OPEN-SOURCE DATA AND IMPROVED METHODS FOR ESTIMATION OF PNEUMOCOCCAL INVASIVENESS INCHILDREN AND ADULTS

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Background

The replacement of high-invasiveness serotypes with low-invasiveness serotypes in the carried pneumococcal population is critical for PCV effectiveness. Quantifying invasiveness, and understanding whether it is consistently associated with serotypes, particularly in pre- and post- PCV periods, is crucial for optimal vaccine design and deployment.

Disease: Progress from carriage	Capsule: 48 serogroups, over 100 serotypes
Disease: Estimations/predictions/vaccines	Invasiveness: Disease per carriage per unit time.

Methods and data

Publicly available datasets from serotyped and genotyped pneumococcal case-carrier studies were aggregated for meta-analyses. A novel open-source Bayesian framework was used to fit different models of pneumococcal invasiveness across serotypes and locations. Identification of the most appropriate model used bridge sampling.

Poisson model:

$$d_{i,x} \sim Pois\left(N_i t_i \upsilon_x \rho_{i,x}\right)$$

Negative binomial model:

$$d_{i,x} \sim NB\left(N_i t_i \upsilon_x \rho_{i,x}\right)$$

Parameters:

N_i: population size for study i;
t_i: time interval for study i;
$\rho_{i,x}$: carriage prevalence for type x in study I;
υ_x: progression rate per time for type x;
υ_j: serotype only;
υ_k: strain only;
$\upsilon_j \upsilon_k$: primarily by serotype, modified by strain;
$\upsilon_k \upsilon_j$: primarily by strain, modified by serotype.
$\upsilon_{j,k}$: by serotype and strain.

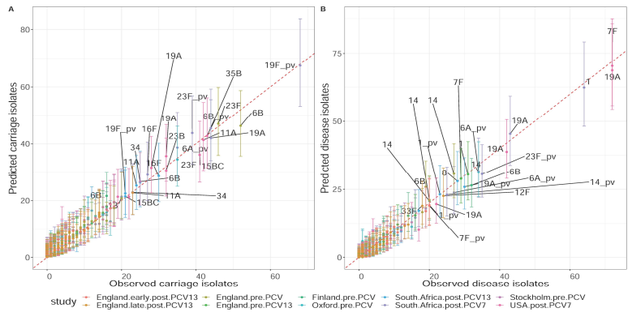
Bayes factor of all fitted model with filtered serotype/strain infant data set:

Model	log(Bayes factor)
serotype_then_strain_type_specific_poisson	0.000000
serotype_type_specific_negbin	-4.519831
serotype_then_strain_type_specific_negbin	-5.710913
strain_then_serotype_type_specific_poisson	-22.547553
serotype_type_specific_poisson	-22.888300
strain_then_serotype_type_specific_negbin	-28.084058
combined_serotype_and_strain_type_specific_poisson	-33.306329
strain_type_specific_negbin	-35.237732
combined_serotype_and_strain_type_specific_negbin	-38.836922
strain_type_specific_poisson	-49.901976

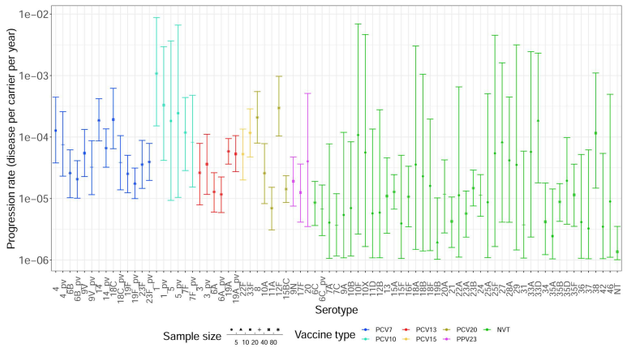
Results

These new methods successfully distinguished the reduced invasiveness of some vaccine serotypes post-PCV provided evidence for direct protection from invasive disease from vaccine-induced immunity.

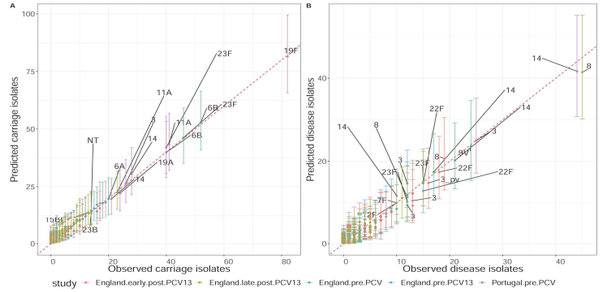
Infants, observation and prediction of case to carrier ratio:



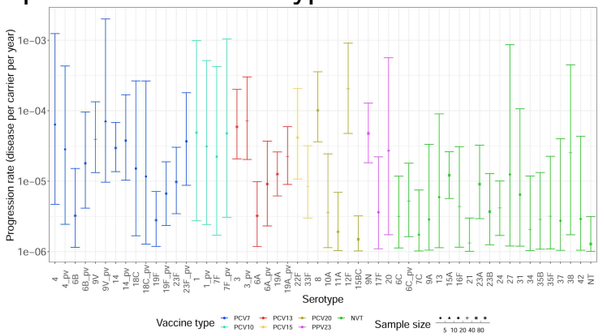
Infants, invasiveness estimates with post- vaccine serotypes:



Adults, observation and prediction of case to carrier ratio:



Adults, invasiveness estimates with post- vaccine serotypes:



Conclusions

We developed novel open-source methods and datasets for estimating serotype- and strain-specific invasiveness across, and within, case-carrier studies. These methods can be used to build an improved evidence base for disease predictions and future vaccine policy.

References
1. *https://github.com/nickjcroucher/progressionEstimation*
2. *Løchen, A., Truscott, J. E., & Croucher, N. J. (2022). Analysing pneumococcal invasiveness using Bayesian models of pathogen progression rates. PLoS computational biology, 18(2), e1009389.*

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