Conceptual Economic Model Methodology for Infant Pneumococcal Conjugate Vaccine Program and its Impact on Antimicrobial Resistance

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BACKGROUND

- Antimicrobial resistance (AMR) is a global threat to effective prevention and treatment of an increasing range of infections that are no longer susceptible to common interventions[1]
- Vaccines prevent disease in individuals, reduce the need for antibiotic prescriptions, and reduce circulation of resistant pathogens, deriving benefit in those not vaccinated[2]
- Since 2000, pneumococcal conjugate vaccines (PCVs) used in infant national immunization programs (NIP) have reduced the burden of pneumococcal disease (PD) as well as AMR pneumococcal infections[3]
  - After the U.S. introduced 7-valent PCV (PCV7), antibiotic prescribing for otitis media (OM) in children under 2 years of age dropped by 42%, and rates of resistant infections with serotypes included in the PCV7 dropped by 87%[4]
  - Six years after introduction of the 13-valent PCV (PCV13), significant reductions in PCV13-type invasive pneumococcal disease (IPD) incidence, mainly driven by serotypes 19A and 7F, were observed in children under 5 years of age with an 85% lower incidence rate[5]

RESEARCH PROBLEM

- Cost-effectiveness and cost-savings of infant PCVs is well acknowledged[6]
- While the impact of PCVs on AMR and prescribing is well documented, ascribing economic value in cost-effectiveness analyses (CEA) and quantifying reduction in AMR or prescribing has not been considered

OBJECTIVE

- Develop a methodologic cost-effectiveness and public health impact modeling framework to capture additional value of PCV program impact on AMR-PD manifestations

MODELING METHODOLOGY

- A methodologic framework was designed to augment existing PCV CEA methodology, generating outcomes incrementally attributable to AMR-PD, including costs, quality-adjusted life-years, AMR cases averted, healthcare resource utilization, and number of antibiotic prescriptions
- Building on the framework of Atkins et al.[7] we developed a conceptual flexible framework to function within different pneumococcal modeling methodologies (Static, Dynamic, agent based, etc.) for a health economic evaluation of a PCV program
  - We considered impact of PCVs on PD specifically related to clinical management of AMR-PD, including AMR epidemiology, antibiotic prescribing patterns, and healthcare resource utilization to quantify impact of PCVs on cases and outcomes of AMR-PD
- Conceptual modeling methodology presented in **Figure 1**
  - Proposed framework considers impact of PCVs on antimicrobial prescribing due to (**IPD**), community-acquired pneumonia (**CAP**), and acute otitis media (**AOM**)
  - Data inputs clustered into 3 pathways: **Population**/**Pathogen, Care,** and **Health Outcomes**
  - Impact of PCV on AMR-PD stems from age- and disease-specific data inputs.
  - Different model structures will require different input approaches

Population & Pathogen Level

- Pathway characterizes epidemiology of pneumococcal serotypes.
- For each disease manifestation, serotype specific inputs are required for:
  - Incidence of disease
    - Proportion of AOM and CAP attributable to pneumococcus
  - Serotype distribution within each disease manifestation
  - Serotype resistance profiles to specific antibiotics

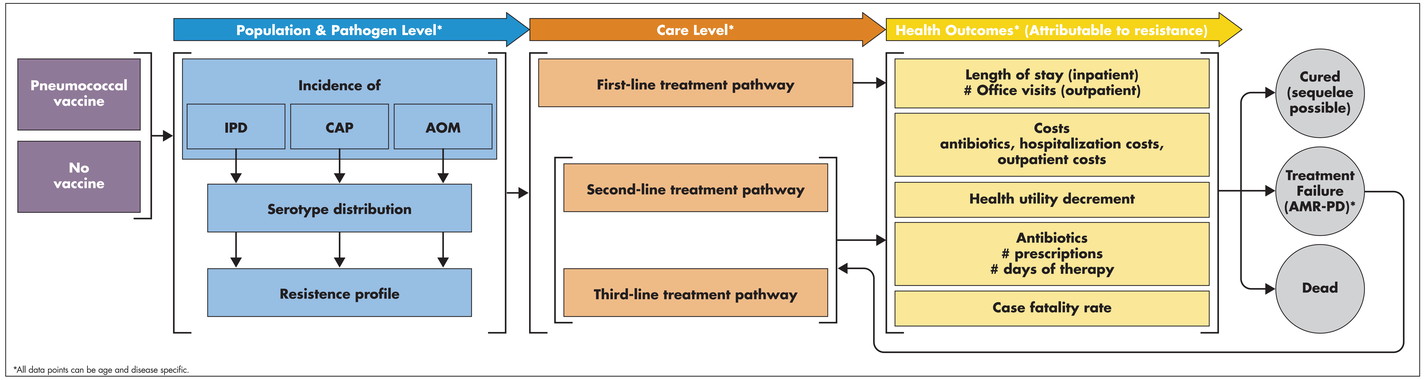
Care Level Pathway

- Pathway characterizes country-, age-, and risk-factor–specific clinical management for each disease manifestation
- Given PD, patient seeks treatment that could potentially lead to antibiotic prescribing among other protocol-driven healthcare interventions
- Treatment protocols may be determined by national guidelines, hospital protocols, society guidelines, available healthcare resources, licensed antibiotics, and antibiotic stewardship practices
- If PD encounters treatment with an antibiotic within that serotype's resistance profile, a probability of treatment failure follows
- Failure may lead to death or require a next-line treatment, which could entail further healthcare encounter (re-hospitalization, additional office visit, or increased length of hospital stay), additional antibiotics prescribed, and potentially worse outcomes (see **Health Outcomes** pathway)
- Second-line treatments follow country-, age-, and risk-factor–specific clinical practice
- Second-line failure may require third-line treatment
  - For model tractability, framework limited to 3 treatment lines (2 failures)

Health Outcomes

- Pathway characterizes AMR-attributable–PD health outcomes requiring input values impacted by antibiotic-resistant cases
  - Longer hospital length of stay
  - Additional office visits or rehospitalization
  - Increased costs of case management and additional antibiotic prescriptions
  - Decreased health-related quality of life (measured by health utility decrements)
  - Number of dispensed antibiotic prescriptions
  - Increased case fatality rates
- Cost-effectiveness model leverages inputs from all 3 pathways to define treatment success (**Cured**), a resistant case requiring a second- or third-line treatment (**treatment failure**), or a fatal case leading to **death**

Figure 1. Conceptual Framework for Inclusion of Health Economic Value of Antimicrobial-Resistant Pneumococcal Disease into a Cost-effectiveness Model



*All data points can be age and disease specific.

IMPLICATIONS

- Framework provides a method for capturing health economic benefits of attributable reduction in AMR outcomes
- However, numerous data points are required to inform data-heavy models. These data remain incomplete, and assumptions are required to fully parameterize the benefits of PCVs in reducing AMR
- Framework is incomplete in that it measures direct impact on AMR-PD but does not capture broader impacts of reducing antibiotic prescribing on non-focal bacteria

CONCLUSIONS

- **This framework presents a generalizable methodology to quantify health economic impact of PCVs on cases and outcomes of AMR-PD, potentially an important consideration of a PCV's public health and economic value**
- **Modeling vaccine-preventable burden of AMR-PD requires data extrapolations and assumptions due to the myriad of interconnected pathways**
- **Further work is needed to validate assumptions and linkages across incomplete data sources**

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DISCLOSURES

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