

Invasive *Streptococcus pneumoniae* serotype 35B in South Africa, 2005-2016

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Background

- Since PCV introduction in children in 2009 (PCV7) and 2011 (PCV13), vaccine-serotype invasive pneumococcal disease (IPD) has declined in South Africa, predominantly in children aged <2 years and adults aged 25-44 years
- In the USA, penicillin non-susceptible serotype 35B increased following PCV introduction, primarily due to expansion of sequence type (ST) 558
- Novel serotype 35D, non-reactive with factor serum 35a and harbouring a disrupted *wciG* gene, was recently described in Australia and the USA, although prevalence was low

Aim

- To describe serotype 35B disease and detect putative 35D in South Africa, pre- and post-PCV introduction

Methods

- We reviewed IPD cases reported through national, laboratory-based surveillance from 2005-2016
- Incidence rates for non-vaccine-serotype IPD, per 100,000 population, were calculated for 2005-2008 (pre PCV) and 2016 (post PCV) using population denominators from Statistics SA
- 249 serotype 35B isolates, spanning 2005-2014, originally serotyped by Quellung as part of routine IPD surveillance, were re-serotyped using Quellung (22 isolates were no longer viable) (Fig. 1)
- A subset of 35B isolates was characterised by whole genome sequencing (Fig. 1)
 - MLST-defined genotypes were determined for 62 isolates
 - In silico* serotype was determined for 50 isolates and these genomes were also investigated for a disrupted *wciG* gene
- A population snapshot of serotype 35B sequence types was generated using eBURST v3 (eburst.mlst.net)

Results

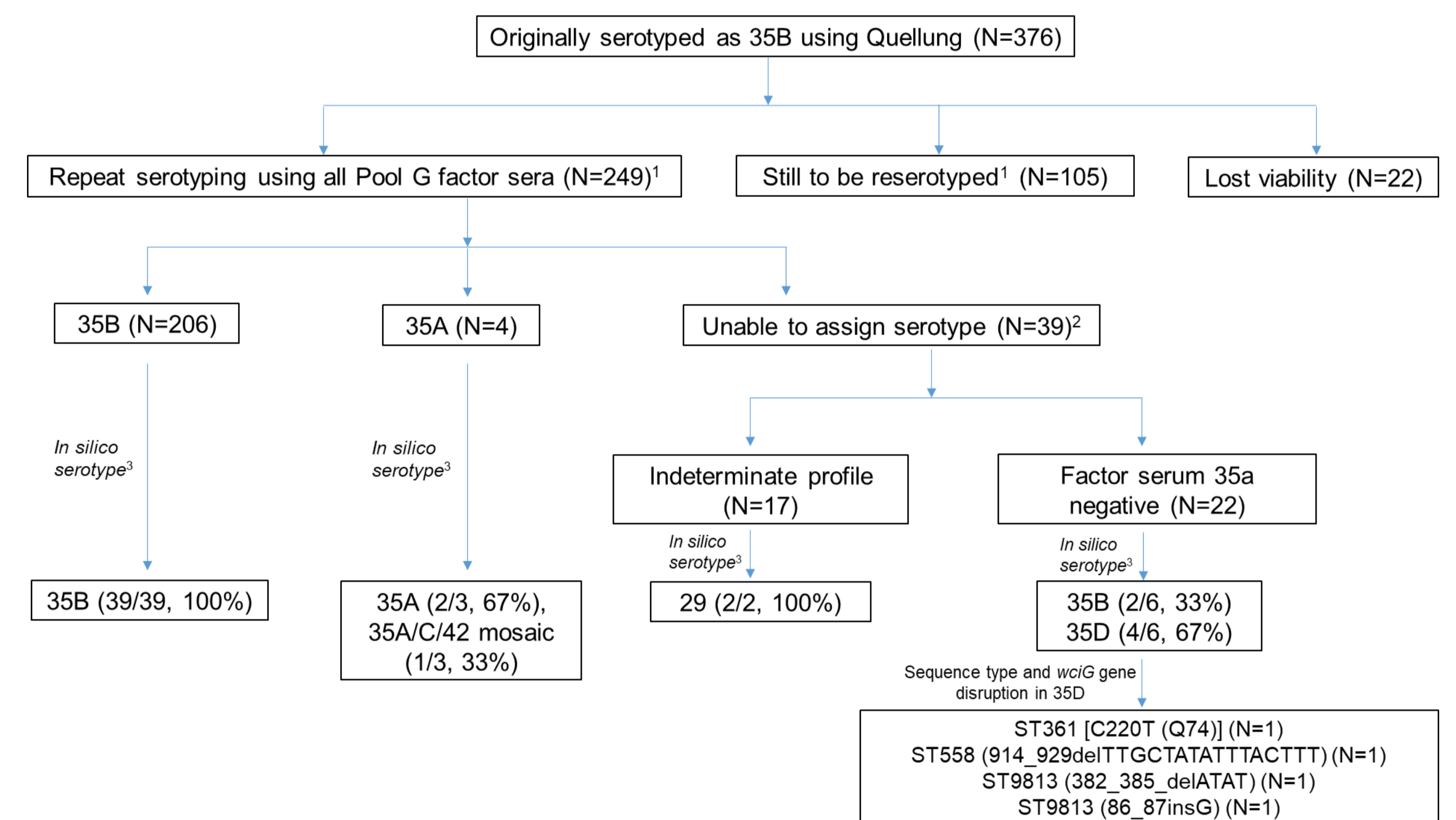
- Surveillance identified 45,852 IPD cases, of which 376/31,513 (1%) were originally 35B by Quellung and 57% (214/376) were non-susceptible to penicillin
- Non-vaccine-serotype IPD increased 29% (95% CI, +9%, +54%) in children aged <5 years and 15% in adults (≥25 years) (95%CI, +7%, +23%) (Fig. 2a & b)
 - Serotype 35B incidence increased 4.5-fold in children aged <5 years (95% CI, 2.25-9.04; rates: 0.08 to 0.36) (Fig. 2a)
 - In adults (≥25 years), serotype 35B incidence rates doubled from 0.05 to 0.10 (95% CI, 1.20-3.21) (Fig. 2b)
- Serotype 35B was predominantly penicillin non-susceptible ST361 and associated single-locus variants (31/62, 50%), or penicillin-susceptible ST9813 (18/62, 29%) (Fig. 3)
- Only one serotype 35B isolate was ST558
- 22/249 (9%) serotype 35B isolates did not react with factor serum 35a (Fig. 1)
 - Of these, 4/6 with genomic data had a disrupted *wciG* gene and were ST361 (n=1), ST558 (n=1) or ST9813 (n=2) (Fig. 1)

Conclusions

- Serotype 35B incidence increased post PCV in children and adults
- Half of the 35B isolates (with known MLST data) belonged to penicillin non-susceptible ST361
- Genetically confirmed 35D was detected in unrelated lineages, at low frequency
- Phenotypic detection of 35D using Quellung is currently unreliable

Acknowledgements

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¹ Includes all viable isolates collected in 2005-2014. Re-serotyping (Quellung) still in progress for years 2015-2016. ² Profiles did not match serotype 35A/B/C/F, 29, 34, 42 or 47. ³ *In silico* serotype available for a subset of isolates (N=50).

Figure 1. Summary of *S. pneumoniae* serotype 35B phenotypic and genotypic characterisation, 2005-2016

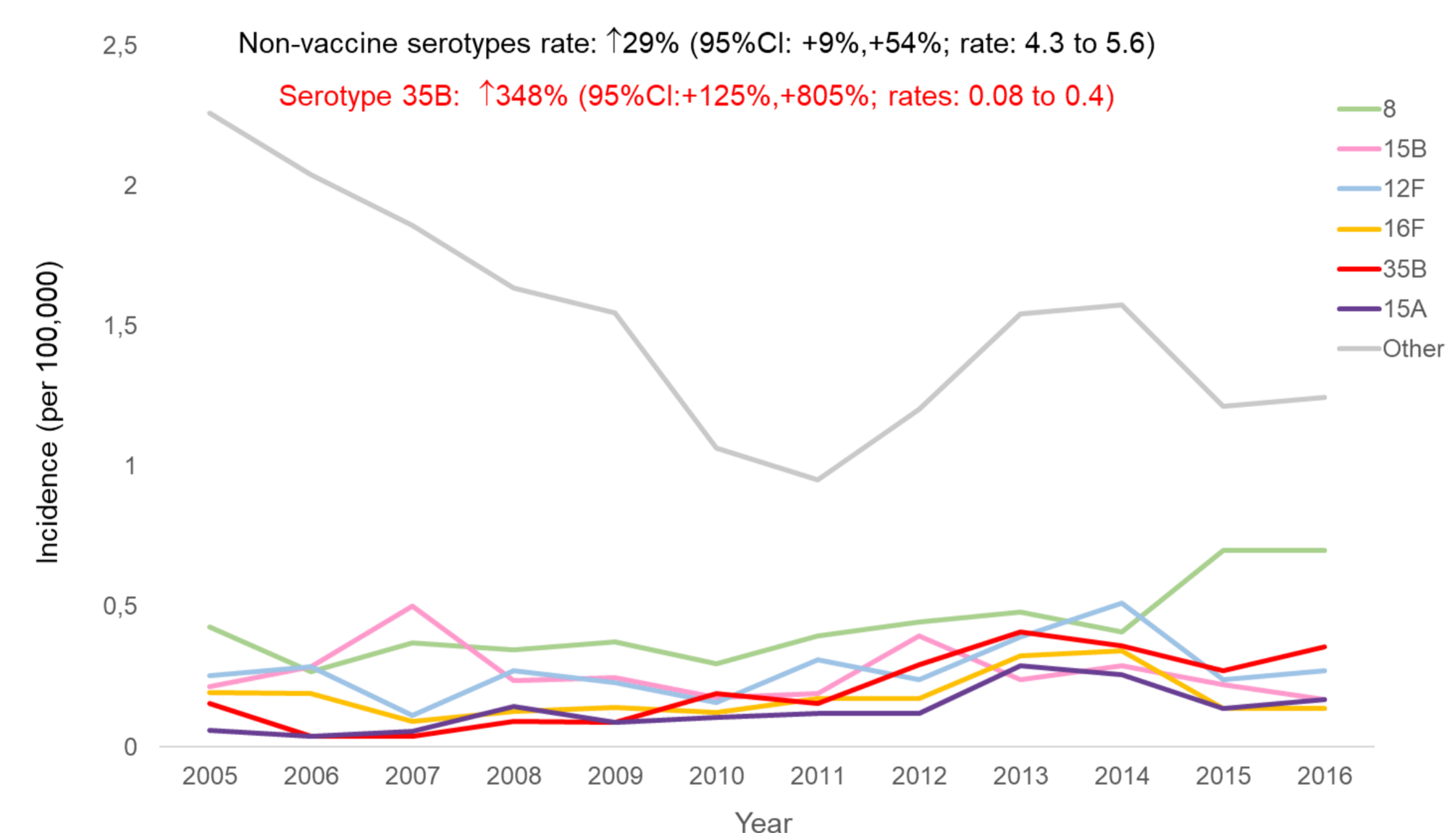


Figure 2a. Incidence of invasive pneumococcal disease episodes with viable isolates caused by non-vaccine serotypes in individuals aged <5 years, 2005-2016, South Africa

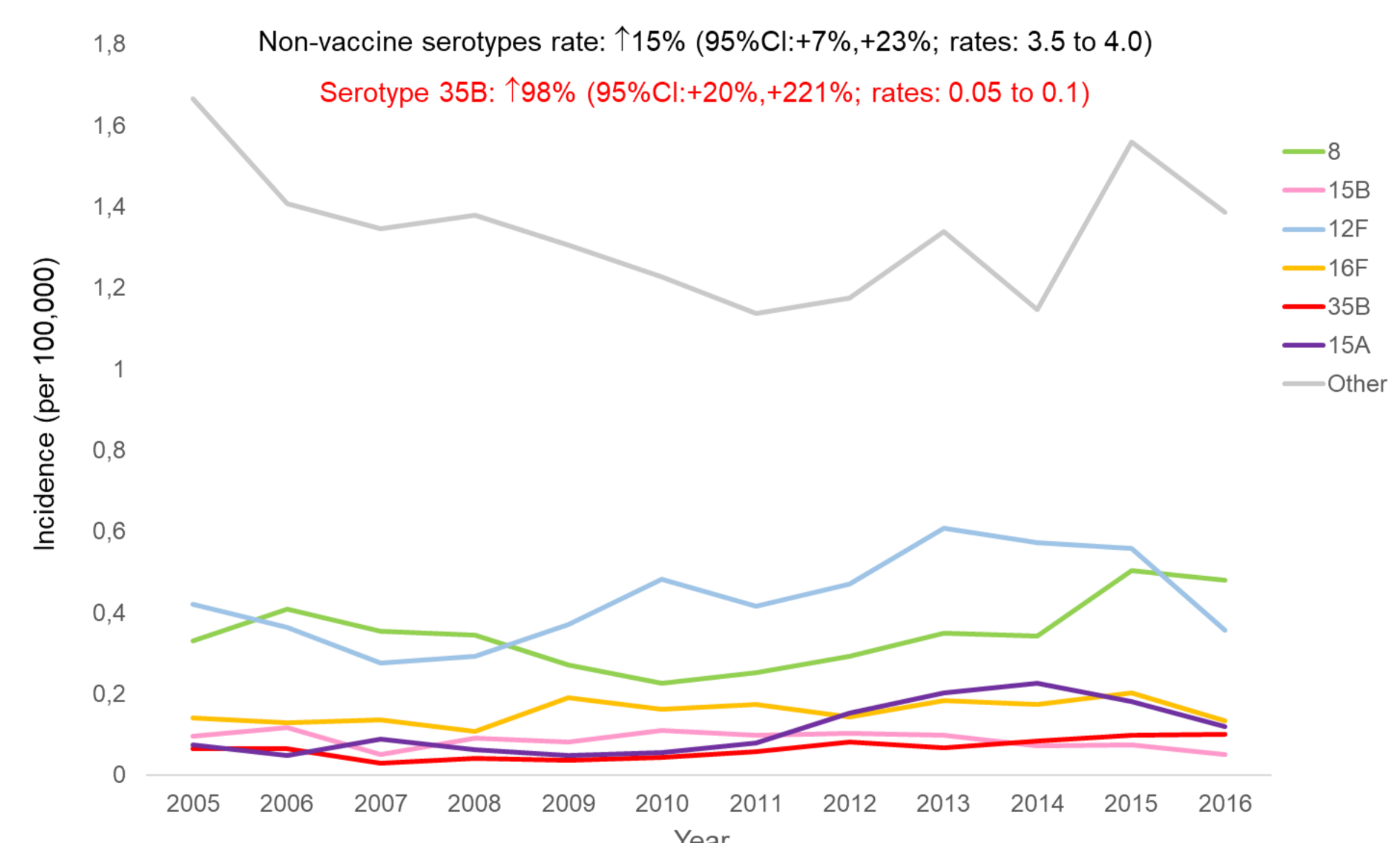


Figure 2b. Incidence of invasive pneumococcal disease episodes with viable isolates caused by non-vaccine serotypes in individuals ≥25 years, 2005-2016, South Africa

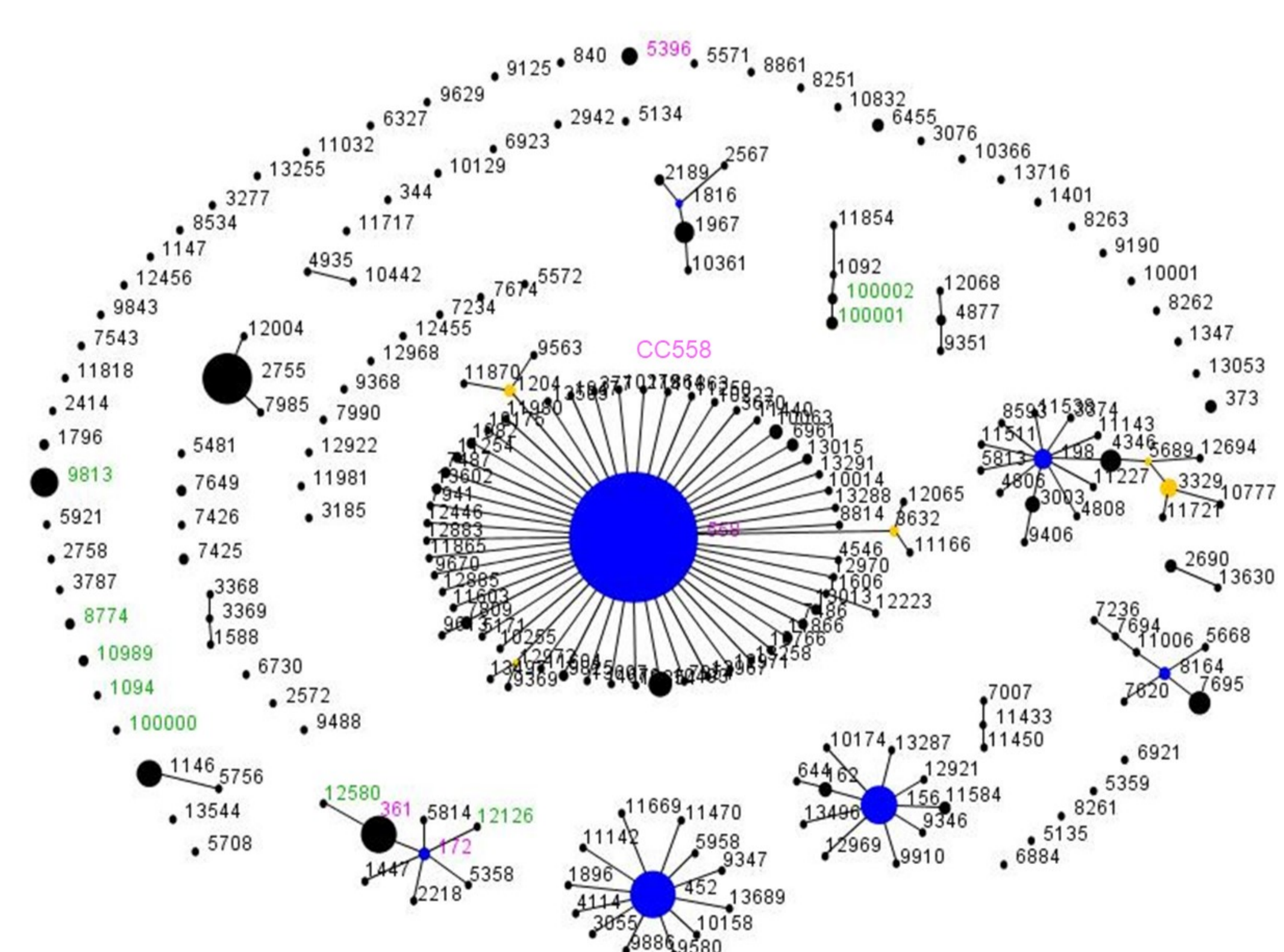


Figure 3. eBURST population snapshot showing relationships among sequence types for *S. pneumoniae* serotype 35B, South Africa (n=62, green) compared to serotype 35B's available in the global PubMLST database (N=855, black) (<https://pubmlst.org/spneumoniae/>). Sequence types in pink were present in both data sets. Blue and yellow circles denote founding and co-founding genotype, respectively, and the size of each circle corresponds to the number of isolates.