GENOMIC EPIDEMIOLOGY OF PNEUMOCOCCI IN THE UK FROM PRE-PCV7 TO POST-PCV13 MODELLING OF CARRIAGE ADN DISEASE DYNAMICS

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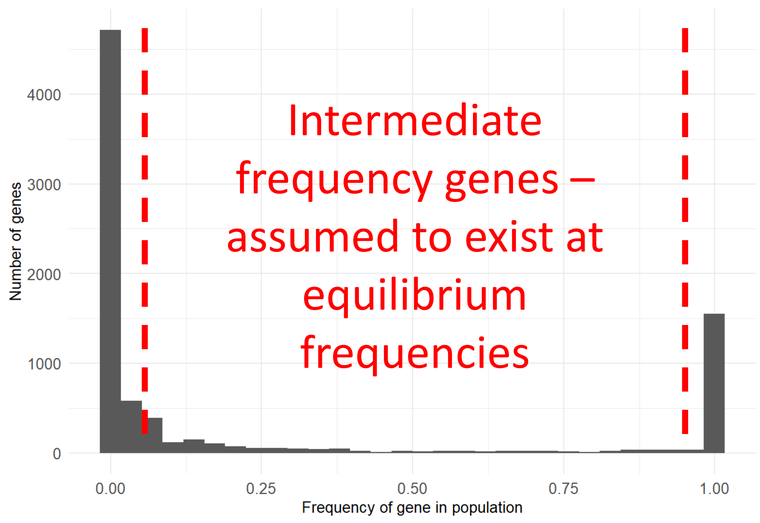
Background

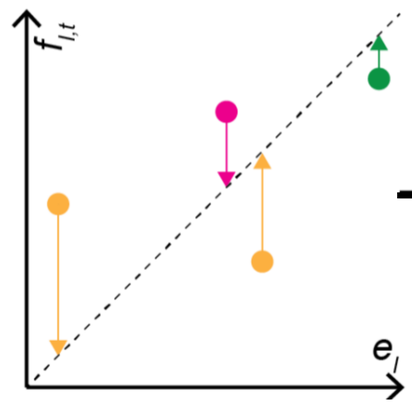
Pneumococcal carriage population dynamics in England have been monitored by five nasopharyngeal surveys undertaken by the UK Health Security Agency (previously Public Health England): pre-PCV7 (2001-2002); post-PCV7 (2008-2009); and post-PCV13 in 2012-2013, 2015-2016 and 2017-2018. A previous study sequenced 877 of these isolates. Contemporaneous isolates from child and adult invasive disease across England (N=1546) were also sequenced to compare the dynamics of disease and carriage.

Methods and data

Isolates were serotyped using PneumoCAT and categorised into strains using PopPUNK. The distribution of genes across isolates was analysed with Panaroo. Simulations used an updated version of the multi-locus negative frequency-dependent selection (NFDS) model (https://github.com/nickjcroucher/multilocusNFDS).Parameters were estimated through approximate Bayesian computation using the ELFI package.

Negative frequency-dependent selection (NFDS) Simulation:





NFDS genotype fitness
$= (1 + \sigma_f)^{\pi_{i,t}}$

Heterogeneous NFDS parameters:
i, Migration rate,
v, Vaccination pressure
s, Strong NFDS strength
j, Weak NFDS strength
y, Fraction of strong NFDS strength

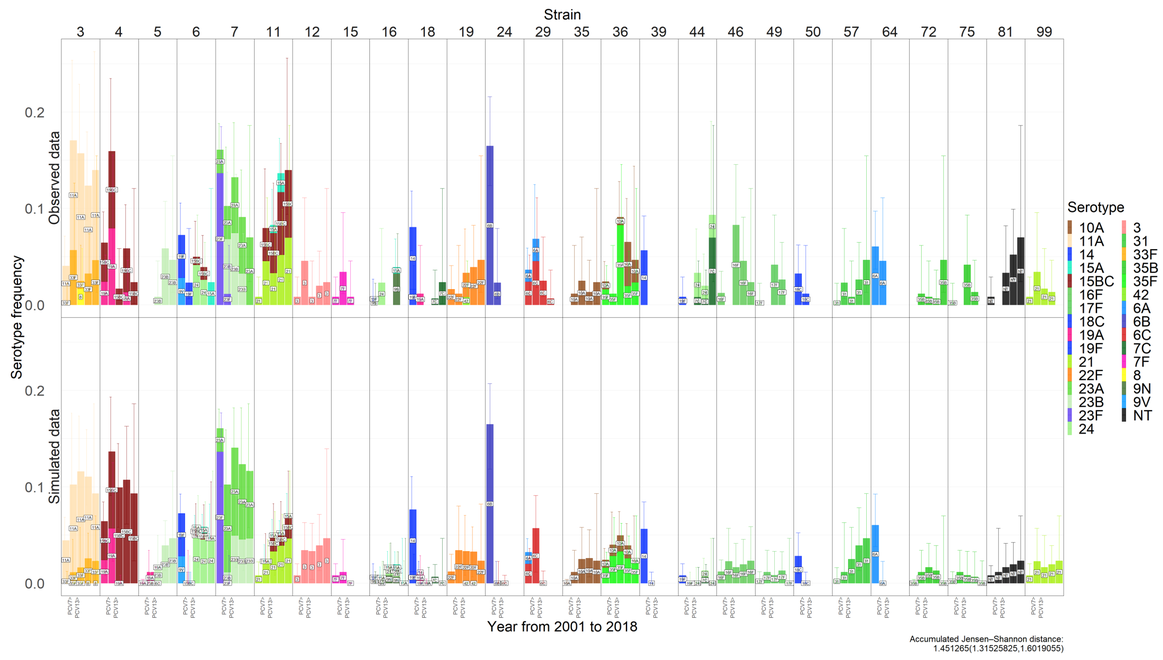
Results

Estimates of NFDS strength were similar to those from fits to independent datasets that only spanned the introduction of PCV7, confirming NFDS models more accurately replicated the population dynamics than equivalent neutral models. Simulations reproduced the elimination of vaccine-type strains, expansion of some non-vaccine-type strains, and serotype switching within strains. Forward simulations were used to predict carriage dynamics post-PCV15 and post-PCV20.

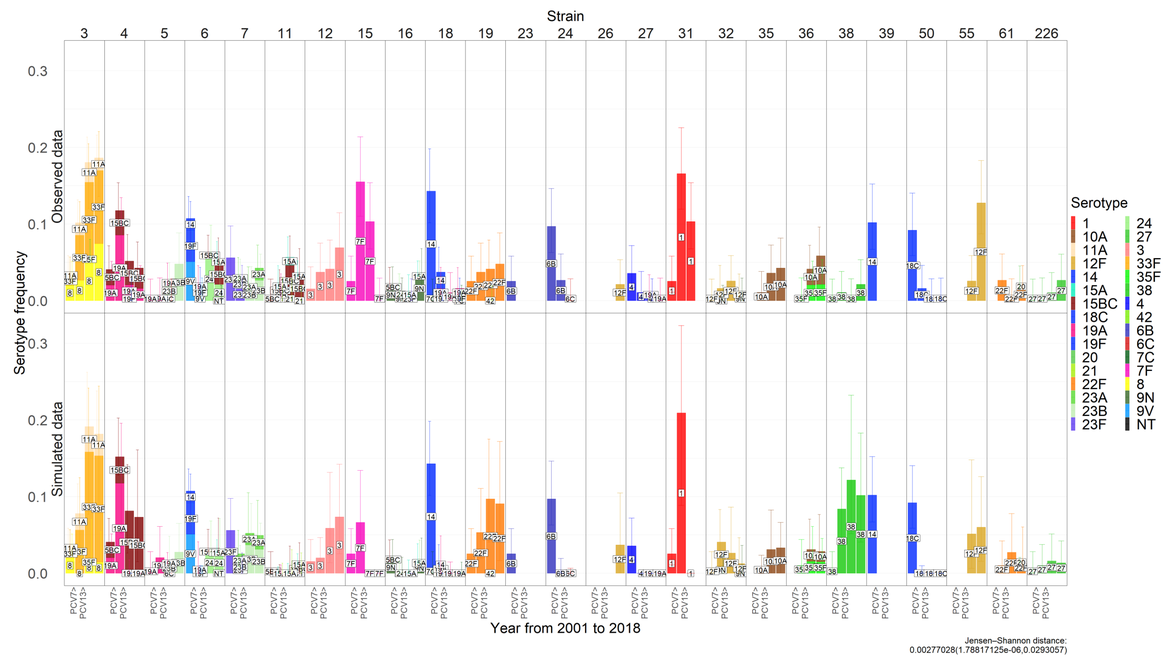
Results

When combined with estimates of genotype invasiveness in children and adults, these enabled the forecasting of invasive disease burdens after the next generation of conjugate vaccines.

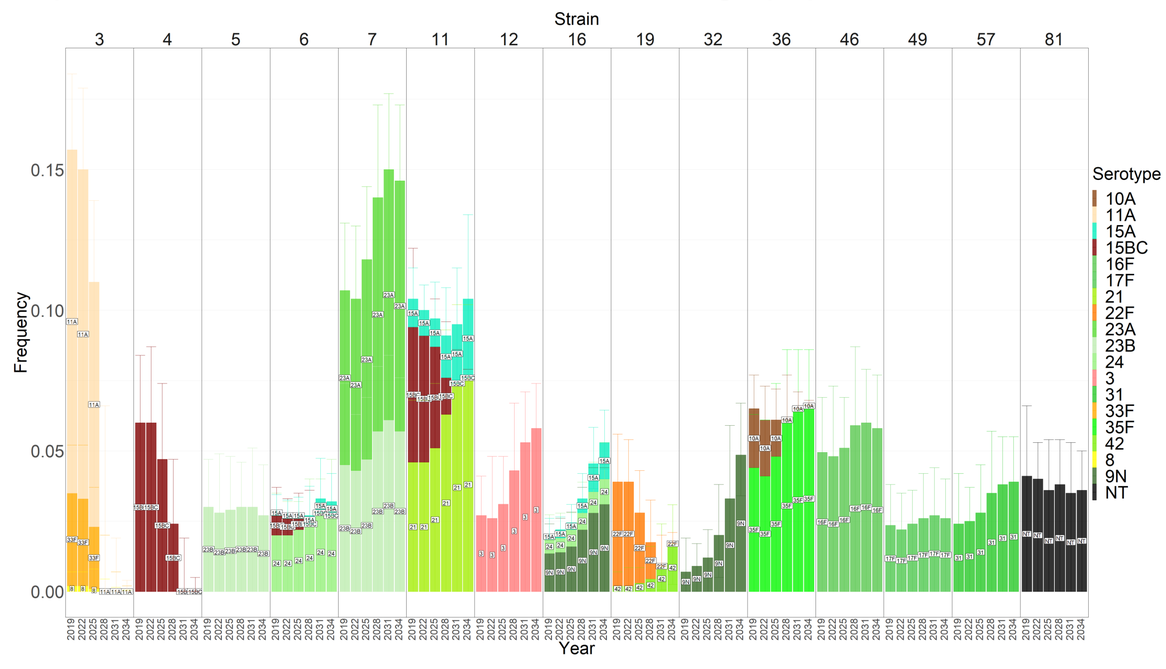
Children carriage dynamics:



Children disease dynamics:



Impact of PCV20 forecast on children carriage populations:



Conclusions

Genomic data and models can improve our understanding of the PCV-associated changes in the carried pneumococcal populations. Forecasts of carriage dynamics combined with invasiveness estimates can be used to predict PCV effectiveness, and highlight the serotypes most likely to cause a substantial burden of disease in children and adults post-PCV.

References
1.https://github.com/nickjcroucher/multilocusNFDS
2.Corander, J. (2017). Nature ecology & evolution, *1*(**12**), 1950-1960
3.Sheppard, C. L. (2019) Genes, *10*(**9**), 687.

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