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Cost-effectiveness of next-generation vaccines: The case of pertussis

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ABSTRACT

Despite steady vaccination coverage rates, pertussis incidence in the United States has continued to rise. This public health challenge has motivated calls for the development of a new vaccine with greater efficacy and duration of protection. Any next-generation vaccine would likely come at a higher cost, and must provide sufficient health benefits beyond those provided by the current vaccine in order to be deemed cost-effective. Using an age-structured transmission model of pertussis, we quantified the health and economic benefits of a next-generation vaccine that would enhance either the efficacy or duration of protection of the childhood series, the duration of the adult booster, or a combination. We developed a metric, the maximum cost-effective price increase (MCPI), to compare the potential value of such improvements. The MCPI estimates the per-dose price increase that would maintain the cost-effectiveness of pertussis vaccination. We evaluated the MCPI across a range of potential single and combined improvements to the pertussis vaccine. As an upper bound, we found that a next-generation vaccine which could achieve perfect efficacy for the childhood series would permit an MCPI of $18 per dose (95% CI: $12–$31). Pertussis vaccine improvements that extend the duration of protection to an average of 75 years would allow for an MCPI of $22 per dose for the childhood series (CI: $10–$33) or $12 for the adult booster (CI: $4–$18). Despite the short duration of the adult booster, improvements to the childhood series could be more valuable than improvements to the adult booster. Combining improvements in both efficacy and duration, a childhood series with perfect efficacy and average duration of 75 years would permit an MCPI of $39 per dose, the highest of any scenario evaluated. Our results highlight the utility of the MCPI metric in evaluating potential vaccines or other interventions when prices are unknown.

1. Introduction

A resurgence of pertussis in the United States (US) has resulted in the highest incidence in over half a century [1,2]. Several hypotheses have been postulated to explain the rising incidence [3–6], with the prevailing view that the increase is attributable to shortcomings in the current vaccine series [7,8]. The acellular pertussis (aP) vaccines currently used in the US are the second generation of pertussis vaccines, licensed during the 1990s in response to concerns about severe side effects associated with whole-cell containing (wP) vaccines [9]. Elevated pertussis in adolescents, who represent the first cohorts vaccinated with the aP vaccine, has led to the suggestion that the protection conferred by the acellular vaccines wanes faster than that of the wP vaccines [10–12]. Additionally, the first doses in the acellular childhood series at 2 and 4 months confer incomplete protection against disease for infants, who have the highest burden of severe pertussis-related disease and mortality [13,14]. Recent studies have demonstrated that administration of a maternal pertussis booster vaccine during pregnancy substantially and cost-effectively reduces disease burden in newborns prior to receipt of their first dose [15–17]. Nevertheless, the apparent shortcomings of the current childhood and adult vaccination series have renewed interest in a next generation of pertussis vaccine

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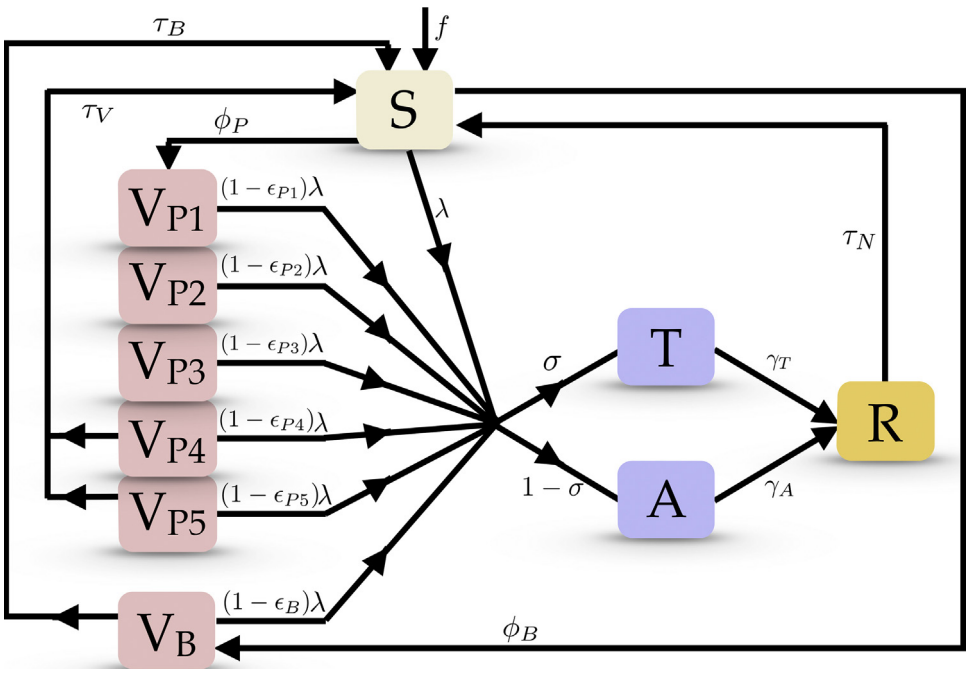

Fig. 1. Dynamic transmission model schematic.

that would provide higher efficacy for infants, a longer duration of protection, or both [7,8].

If such an improved vaccine were brought to market with a price per dose equal to the current vaccine, the decision to switch to the new vaccine would be straightforward. However, the investment that would be required to develop a new vaccine entails a higher cost per dose than that for the current vaccines. Additionally, new recommendations for maternal aP vaccination during pregnancy for infant protection [15,16] may render any health benefits of a new vaccine insufficient to justify the increased cost.

Cost-effectiveness analysis is often conducted when considering the implementation of a vaccine that has already been developed [18–22], or hypothetical vaccines against pathogens for which no vaccine exists [23–29]. While — for instance — a study of adding protection against multiple pathogens causing otitis media to the pneumococcal vaccine has identified break-even and cost-effective thresholds in vaccine price [30], no previous analysis has assessed the potential health impact and economic value of replacing a current vaccine with an improved hypothetical vaccine. With pertussis — and in similar cases where the current vaccine may have multiple shortcomings — calculating the relative value of improvements in either duration or efficacy could inform the design of a next generation vaccine to optimize public health benefit.

Here, we use a previously validated dynamic cost-effectiveness model of *B. pertussis* transmission in the US [17] to evaluate the potential health benefits and economic value of developing a next-generation pertussis vaccine. We consider three potential improvements: 1) increased efficacy of the childhood vaccination series, 2) extended duration of protection for the childhood series, and 3) extended duration of protection for the adult booster, as well as combinations of improvements. We formulate the maximum cost-effective price increase (MCPI), as a metric of the value of a new vaccine under the constraint that the vaccine remains cost-effective. The MCPI metric has general applicability to inform decision-making regarding investment in the development and the pricing of potential vaccines.

2. Methods

2.1. Transmission model structure

We modeled the epidemiological states (Fig. 1) as susceptible (S), infectious (T: typical infection, defined in the Acellular Pertussis Vaccine Trial (APERT) as a cough lasting at least 6 days [31]; A: atypical infection, all other cases), recovered (R), and vaccinated (V_P: DTaP vaccination, V_B: Tdap vaccination), keeping track of the participation of parents and their infants in a program of parental vaccination [17]. A model population of 316 million individuals was age-stratified to reflect the 2013 US population [32]. We specified the force of infection for each age class based on empirical age-specific social contact rates for the US [33]. We also incorporated parents of newborns, and parameterized the extensive contacts that they have with their infants based on time-use studies conducted in the US [17,33].

2.1.1. Parameterization and fitting

Our base case and uncertainty distributions for epidemiological and economic parameters (Tables S1 and S2) were provided by fitting our model to US incidence data from 2003 to 2012 [1]. We used empirically derived reporting rates for typical infections for four age groups: 1.38% for <1 years, 0.93% for 1–6 years, 0.45% for 7–10 years, and 0.30% for 11+ years) [17]. We assumed that the less severe atypical cases were neither hospitalized nor reported.

2.1.2. Scenarios of next-generation pertussis vaccines

Scenarios for improvement of the pertussis vaccine included: 1) increasing the efficacy of the childhood vaccination series, 2) extending the duration of protection for the childhood series, and 3) extending the duration of protection for the adult booster (Table 1).

We define efficacy, E, as the proportional reduction in the risk of infection for vaccinated individuals relative to that of a susceptible, unvaccinated individual [34]. We parameterize the efficacy of each of the first three doses of the pertussis vaccine using data from a case-control study [13]. These case-control studies

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