Parent “cocoon” immunization to prevent pertussis-related hospitalization in infants: The case of Piemonte in Italy

Michela Meregaglia, Lorenza Ferrara, Alessia Melegaro, Vittorio Demicheli

**Abstract**

Pertussis incidence in Piemonte (Italy) is now at the lowest level ever reached (0.85 per 100,000 in 2010) but the disease is still endemic in infants (54 per 100,000 in 2005–2010).

Parental “cocoon” immunization has been proposed in some countries (i.e. United States, France) as a measure to protect newborns from serious pertussis outcomes. We assessed the number needed to vaccinate (NNV) to prevent hospital admissions in infants (<12 months) and the potential cost-effectiveness of this strategy in Piemonte. The NNV for parental immunization was at least 5000 to prevent one infant hospitalization in the latest epidemic cycle (2005–2010) at the cost of >€100,000. The “cocoon” programme leads to net costs from a National Health Service (NHS) perspective (ROI < 1).

In contexts of low incidence and without reliable data on a high parent-attributable infant risk, the parental “cocoon” programme is poorly efficient and very resource intensive in preventing pertussis in infants.

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1. Introduction

Pertussis, or whooping cough, is a highly infectious respiratory disease caused by the bacteria *Bordetella pertussis* or occasionally *B. Parapertussis* [1,2]. Transmission occurs primarily through contact with respiratory droplets or secretions from infected persons [1]. Pertussis in adolescents and adults is generally mild and passes unnoticed while the infection may be severe in infants, with complications including pneumonia, seizures and encephalopathy. Very young infants experience the highest rates of morbidity [3].

In Italy, pertussis immunization of infants has been recommended since the 1960s but only in 2002 it was included among the vaccinations to be offered free of charge to children [4] and the immunization coverage is high (97% in 2010). It has been suggested that vaccine-induced immunity wanes after 4–12 years [5] and, as a consequence, the distribution of cases appears to have shifted to adolescents and adults [6], who represent an important source of infection for susceptible infants. Paediatrician schedules recommend routine immunization beginning at 8 weeks of age, so that younger infants are at high risk of infection. To cover this short interval of risk, the “cocoon” strategy has been proposed in some countries such as the United States, France, Germany and Belgium.

In 2012, South Korea introduced the Tdap Immunization of individuals 11–64 years with frequent contacts with infants [7].

According to the “cocoon”, parents and other close contacts should receive a booster dose during pregnancy or immediately after delivery. A number of economic analyses estimated that cocooning is cost-effective and even cost-saving from a societal perspective [1,8]. However, a recent study [9] revealed that the number of parents needed to vaccinate in order to prevent serious pertussis-related outcomes in infants is too high in a context of low pertussis incidence. Caution on “cocoon” strategy is shared also by the WHO [10]. This study is aimed at estimating the number needed to vaccinate (NNV) within parental “cocoon” immunization in order to prevent hospital admissions in infants and determining its potential cost-effectiveness.

2. Methods

Notification of pertussis has been mandatory in Piemonte since 1934. The case definition is based on clinical diagnosis. Notifications do not capture all cases of disease [1], as pertussis may take a modified clinical course in adults and the elderly [2]. To address underreporting, the yearly incidence was estimated for the youngest age groups by means of hospital admissions, which appeared to be higher than the number of reported cases. Data on pertussis-related hospitalizations (ICD9 codes: 0330; 0331; 0338; 0339 and 4843) were derived from the regional hospital discharge database (SDO) for the years 2000–2010. Official statistics
NNV and costs to prevent hospitalization in infants through parent cocoon immunization (by age categories in months).

<table>
<thead>
<tr>
<th>N. hospital admission</th>
<th>Risk of pertussis hospitalization (per 100,000)</th>
<th>Percentage attributed to a parent</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Scenario A: 32%</td>
</tr>
<tr>
<td>&lt;3 months</td>
<td></td>
<td>14,753</td>
</tr>
<tr>
<td>2005–2010</td>
<td></td>
<td>273,668</td>
</tr>
<tr>
<td>Cost (€)</td>
<td></td>
<td>11,400</td>
</tr>
<tr>
<td>2009 (high hosp)</td>
<td></td>
<td>211,470</td>
</tr>
<tr>
<td>Cost (€)</td>
<td></td>
<td>31,350</td>
</tr>
<tr>
<td>&lt;12 months</td>
<td></td>
<td>581,543</td>
</tr>
<tr>
<td>2005–2010</td>
<td></td>
<td>9289</td>
</tr>
<tr>
<td>Cost (€)</td>
<td></td>
<td>172,311</td>
</tr>
<tr>
<td>2009 (high hosp)</td>
<td></td>
<td>7486</td>
</tr>
<tr>
<td>Cost (€)</td>
<td></td>
<td>138,865</td>
</tr>
<tr>
<td>&lt;12 months</td>
<td></td>
<td>18,578</td>
</tr>
<tr>
<td>2005–2010</td>
<td></td>
<td>344,622</td>
</tr>
</tbody>
</table>

NNV = infant hospitalization risk ×% of infants infected by parents - adult VE

Assuming that the vaccine-induced immunity lasts 4–12 years on average [5], other children will also benefit from cocooning. The NNV was then divided by the fertility rate (1.4 in 2010) [15]. The NNV was calculated for the most recent epidemic cycle (2005–2010), including years with the highest (2009) and lowest (2005) incidence estimates.

A cost-benefit analysis (CBA) was performed. The 2011 retail price of a single dose of Tdap adults vaccine was €12.34. The vaccine administration cost was assumed at €0.21/dose [16]. For pertussis related hospitalizations, Italian DRG-based average cost per case was used. It was assumed that no indirect costs were incurred for infants aged 0–12 months owing to Italian compulsory and optional maternity leaves. The main economic measure was the benefit-to-cost ratio (BCR), defined as the net savings deriving from vaccination (in terms of hospitalizations avoided) divided by the vaccination costs.

3. Results

The annual incidence rates (per 100,000) of pertussis were analyzed over the period 1995–2010. An epidemic occurred in 1998, when incidence peaked at 15.5; then it began to fall reaching a low of 0.85 in 2010. Pertussis continued to be the cause of significant morbidity in young infants (<12 months) with epidemic peaks regularly occurring every 2–3 years and with peak incidence at the third month of life. The average infant hospitalization rate was 54 per 100,000 between 2005 and 2010, while the average length of stay was about one week.

Available studies estimating the source of pertussis infection in infants were reviewed [3,17,18]. As the source of infection was only partially identified (between 59% and 80% of the cases), a range of values was derived from two recent studies [3,18] and the NNV was estimated on the basis of a parent-attributable infant risk of 32%, 40% and 55%.

<table>
<thead>
<tr>
<th>Hospitalization</th>
<th>No cocoon</th>
<th>Cocoon (32%)</th>
<th>Cocoon (40%)</th>
<th>Cocoon (55%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effectiveness (%)</td>
<td>46</td>
<td>33</td>
<td>30</td>
<td>23</td>
</tr>
<tr>
<td>BCR (RO1)</td>
<td>28.3</td>
<td>34.8</td>
<td>50.0</td>
<td></td>
</tr>
</tbody>
</table>

There were limited direct VE data for a single dose of acellular pertussis vaccine in adults [9]; thus, for the present study, an estimate of 89% was used [5].

For the period 2005–2010, the NNV to prevent one hospitalization in infants aged <12 months, assuming that parents account for 32% of infant illnesses (lower bound scenario), reached almost 10,000 (Table 1). The corresponding vaccine cost per pertussis case prevented was estimated at ~€170,000. Even in the upper bound scenario (55%) the NNV would still exceed 5000 and the cost per avoided case would be over €100,000. During a period of low incidence (2005) the NNV increases up to ~18,500 at the cost of ~€345,000. The parental NNV to prevent hospitalization in infants <3 months is even higher (between 8000 and 15,000 parents to be vaccinated) owing to the abbreviated period of risk.

In the absence of parental “cocoon” immunization, there were 46 pertussis-related hospitalizations in infants <12 months in 2009–2010 (Table 2). Had the “cocoon” strategy been adopted, this number would have decreased to 33, 30, and 23 respectively under different assumptions of the proportion of children infected by parents. The average cost of hospitalization per infant (<12 months) in 2009–2010 was €1795 [19] and the total cost of pertussis-related hospitalization in infants was ~€82,595 (Table 3). The parental “cocoon” strategy under all assumptions would determine net costs instead of net savings in Piedmont.

To test the results, a sensitivity analysis was performed by varying the values of incidence rate and vaccination costs.

To achieve the cost-effectiveness threshold (at which the cost of a case prevented by “cocoon” is equivalent to the average cost of an

<table>
<thead>
<tr>
<th>Hospitalization costs</th>
<th>No cocoon</th>
<th>Cocoon (32%)</th>
<th>Cocoon (40%)</th>
<th>Cocoon (55%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccination costs</td>
<td>0</td>
<td>2,854,400</td>
<td>2,854,400</td>
<td>2,854,400</td>
</tr>
<tr>
<td>Total medical costs</td>
<td>82,595</td>
<td>2,913,487</td>
<td>2,907,605</td>
<td>2,896,575</td>
</tr>
<tr>
<td>Net costs or savings</td>
<td>2,930,892</td>
<td>2,825,010</td>
<td>2,813,980</td>
<td>2,802,957</td>
</tr>
<tr>
<td>BCR (RO1)</td>
<td>0.0082</td>
<td>0.0103</td>
<td>0.0142</td>
<td>0.0174</td>
</tr>
</tbody>
</table>
infant hospitalized), the risk of hospitalization should be approximately 100 times higher, while the vaccination cost should be less than €1.

4. Discussion

According to regional-specific data, our study found a very high NNV for the parental “cocoon” programme. The NNV remained high when the fertility rate per woman was included in the formula [15] to account for successive births. The cost per case prevented was consequently extremely (>€100,000). The economic evaluation of cocooning was performed through a CBA, as the monetary approach is generally welcomed by public decision-makers, especially in the Italian setting [16]. The alternative use of quality-adjusted life years (QALYs) as a benefit measure could have been problematic in the case of pertussis since QALY data are not directly available and the quality of life may not be the relevant outcome. CBA demonstrates that the introduction of parental “cocoon” vaccination would be poorly effective in reducing the burden of hospitalized cases and that the programme would determine net costs instead of net savings.

Our findings are consistent with those of the study conducted in 2011 [9] in two Canadian provinces (Québec and British Columbia), both experiencing low rates of pertussis (1.4 and 2.8 respectively in 2010). The NNV for death was at least 1 million, for intensive care unit admission it was ~100,000 and for averted hospitalization it was >10,000 based on 35% parent-attributable infant risk.

Our study only assessed direct infant hospitalization costs (3% of “cocoon” cost). We did not include direct costs due to pertussis morbidly in adults or other herd immunity effects. A study conducted at Anna Meyer’s Children’s Hospital in Florence demonstrated that the hospitalization cost of a paediatric case is higher than that calculated through the DRG (~€511 per day) [20]. If this value is used, Piemonte hospitalization costs would be higher (~€197,450) but the economic performance of cocooning wouldn’t be modified.

These results contradict more optimistic outcome estimates [18] and confirm that a parental “cocoon” strategy is not favourable in a context of low pertussis incidence. Cocooning shows to be extremely resource intensive and poorly efficient in reducing pertussis-related hospitalizations. Therefore, a recommendation for the “cocoon” programme is crucially dependent upon the epidemiological context in which it is proposed. Further studies assessing the proportion of cases due to transmission from household members should be encouraged.

References


