Diverse and distinct *Streptococcus pneumoniae* cause invasive disease in Papua New Guinea: implications for vaccination

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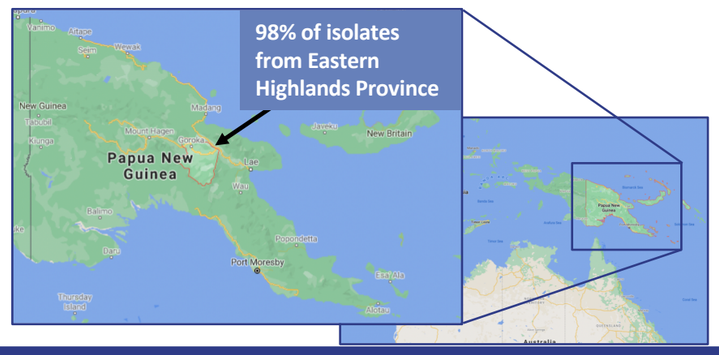
Aim: Characterise the *S. pneumoniae* population causing invasive disease in children in Papua New Guinea (PNG), prior to introduction of PCV13

Background: *S. pneumoniae* in Papua New Guinea

- Common cause of pneumonia and meningitis
- Key contributors to childhood morbidity and mortality (child mortality <5 years-of-age 57/1000)
- ~21.5% of isolates from children with meningitis are penicillin-resistant
- Some common serotypes are rarely observed elsewhere
- High carriage rates and rapid colonisation of infants
- 13-valent pneumococcal conjugate vaccine (PCV13) added to the child immunisation programme in 2014

Methods

- Whole-genome sequencing (WGS) of 191 isolates from children <8 years with meningitis and/or pneumonia (1989-2017)
- Most isolates (88%) from children ≤2 years-of-age
- 70.2% derived from CSF samples, 29.8% from blood
- *In silico* prediction of antimicrobial resistance (AMR), multi-locus sequence typing (MLST), serotyping using SeroBA, and global pneumococcal sequencing clusters (GPSC) using PopPUNK
- Characterisation of relationships amongst lineages, serotypes and AMR traits
- Serotypes of interest were contextualised using the Global Pneumococcal Sequencing (GPS) project database (~26k isolates)



Results

Diverse and distinct *S. pneumoniae* population

- 33 serotypes across 48 GPSCs
- 17 GPSCs (n=29 isolates) and MLST of a further 34 isolates were unique* to PNG
- The most common serotypes differ from those in neighbouring Indonesia

Potential for rapid serotype replacement

- Multiple GPSCs expressed both PCV13 and non-PCV13 serotypes, indicating potential for serotype replacement and vaccine evasion by these lineages

Impact of PCV13 may be limited, particularly upon meningitis burden

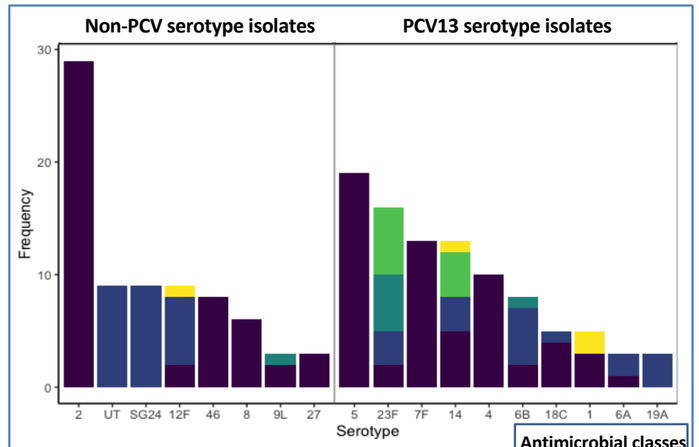
- Almost half of isolates (47.6%) expressed non-PCV13 serotypes
- Serotype coverage of PCV13 serotypes is higher for blood than CSF origin isolates
- Non-PCV13 serotype isolates have higher odds of association with meningitis than PCV13 serotype isolates (OR 3.57 [1.26,11.11], p 0.009)

PCV13 may reduce MDR but not penicillin resistance

- PCV13 serotype isolates have higher odds of being MDR (OR 13.6 [95%CI [1.96, 589.25], p 0.001)
- >30% isolates predicted to be resistant to ≥1 antimicrobial, with no difference in odds of AMR between PCV13 and non-PCV13 serotype isolates (including penicillin)

Two distinct clusters of the most common serotype within GPSC 96

- A highly clonal cluster of serotype 2 isolates unique to PNG (ST 1504) spanning 1989-2002
- A distinct second cluster suggestive of intercontinental transmission (ST 1504~), observed in 2000 and 2001



Summary of predominant serotypes, coloured by number of antimicrobial classes to which isolates were resistant. (UT = untypable, SG24 = serogroup 24)

Conclusions

The resolution afforded by genomic data and contextualisation using the GPS collection has highlighted the distinct *S. pneumoniae* population observed in PNG, with multiple GPSCs unique to PNG.

The impact of PCV13 upon the invasive disease burden may be limited as almost 50% cases were caused by non-PCV13 serotypes. Affinivax PCV24 (in development) could provide enhanced coverage (~75%) of invasive pneumococcal disease cases.

Ongoing surveillance, including WGS and more representative sampling, is required to monitor the impact of the national PCV-13 programme upon the *S. pneumoniae* population, including serotype replacement and antimicrobial resistance.

*Not observed in GPS or PubMLST databases

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