Impact of mechanisms of antibiotic resistant strain competition on dynamics of *Streptococcus pneumoniae* following introduction of PCV: a modelling study

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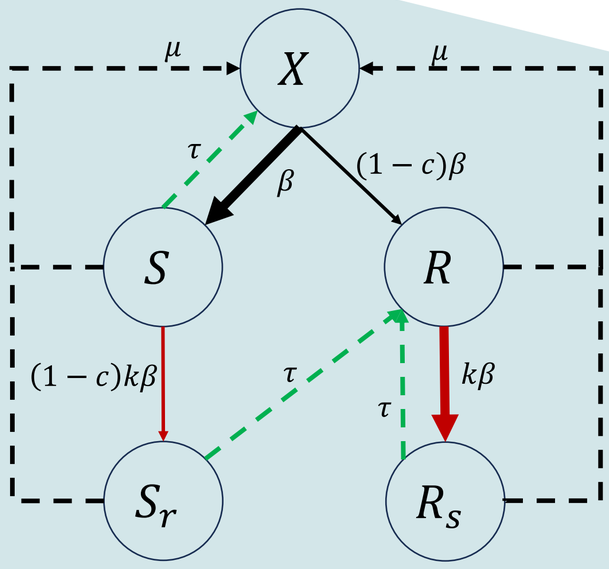
Background

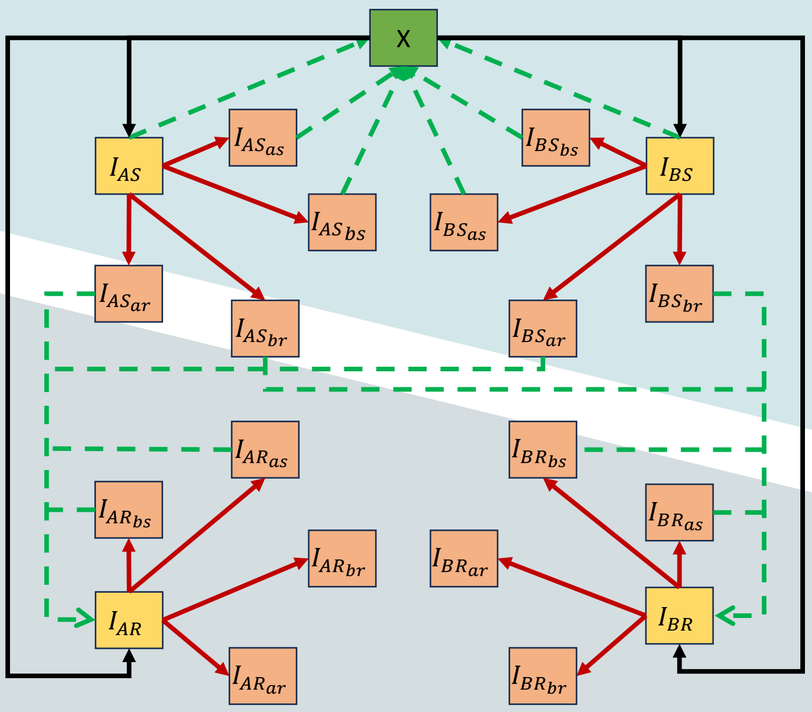
- *S. pneumoniae* (pneumococcus) is a bacterial opportunistic pathogen of the respiratory tract. Pneumococcal conjugate vaccines (PCVs) are a crucial component of pneumococcus infection prevention.
- Antibiotic resistant strains of pneumococcus are a leading cause of mortality attributable to antibiotic resistance. **Estimates of the long-term impact of PCVs need to include the post-vaccine epidemiology of antibiotic resistant strains of pneumococcus.**
- There is a lack of validated mathematical models that capture the serotype-specific epidemiology of sensitive and resistant strains of pneumococcus.
- Multiple models can explain fundamental epidemiology such as the co-existence between sensitive and resistance pneumococcal strains. **These models lead to divergent predictions of vaccine impact on resistant strain prevalence.**
- **We will develop a suite of models, making testable prediction of the impact of vaccination on resistant carriage under each mechanism. We will test predictions against data from a controlled vaccine trial.**

1. Single serotype model

We use a compartmental ODE model structure. Individuals can be uncolonised (X), singly colonised with sensitive (S) or resistant (R) strains, or can be co-colonised with both strains. Co-colonisations have a major and a minor population. Coexistence of S and R strains is maintained in this model because although there is a cost to transmission for resistant strains, treatment of co-colonisations can benefit resistant type.



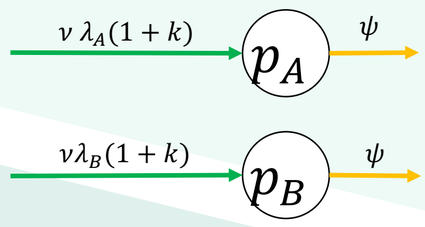
2. Expand to two-serotype model



The single serotype models were expanded to two groups of serotypes, for vaccine and non-vaccine serotypes. We allow for co-colonisation between serotypes and track co-colonisation between two members of the same serotype and antibiotic susceptibility group. Both the single serotype and the expanded two serotype models are structurally neutral with respect to resistance transmission. Natural clearance not shown.

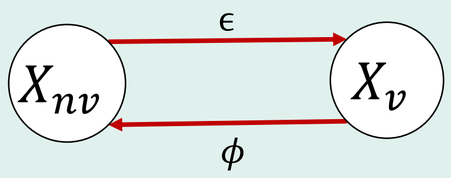
3. Serotype-specific immunity

In the two-serotype model, we need to take serotype-specific immunity into account:



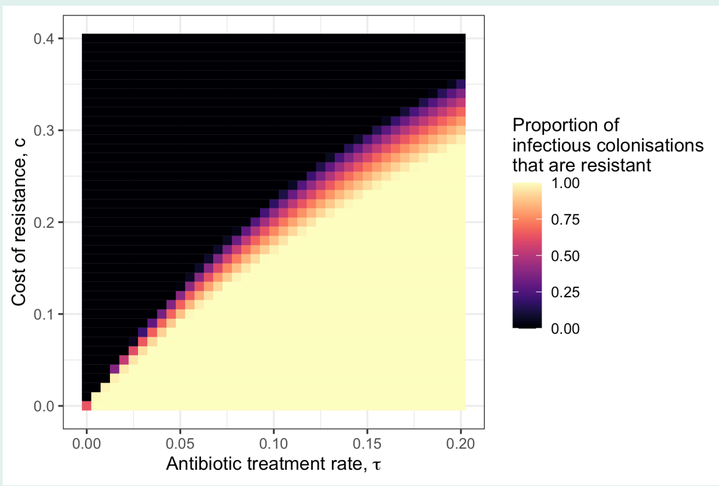
- Population-level probability of immunity to serotype
- All colonisations contribute to population-level immunity (by factor ν)
- Immunity wanes over time

4. Vaccination dynamics



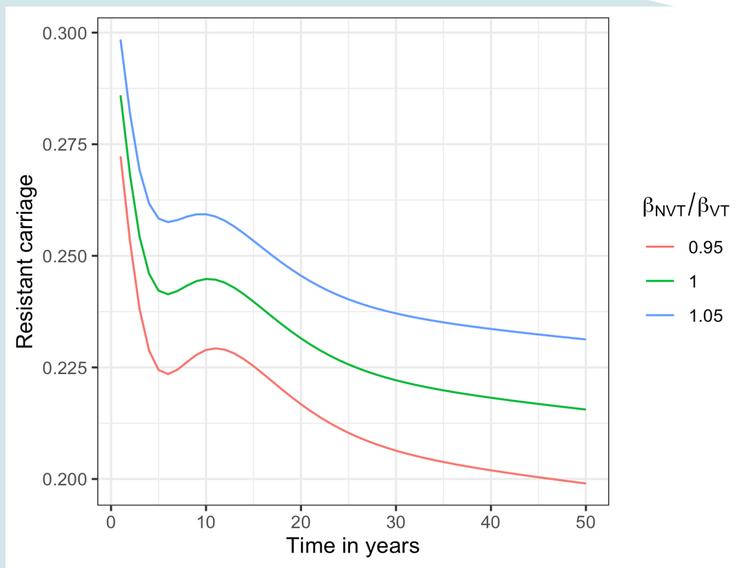
- We add vaccinated and unvaccinated versions of each disease state
- Reduced rate of acquisition of vaccine serotypes among vaccinated, e.g. $(1-\alpha)\lambda_{AS}$

Preliminary results: Co-existence dynamics



- Two-strain, two-serotype model replicates dynamics of two-strain model
- Co-existence is possible when the treatment rate, τ, and the cost of resistance, c, are balanced
- Implies narrow region of co-existence: is this realistic?

Preliminary results: Impact of vaccine introduction on prevalence of resistant colonisations (resistant carriage)



- Resistance carriage decreases after a vaccine is introduced due to reduction in transmission of vaccine-types
- The transmission rate of the vaccine and non-vaccine type impacts resistance carriage: greater transmission promotes co-colonisation, which increases colonisation opportunities for resistant strains

Conclusions

- Can obtain co-existence of sensitive and resistant strains and two serotypes in two-serotype model structure
- Resistant carriage could decrease after vaccination, but depends on model structure and model parameters

Next steps

- We will develop two-serotype models for different hypotheses for mechanisms of sensitive/resistant strain coexistence. We will also incorporate age dynamics and time-varying vaccine coverage
- Fit each of the suite model to data from a controlled trial of PCV10 from Vietnam, obtaining WAIC (or similar) for each mechanism. The data comprises sequencing of multiple pneumococcal isolates per participant from the community, at baseline and over 4 years of a catch-up vaccination campaign.

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