Title: Return on Investment of Preventively Vaccinating Healthcare Workers against Pertussis: a Dutch case study

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ABSTRACT (298 words)

Background
Healthcare workers (HCW) are at particular risk of acquiring pertussis and transmitting the infection to high-risk susceptible patients and colleagues. In this paper, the return on investment (ROI) of preventively vaccinating HCW against pertussis to prevent nosocomial pertussis outbreaks is estimated using a hospital ward perspective, presuming an outbreak occurs once in 10 years.

Methods
Data on the pertussis outbreak on the neonatology ward in 2004 in the Academic Medical Center Amsterdam (The Netherlands) was used to calculate control costs and other outbreak related costs. The study population was: neonatology ward staff members (n=133), parents (n=40), neonates (n=20), and newborns transferred to other hospitals (n=23). ROI is presented as the amount of Euros saved in averting outbreaks by investing one Euro in preventively vaccinating HCW. Sensitivity analysis was performed to study the robustness of the ROI. Results are presented at 2012 price level.

Results
Total nosocomial pertussis outbreak costs were €48,682. Direct control costs (i.e. Antibiotic therapy, laboratory investigation and outbreak management control) were €11,464. Other outbreak related costs (i.e. sick leave of HCW; restrictions on the neonatology ward, savings due to reduced working force) accounted for €37,218. Vaccination costs would be €12,208. The ROI of preventively vaccinating HCW against pertussis was 1:4, meaning 4 Euros could be saved by every Euro invested in vaccinating HCW to avert outbreaks. ROI was sensitive to a lower vaccine price, considering direct control costs only, average length of stay neonates on the neonatology ward, length of patient uptake restrictions, assuming no reduced work force due to ward closer and presuming more than one outbreak to occur in 10 years’ time.

Conclusion
From a hospital ward perspective, preventive vaccination of HCW against pertussis to prevent nosocomial pertussis outbreaks results in a positive ROI, presuming an outbreak occurs once in 10 years.

Key words: Pertussis; Nosocomial outbreak; Healthcare workers; Return on investment; Vaccination; Cost
BACKGROUND

Pertussis among healthcare workers (HCW) is of special concern because of the potential for nosocomial exposure to susceptible patients and other HCW [1]. HCW are at particular risk of acquiring pertussis and may transmit the infection to young infants and colleagues [2]. Compared to the general adult population, HCW are reported to have an almost 1.7-times higher risk of pertussis [3]. In literature, reports of nosocomial pertussis outbreaks following community or hospital exposures of HCW are available [4-7]. Nosocomial outbreaks not only generate a considerable disease burden in humans, but can also result in substantial control costs and other outbreak related costs for hospitals. The type of expenses include diagnostic testing, provision of antibiotic treatment or prophylaxis, costs associated with furlough of employees, and time spent by occupational health infection control staff to track and identify exposed individuals, as well as costs associated with dissemination of information [2]. Previous studies estimating the nosocomial pertussis outbreak costs among HCW concluded that these outbreaks resulted in serious adverse health and economic consequences to the hospitals, HCW, patients and their families [1,5,8,9]. Using a hospital perspective, Ward et al., [5] estimated the total outbreak costs among HCW at €46,691 (Euro 2002 estimate) (€55,579 2012 estimate\(^1\)) for 91 cases in a French hospital. Calugar et al., [1] calculated the total outbreak costs at $81,382 (USD 2004 estimate) (€76,945 2012 estimate\(^{1,2}\)) for 17 cases in a hospital in the United States. From the hospitals’ perspective, Baggett et al., [8] calculated costs of two hospital outbreaks in the United States at $121,130 and $263,357 (USD 2004 estimates) (€114,526 and €248,998 2012 estimates\(^{1,2}\)), respectively. Zivna et al., [9] estimated the total outbreak costs to be $85,066-$98,456 (USD 2004 estimate) (€80,428 - €93,088 2012 estimate\(^{1,2}\)) in a tertiary care medical center in the United States. According to Calugar et al., [1] cost savings and benefits can be accrued by vaccinating HCW against pertussis, with benefits for the hospital estimated at 2.38 times a dollar invested in vaccinating HCW (USD 2004 estimate). Therefore, prevention of


\(^{2}\text{Exchange rate from USD 2012 to EURO 2012: 0.778 (http://stats.oecd.org/index.aspx?queryid=169)}\)
nosocomial pertussis outbreaks by preventively vaccinating HCW can be beneficial and has the potential to reduce the overall disease and economic burden of pertussis. In the Netherlands, infants are vaccinated against pertussis on the age of 2, 3, 4, 11 months, and 4 years in the National Immunization Program (NIP) [10], meaning in the first four months, infants are not fully protected against pertussis. A national vaccination recommendation of HCW has yet to be made in the Netherlands. Nosocomial pertussis outbreaks have occurred in the Netherlands in the past decade [11,12]. However, economic consequences of such pertussis outbreaks and the potential benefits of preventively vaccinating HCW have not been evaluated. In this paper, we aim to calculate the return on investment (ROI) of preventively vaccinating HCW against pertussis to prevent nosocomial pertussis outbreaks using a hospital ward perspective. Data on the nosocomial pertussis outbreak on the neonatology ward in the Academic Medical Center Amsterdam (AMC) in The Netherlands in the year 2004 (Box 1) were used as a case study to examine the economic impact of a pertussis outbreak in a neonatology ward.
**BOX 1: Case study**

**Nosocomial pertussis outbreak on the neonatology ward in the AMC in the Netherlands in 2004**

On June 11, 2004 a secretary of the neonatology ward of the AMC experienced cold symptoms with cough. From June 28 onwards, this staff member was on sick-leave. On July 6, the occupational health service performed serological tests for pertussis, which resulted in high antibodies of *Bordetella pertussis*, caused by a recent pertussis infection. Two nurses and a physician working on the neonatology ward were infected. Laboratory investigations reported additional five infected cases. In total, nine pertussis cases were reported. Several outbreak-containment measures were undertaken in the hospital related to patients, their parents, and staff members of the neonatology ward.

**Patients and parents**

All newborns (n=20) were tested on pertussis with Polymerase Chain Reaction tests (PCR) on nasopharyngeal swabs and blood samples for serology were taken. All newborns received erythromycin during 14 days. Their parents (n=40) were treated with azithromycin during three days (i.e. fathers (n=20) and non-lactating mothers (n=7)) or erythromycin during 14 days (i.e. lactating mothers (n=13)). There were also newborns transferred to another hospital (n=23). Their parents were informed (telephone calls) about their child being at-risk of developing pertussis.

**Staff members**

Of the 133 staff members, including consultants, domestic cleaners, and all other persons who visited the ward at least once during the outbreak period most received azithromycin during three days. Erythromycin during 14 days was only given to lactating and pregnant staff members (n=5). Only one staff member refused to receive prophylaxis and wore a surgical mask for three weeks. Nasopharyngeal swabs for PCR (n=24) and blood samples for serology (n=27) were taken.
Other measures

In the hospital, crisis meetings (n=5) were organized during the outbreak period with ten HCW present at every meeting. In addition, one neonatologist spent one whole week working on controlling the outbreak. Furthermore, a survey was performed by the occupational health service department to investigate the experience of all staff members (n=133) on receiving prophylaxis. Also, there was a restriction on the intake of new patients on the neonatology ward for ten days.

For more information on the nosocomial pertussis outbreak in the AMC in The Netherlands, please see Zwart et al., [11].
METHODS

Data collection & study population

During the outbreak period, data were collected by the occupational health service department of the AMC (hereafter referred as “AMC database”) on all control measures undertaken related to newborns, their parents, staff members, and to the organization within the hospital. The study population consisted of: neonatology ward staff members (15 neonatologists, 100 nurses, 18 assistants), parents of newborns (20 fathers, 13 lactating mothers, 7 non-lactating mothers), neonates (20 infants) and parents of 23 newborns who were transferred to another hospital.

Assumptions

The following assumptions were made in this study as the AMC database did not capture all data on the outbreak:

- Due to patient uptake restrictions, we assumed that the following activities were performed during regular working hours (i.e. not resulting in additional costs for the hospital ward):
  - telephone calls made to parents whose children were transferred to another hospital;
  - time spent by the neonatologist working on controlling the outbreak;
  - survey performed by the occupational health service department as this is normal procedure during an outbreak in the AMC;
  - all drug and vaccination administrations;
  - PCRs done on nasopharyngeal swabs and blood samples taken for serology;

- Based on average Dutch working population [13] we assumed that an average working week of staff members other than neonatologists consisted of 32 hours; neonatologists were assumed to work 42 hours/week [14];

- No further transmission of the pertussis infection took place after restrictions on the patient uptake on the neonatology ward were lifted;
Reduced work force was required to run the neonatology ward during the period of restrictions on the patient uptake. We assumed that on day 1, 2, 3 and 4, 0%, 5%, 10% and 15% reduced work force was required, respectively. On day five and onwards, this assumption was set at 20%.

Cost estimations

Total outbreak costs were calculated by considering:

- direct control costs (i.e. (i) medical consumption costs containing antibiotics, (ii) laboratory investigation costs, (iii) outbreak control management costs) and
- other outbreak related costs (i.e. (iv) replacing costs for sick hospital staff members, (v) losses due to restrictions on patient uptake on the neonatology ward and (vi) savings due to a reduced work force required on the neonatology ward during patient uptake restriction period).

Dutch prices were used to derive medication costs and other resource unit costs [14-17], and where necessary updated to 2012 using Dutch consumer price index (CPI) [13].

Vaccination costs were calculated by considering:

- catch-up vaccination: vaccination of all HCW (n=133) one year after the outbreak based on the list price for Infanrix® IPV (diphtheria, tetanus, acellular pertussis and inactivated poliomyelitis) vaccine (€34.50 per vial) [18, 19];
- vaccination of newly employed HCW staff (assumption 10% per year) for a period of 10 years. New HCW were assumed to be unvaccinated but would be vaccinated upfront when hired at 100% coverage rate;
- booster vaccination to be provided eight years after first vaccination due to the declining vaccine effectiveness [20].

Return on Investment (ROI)
ROI of preventively vaccinating HCW was calculated by dividing the return on investment (i.e. averted outbreak costs, using the AMC outbreak costs as proxy) by the cost of the investment (i.e. cumulative vaccination costs including booster vaccination):

\[ ROI = \frac{\text{Averted outbreak costs}}{\text{Vaccination costs}} \]

and it is presented as a ratio: the amount of Euros saved by averting an outbreak times one Euro invested in vaccinating HCW. All costs are presented in Euro at 2012 price level and without time-discounting. Discounting is applied in sensitivity analysis.

**Model**

The analysis was conducted in MS Excel, version 2007 based on the study population and the input parameters displayed in Table 1. The outcome measures were:

- total nosocomial pertussis outbreak costs, split up as costs of antibiotics, costs of laboratory investigations, costs of outbreak control management, costs due to work absence of sick staff members, losses due to restrictions on patient uptake and reduced costs (=savings) due to reduced working force;
- ROI of preventively vaccinating HCW assuming one outbreak within 10 years’ time.

**Sensitivity analysis**

Univariate sensitivity analysis was performed on several input parameters to further test the robustness of the outcomes. In table 2, the scenarios for the sensitivity analysis together with the values of input parameters are displayed. Amongst other variables, the impact of discounting future outbreak costs and vaccination costs on the ROI was estimated, using a discount rate of 4%, according to Dutch health economic guidelines [14]. Also, the number of pertussis outbreaks in a period was varied (i.e. once or twice in 10 years, once in 20 years).
RESULTS

Total nosocomial pertussis outbreak costs in the AMC in the Netherlands were €48,682. Direct control cost account for less than 25%. The majority of the costs were caused due to patient uptake restrictions on the neonatology ward, including savings due to reduce working force (33%), and due to absenteeism of HCW (43%). Medical consumption costs were €785, laboratory investigation costs accounted for €6,982, outbreak management control costs were €3,697, costs due to absenteeism were €21,008, and costs due to patient uptake restrictions were €16,210. Cumulative vaccination costs, including boostering, were €12,208. The return on investment of vaccinating HCW was 1:4, meaning 4 Euros can be saved by investing one Euro in vaccinating HCW to prevent a nosocomial pertussis outbreak (Table 3).

Sensitivity analysis

Vaccine price, inclusion of direct control costs only, average length of stay neonates on the neonatology ward, length of patient uptake restrictions, assuming no reduced work force due to ward closer, and presuming two outbreaks would occur in 10 years time had an impact on the ROI (Table 4). The ROI increased to 1:6.6 when vaccine price was decreased to €18.30 per dose. When only direct control costs were considered in the ratio, ROI was slightly negative (1:-0.9). The ROI was 1:7.8 when average length of stay of neonates in the ward was assumed to be shorter (i.e. 7 days versus 14 days), and would be 1:2.7 if average length of stay of neonates would be 21 days. A shorter and a prolonged length of patient uptake restrictions resulted in a lower (1:2.9) and a higher (1:6.9) ROI, respectively. Assuming no reduction in the work force on the neonatology ward resulted in a ROI of 1:6.5. Presuming an outbreak would occur twice in 10 years, the ROI would be 1:7.9, if undiscounted and 1:7.4 if discounted. All other factors, including discounting, changed only slightly the calculated ROI (see Table 4).
DISCUSSION

The return on investment of preventively vaccinating HCW against pertussis to prevent a nosocomial pertussis outbreak was 1:4, meaning 4 Euros can be saved by investing one Euro on preventive vaccination of HCW to prevent a pertussis outbreak. Total nosocomial pertussis outbreak costs in the AMC were €48,682. Direct control costs and other outbreak related costs were 24% and 76% of total costs, respectively. The majority of the costs were caused due to patient uptake restrictions on the neonatology ward of the hospital and by absence of the infected HCW. ROI was sensitive to a lower vaccine price (higher ROI), inclusion of direct control costs only (negative ROI), average length of stay neonates on the neonatology ward (lower/higher ROI), length of patient uptake restrictions (lower/higher ROI), assuming no reduced work force due to ward closer (higher ROI), and presuming two outbreaks would occur in 10 years’ time (higher ROI). Discounting costs, however, had only a marginal impact on the ROI.

Comparison with previous studies

Our findings on total outbreak costs were in accordance with Calugar et al., [1] and Ward et al., [5]. However, costs reported by Baggett et al., [8] were much higher compared to our study, which was primarily the result of higher personnel costs used in Baggett et al., [8]. Our estimate of the ROI was slightly higher than calculated by Calugar et al., [1] but still in the same order of magnitude.

Limitations & Assumptions

A major limitation of this study is the possibility of recall bias because the data on the pertussis outbreak were recalled from the year 2004. Another limitation is the narrow perspective (i.e. hospital ward) used in this study. However, using a broader perspective and including additional costs would have led to even a more favourable (i.e. higher) ROI. The assumptions made in this study led to outbreak cost estimates which can be considered as conservative. First, handling costs of several activities (e.g. drug and vaccination administration, PCRs, blood samples, and survey) were not
considered as it was assumed that these activities were performed by the staff themselves during their regular working hours. Including the costs of these activities would lead to higher total outbreak costs and a higher ROI. Second, it was assumed that no further transmission of the infection took place when patient uptake restrictions on the neonatology ward were lifted. In practice, additional infections could occur after these restrictions would be lifted, which would lead to additional outbreak costs and a higher ROI. Third, additional costs related to the spread of the infection by children who were brought to other hospitals were behind our perspective (i.e. the hospital ward) and therefore not considered. But also productivity losses due to work absence of sick parents (i.e. only fathers as mothers would be on maternity leave) were disregarded because of the restricted perspective. Both - negative externalities to the Dutch society - might be omitted if the HCW would have been vaccinated. Fifth, psychological impact on parents with newborns due to a prolonged stay and treatment in the hospital was not quantified. Sixth, the prevented outbreak costs were based on one single outbreak. A larger or a smaller outbreak in a slightly other setting might lead to higher or smaller ROI than presented in the current study. Finally, the ROI estimated in this study is based on preventing one nosocomial pertussis outbreak. In practice, more nosocomial outbreaks could possibly be prevented by preventive vaccination of HCW, which would lead to a higher ROI.

**Policy implications**

In the Netherlands, a national vaccination recommendation of HCW against pertussis has yet to be made. In the Dutch society, infants are not fully protected against pertussis in the first few months of their life. To provide protection to this vulnerable group, preventive vaccination of HCW working with vulnerable infants who are not fully protected could be a relevant intervention. Also, it could be argued that hospitals as employers should have some responsibility in preventing nosocomial infections and protecting both, patients and staff members. Therefore, within policy decision making on vaccination recommendations, vaccinating HCW should also be recommended.
CONCLUSION

In conclusion, the current study demonstrated that from a hospital ward perspective, preventive vaccination of healthcare workers against pertussis to prevent nosocomial pertussis outbreaks does result in a positive return on investment (1:4). Therefore, preventive vaccination of healthcare workers can be considered a wise use of healthcare resources enabling the prevention of nosocomial pertussis outbreaks with the tendency to reduce, both the economic and disease burden of pertussis in both, hospital setting and the society.
LIST OF ABBREVIATIONS USED

HCW: Healthcare Workers
ROI: Return on Investment
USD: United States of America Dollar
AMC: Academic Medical Center Amsterdam
PCR: Polymerase Chain Reaction test
IPV: Inactivated Polio Vaccine

COMPETING INTERESTS

This study was conducted in collaboration between the Academic Medical Center Amsterdam (AMC), the Julius Center for Health Sciences and Primary care of the University Medical Center Utrecht (UMCU), Utrecht University (UU), and GlaxoSmithKline (GSK) in The Netherlands. The data on the nosocomial pertussis outbreak was collected in the AMC. Data analysis was performed in collaboration between the AMC, UMCU, UU and GSK. One of the authors (LT) works for the pharmaceutical industry (GSK). Parallel to this employment, LT is a professional PhD-researcher at the Utrecht Institute for Pharmaceutical Sciences at UU. This study was not financially supported by any source. However, UMCU received a consult fee from GSK to enumerate the work done by MJM, i.e. checking the cost-analysis performed in this study and helping with the manuscript. But MJM is employed and paid by UMCU. The authors declare that they have no further competing interests.

AUTHORS’S CONTRIBUTIONS

LT, GF, and HdB conceptualized the design of the study. LT, MJM, and HdB performed the data acquisition. LT, MJM, and HdB developed the model and performed data analysis and interpretation. All authors contributed in drafting and revising the manuscript. All authors approved the final version of the manuscript.
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5&D2=0&D3=194,219&HDR=G1,T&STB=G2&VW=T. Accessed June 2012


Table 1: Study population and input parameters (all costs are expressed in 2012 Euros)

Table 2: Scenarios in the univariate and two-way sensitivity analysis

Table 3: Return on investment of preventively vaccinating healthcare workers against pertussis

Table 4: Outcomes of the univariate and two-way sensitivity analysis
Additional files provided with this submission:

Additional file 1: Table 1 Study population and input parameters (all costs are exp, 14K
http://www.biomedcentral.com/imedia/1645961775136555/supp1.docx
Additional file 2: Table 2 Scenarios in the univariate and two-way sensitivity anal, 14K
http://www.biomedcentral.com/imedia/1278351289136555/supp2.docx
Additional file 3: Table 3 Return on investment of preventively vaccinating healthc, 12K
http://www.biomedcentral.com/imedia/1861330593136555/supp3.docx
Additional file 4: Table 4 Outcomes of the univariate and two-way sensitivity analy, 17K
http://www.biomedcentral.com/imedia/1432766563136555/supp4.docx