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Cost-effectiveness of targeted vaccination to protect new-borns against pertussis: Comparing neonatal, maternal, and cocooning vaccination strategies

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ABSTRACT

Pertussis (whooping cough) is a severe infectious disease in infants less than 6 months old. Mass vaccination programmes have been unable to halt transmission effectively. Strategies to protect new-borns against infection include vaccination of the neonate or the mother directly after birth (cocooning), or the mother during pregnancy (maternal). Here we investigate the cost-effectiveness of these three strategies in the Netherlands. Costs for health care utilization and productivity losses, as well as impact on quality of life were calculated for a 10-year vaccination programme, assuming that vaccine-induced immunity lasts 5 years. Cocooning was the most attractive option from a cost-effectiveness viewpoint (€89,000/QALY). However, both cocooning and maternal vaccination would reduce the disease burden in infants and mothers vaccinated (about 17–20 QALY/year). Specifically, with a persistent epidemic as seen in 2012, there is need for reconsidering the vaccination schedules against pertussis in order to increase protection of the vulnerable new-borns.

1. Introduction

Pertussis infection is usually severe in un- or incompletely vaccinated infants less than 6 months old [1]. In the past decades, efforts have been made to reduce the burden of disease, and in particular to protect new-borns [2,3]. In the Netherlands, all four-year olds are offered a booster vaccination dose against pertussis since November 2001 within the National Immunization Programme. In addition, in January 2005 there was a switch from a Dutch whole cell pertussis combination vaccine to a vaccine containing acellular pertussis components. Such a switch was implemented in many western countries because of a more favourable safety profile, compared to whole cell pertussis vaccines [4,5]. Although the changes in the vaccination programme have reduced the incidence of pertussis between the age of 3 months to 8 years [6,7], the efforts are still insufficient to halt transmission completely, and severe cases in young infants continue to occur. Furthermore, vaccine-effectiveness of a booster with the acellular vaccine has shown to decline rapidly, resulting in a limited durability of protection [8,9].

Pertussis resurges every 4–5 years. In 2011–2012, a worldwide increase in pertussis notifications was observed, underpinning the need for improved control strategies [10–12]. The high incidence levels of pertussis underline the need for further measures to protect at least the most vulnerable, the new-borns. It has been found that an infant with pertussis is most likely infected by a household contact [13,14]. A household transmission study conducted in the Netherlands explored the effectiveness of a cocooning vaccination strategy within the family, showed that vaccinating mothers could be the most effective strategy to prevent infection of infants [15].

With the new insights in the limited durability of protection of acellular vaccine, the transmission within the family, and the current increase in incidence, assessing the cost-effectiveness of vaccination to protect the new-borns is warranted, to guide decisions on new vaccination strategies. Three strategies have recently come to the fore: neonatal, parental cocooning, and maternal vaccination. These are potential additions to the current immunization programme for vaccination directly targeted to protect infants. Our aim was to perform cost-effectiveness analyses of the above mentioned vaccination strategies.

2. Methods and data

Quality adjusted life years (QALY) are gained due to less disease and fewer deaths due to vaccination, in new-borns and vaccinated

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mothers. In the analyses, each vaccination strategy was compared to the current situation in the Netherlands, i.e., in the absence of neonatal, cocooning and maternal vaccination, in an incremental cost-effectiveness ratio (ICER), with the time perspective of 10 years.

We analyzed a baseline scenario based on notifications from Dutch surveillance incidence data over the period 2002–2011. Costs of vaccination and treatment, and effectiveness of vaccination were based on earlier research [13,16]. The relevant data were retrieved from the Dutch birth registries [17], from the literature, the Dutch disease notification system (OSIRIS), and from our earlier studies [6,13,15,16,18] (Table 1). All prices are expressed in Euros (€) in 2009 year's price level. Future costs are discounted at 4% and life years gained with 1.5% following the Dutch guidelines [19]. A reasonable threshold for a cost-effective intervention is currently cited to be €20,000–€50,000/QALY [20,21]. All analyses were carried out using Microsoft Excel®.

2.1. Incidence of pertussis

Although pertussis is notifiable in the Netherlands, many infections go by unnoticed. The degree of underreporting has been estimated in cross-sectional serological and household studies to lie between a factor of 100–200, mainly in adults [18,22]. Underreporting forms a problem since asymptomatic infections can transmit an infection, especially in a close-contact relation, such as the one between a mother and her new-born. In infants, pertussis usually leads to disease severe enough to be recognized, resulting in minor underreporting. The average number of notified cases yielded an annual incidence of infections in infants (0–5 months) of 130/100,000 in 2002–2011. During 2002–2011 there have been two deaths due to pertussis registered in infants less than 6 months of age, and therefore we assumed 0.2 deaths annually. Estimation of expected number of infections in parents with a new-born was based on the average number of notifications, in the same time period as for infants, in the age-group 20–40 years [15], adjusted for population size and gender in this age-group [17] and 100 times underreporting, yielding an average, yearly incidence in women of 2606/100,000.

2.2. Vaccination strategies

Differences between the three vaccination strategies regarding costs and effects of vaccination entail the number of vaccinations and the proportion of new-borns that are protected against (severe) disease (Table 2). For the neonatal strategy, the number of vaccinations was based on number of live born children, vaccinated within two weeks from birth. In the cocooning strategy, vaccination of mothers would take place directly after the birth of the child, and the number of eligible women is equal to number of live births corrected for multiple births. We only included vaccination of the mothers, since our analyses indicated that including also fathers would not increase the cost-effectiveness (details available upon request). Maternal vaccination entails vaccination of pregnant women in the last trimester. The number of vaccination doses was calculated as the number of live-born corrected for multiple births and a factor to adjust for intrauterine deaths and dead-born babies. According to available data from the national statistics, the average percentage of dead-born infants from gestation week 30 and deaths within a week from birth was about 0.3% of the live born infants.

In the cocooning strategy all new mothers would be vaccinated every 5th year (not only the first time mothers) in view of waning immunity. Younger siblings born within a 5-year period, would then also be protected against transmission from the mother if she were to be vaccinated, and there would be less pertussis cases and less number of vaccinations needed after the first year of vaccinations. Furthermore, there would be need for a one-year catch-up campaign the year before starting a regular programme, but this extra year was not included in the cost-effectiveness calculations. For the maternal vaccination strategy, the primary goal is to protect the new-born immediately after birth by transplacental transport of maternal antibodies to the foetus. The 50% waning of the maternal antibody concentration within one year after immunization [5] implies that all pregnant women would have to be vaccinated during each pregnancy. We were not able to correct for the cocooning effect of this strategy on subsequent new-borns.

The number of preventable cases was based on number of notified cases in new-borns and mothers, and depended on the vaccine efficacy (90%) and vaccine up-take (75%). In lack of reliable data to decide otherwise, vaccine efficacy is assumed to be the same in all scenarios. Vaccination would not yield instant protection against infection in the new-born for the strategies neonatal and cocooning. To adjust for this we assumed that baby's would not be protected against infection and death for the first 14 days after birth for these two vaccination strategies (Table 3).

We used the results from a Dutch study to estimate the percentage of infections in new-borns that could be prevented by vaccinating the mother in the cocooning strategy, where the infant was not the first case in the household [15]. We assume that cocooning would not protect against infections directly transmitted to the infant from outside the household (Table 1). For neonatal and maternal vaccination, the new-born would potentially be protected against all infections due to the direct protection, depending on vaccine effectiveness and uptake. We assumed that one inoculation would protect against infection in the mother, and in the new-born when vaccinated. Furthermore, we assumed that the infant would not be protected in case of failure of the vaccine to protect the mother.

2.3. Health related quality-of-life

Health Related Quality-of-life (HRQoL) weights for pertussis infection, in combination with the length of disease were used to estimate the QALYs [23]. Infections that had not been notified (the underreported cases) were assumed to induce a lower HRQoL-loss due to infection compared to notified cases [24]. We made no distinction between HRQoL-loss in hospitalized cases compared to non-hospitalized due to the negligible influence on the cost-effectiveness results, because of the small number of hospitalized cases in adults and to the uncertainty about the difference in HRQoL-loss. Since the hospitalizations mainly occur in infants, the age-specific HRQoL-loss reflects this difference in severity of illness. We included life-years lost due to deaths as average life-expectancy at birth (80.6 years) being (discounted: 46.8 years).

2.4. Direct health care costs

The direct health care costs are costs of vaccination and of treatment of disease (in- and outpatient). With regard to the cost-calculations, we used previous estimates of vaccination and treatment costs [16]. The cost of vaccination includes the cost of the vaccine as well as administration costs. For the neonatal strategy a trained nurse or mid-wife would give the injection at a regular check-up, for the cocooning a nurse or mid-wife present at the delivery would give the injection as soon as possible after birth, and vaccination of the pregnant woman (the maternal vaccination) would take place at a regular pregnancy control. Treatment costs entailed average number per infection of physician consultations (general practitioner (GP) and specialist), antibiotics and cough medication, diagnostic tests, and hospitalizations, including at intensive care units.