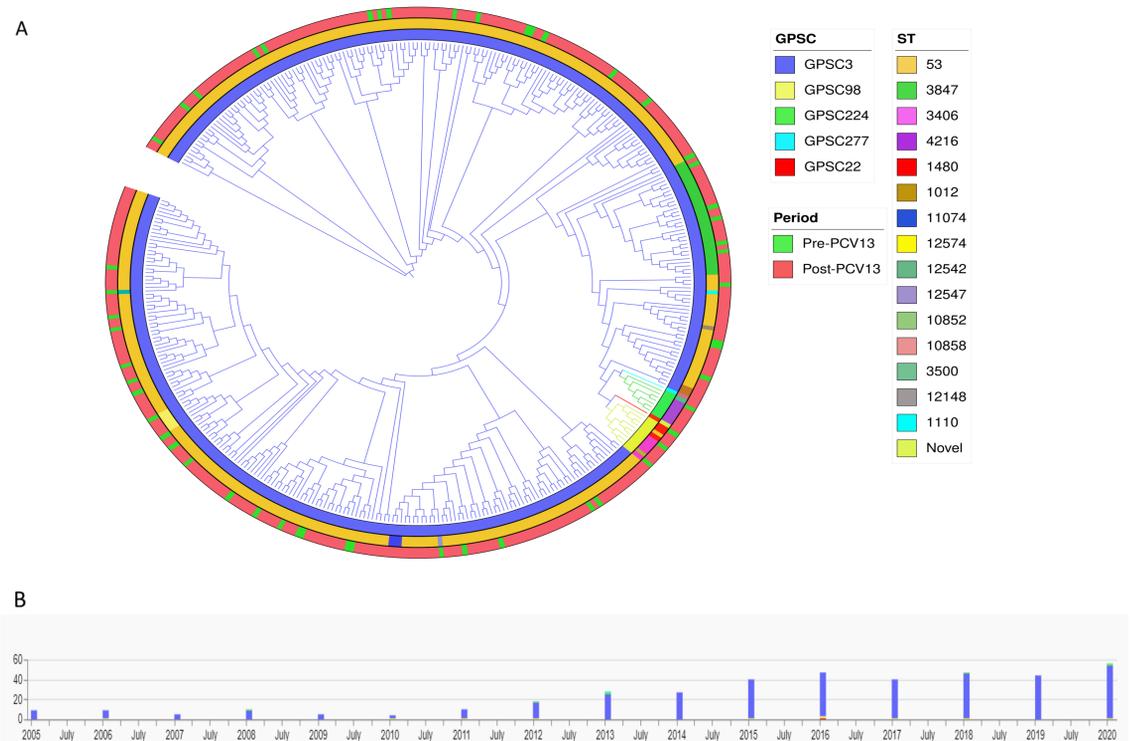


Figure 3: Phylogeographic analysis of pneumococcal serotype 8 (st8) [n=399] using core genome single nucleotide polymorphisms (SNPs). A: phylogenetic tree showing the genetic relatedness among st8 strains: inner colour strip represents GPSC lineages, middle strip represents sequence types and outer strip shows the period. B: timeline showing the number of st8 isolates by GPSC over the 2005-2020 time period