Journal of Infection (2016) xx, 1–10

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Cost-effectiveness and programmatic benefits of maternal vaccination against pertussis in England

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Accepted 14 April 2016
Available online ■ ■ ■

KEYWORDS
Pertussis;
Maternal vaccination;
Cost-effectiveness;
Policymaking;
Programmatic considerations

Summary *Background:* Maternal pertussis immunisation was introduced during the pertussis resurgence in England in 2012 as a temporary measure to protect infants too young to be vaccinated. The programme was shown to be safe and highly effective. However, continuation of maternal vaccination as a routine programme requires a cost-effectiveness analysis.
Method: The estimated prevented disease burden among mothers and their infants was obtained assuming 89% (95% CI: 19%–99%) vaccine efficacy for mothers and 91% (95% CI: 84%–95%) for infants. Future incidence was projected based on the disease rates in 2010–2012, including the four-year cycle of low and high incidence years. Full probabilistic sensitivity analysis was performed for different scenarios.
Results: Assuming a vaccine coverage of 60%, there were 1650 prevented hospitalisations in infants (3.5% discounting, the first 10 years), including 55–60 deaths and ~20,500 cases among mothers, of which around 1800 would be severe. The annual costs of the programme are £7.3 million assuming a price of £10 per dose and £9.4 million assuming £15 per dose. Using discounting of 3.5%, a 200 year time horizon and a price of £10 per dose (+£7.5 administration costs) only 25% of the iterations were below £30,000 per QALY. Using a 35% higher incidence resulted in 88% of the scenarios below this threshold. Assuming that the incidence remains at the level at the height of 2012, then the programme would be highly cost effective, with an ICER of £16,865 (£12,209–£25,976; price of £10 and 3.5%/3.5% discounting).
Conclusion: Maternal vaccination is effective in preventing severe illness and deaths in infants but the cost-effectiveness of the programme is highly dependent on future incidence which is

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http://dx.doi.org/10.1016/j.jinf.2016.04.012

Please cite this article in press as: van Hoek AJ, et al., Cost-effectiveness and programmatic benefits of maternal vaccination against pertussis in England, J Infect (2016), http://dx.doi.org/10.1016/j.jinf.2016.04.012

necessarily uncertain. However, the duration and magnitude of protection against transmission afforded by the current acellular vaccines is also uncertain as are the associated effects on future herd immunity. The direct protection offered by the maternal dose provides the only certain way of protecting vulnerable infants from birth.

Introduction

In October 2012, a maternal pertussis vaccination programme was introduced in England [1] as an outbreak measure in response to the highest number of infant cases and deaths from pertussis in more than a decade in 2012. All the infants who died developed disease before they were eligible to receive the primary course of pertussis vaccine. The maternal programme has been well received in England, with uptake peaking at 60% and evidence of a direct impact in infants under 3 months of age.[1]

Maternal vaccination is offered in every pregnancy, ideally between 28 and 32 weeks, but up to 38 weeks[1] and works in two ways: by passive immunisation of the infant through the transport of antibodies across the placenta and by directly protecting the mother which lowers the probability of her being a source of infection to her infant. The programme effectiveness against infant disease has been estimated to be 91% (84%—95%) in England[1] Maternal vaccination thus offers a safe[2] and effective way of directly protecting those too young to be vaccinated.

Although this programme was introduced as a temporary outbreak response measure, the question now is whether, based on the evidence of effectiveness, maternal vaccination should be added to the routine programme in England. In the England, policy recommendations by the Joint Committee and Vaccination and Immunisation require evidence of cost-effectiveness.

In this paper, we investigate the cost-effectiveness of introducing maternal vaccination programme into the national immunisation schedule, offering a dose to women in every pregnancy.

Methods

Programme under consideration

The programme under study in this analysis is vaccinating pregnant woman in the 3rd trimester with one dose of a pertussis-containing vaccine designed for adult boosting. In practice, women will be offered vaccine at the first appointment in the 3rd trimester (week 28—32, where possible and up to 38 weeks).

Impact of the vaccine

The duration and type of protection induced in the mother and infant differs. The infant is passively protected by maternal antibodies until development of active immunity following receipt of the first dose of pertussis-containing vaccine at 2 months of age. In this analysis, disease up to 3 months of age was considered preventable by maternal vaccination assuming that those hospitalised between 2 and 3 months are either still unvaccinated, or were exposed before they could develop protective antibodies after the first dose of the primary course. Vaccinating the mother will boost her pre-existing immunity which will induce protection for a longer time. This was assumed to be 5 years, based on estimates of the duration of protection after a 5th dose of acellular vaccine given around 5 years of age and antibody persistence after an adolescent acellular booster.[3] However, pertussis antibody titres rapidly decline within a year of boosting[4] and therefore vaccine is recommended in each pregnancy, regardless of vaccine history in order to passively protect the infant. This means that some women will get pregnant again and receive the vaccine for a second time while still protected against disease. Therefore, to take this into account, the effective duration of maternal protection was reduced. Where vaccine recipients do not become pregnant again they enjoy 5 years of protection; when they do have a subsequent pregnancy an average interval between pregnancies was assumed of 3 years based on national maternity data.[5] For the analysis a weighted average duration was calculated based on the observed distribution of first, second, third and fourth pregnancies (see the online material for more detail). The average duration of protection was estimated as 3.89 years or 47 months.

Therefore, for example, if a mother was vaccinated in the 5th month of the programme 2 months before delivery, disease in the mother would be on average prevented from month 5 until month 52 and in the infant from month 7 until the end of month 9 of the programme.

The preventable disease burden

The transmission of pertussis is cyclical, with a 3—4 year interval between high transmission years. Due to the fluctuating disease burden the cost-effectiveness of a dose will change over time within the cycle. Therefore the programme was evaluated over a longer period, using a fluctuating monthly incidence. The fluctuation was simulated by a sine function with a peak every 4 years, oscillating between the maximum and minimum incidence.

As the vaccine prevents both disease in the infant and the mother, separate estimates of the preventable disease burden were made. For infants under 3 months, the burden of disease was estimated from hospital admission data as pertussis at this age is severe and over 90% of cases require in-patient care[6]; it is also the most complete data source as admissions in infants under 3 months are nearly double the number of notified cases in this age group.[6] In contrast, pertussis in adults is often a mild, unrecognised illness so notifications and laboratory confirmed cases will substantially underestimate the true burden of clinical illness; it is conservatively assumed that laboratory confirmed cases comprise only a third of all clinically significant pertussis

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