Reviewer's report

Title: Hospitalization for Pertussis in the United States: Profiles and Case Costs by Age.

Version: Date: 21 March 2005

Reviewer: Grace Lee

Reviewer's report:

General

This study describes the costs of hospitalizations for pertussis in 4 states in the U.S.—California, Florida, Massachusetts, and Washington. The data was derived from utilization data from approximately 1,000 hospitals in these 4 states. Costs were estimated from varied sources that are not exactly clear to the reader. Over a 4-year period, 2,518 cases were admitted to these hospitals for pertussis and 90% were in children less than 1 year. As expected, the mean cost per hospitalization was highest in infants <1 year given the high rate of severe complications.

This study highlights the importance of hospitalized pertussis disease among infants in the U.S. While the results are not surprising, the information may be helpful in quantifying the economic burden of hospitalized pertussis disease. In terms of policy relevance, the major upcoming decision focuses on adolescent and adult vaccination, with the hopeful benefit of potentially reducing disease in the young infants who most frequently suffer severe complications. However, the extent to which herd immunity will occur as a result of adolescent/adult vaccination is not clear. Since the authors focus on hospitalized disease, we only have a small glimpse of the economic burden of adolescent and adult disease where the vaccine might have the greatest impact.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

The methods used in this study to assess costs are not well described and leave the reader confused about what contributes to these costs. It seems that hospital charges were used and a cost-to-charge ratio applied in order to obtain costs, and physician fees were determined by the Physician Fee Schedule or the Florida Medicaid physician fee schedule. In the results section, the authors then describe the relative proportion of costs for each payer (Medicaid, Medicare, managed care) implying that the costs may have been different for each payer? Since the focus of this paper is the economic cost of illness, it would be much more helpful to the reader if each unit of utilization (accommodations, ancillary, physician services, etc.), the source of costs for each unit, and potential adjustments applied (such as cost-to-charge ratios and published payer ratios) were described clearly in the methods. Additionally, a table that describes the average resource utilization for each age group and their respective costs would be helpful to understand the major cost components. In the discussion section, a comparison of this study to other published studies on the costs of pertussis disease would be useful. In particular, the 2 studies published by Pichichero and colleagues on pertussis costs would be a helpful comparison. Finally, the title should state that hospitalization costs reflect data from 4 states, not the entire U.S. as implied.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
Abstract:
- Data sources should be more clearly described in the methods section of the abstract.
- It is surprising the mortality rate is higher in adolescents/adults compared to infants, especially since disease is more severe in young infants. This is likely due to small numbers and wide confidence intervals for adolescents and adults. Can the authors discuss this finding further either in the abstract or the discussion?

Background:
- The incidence of reported pertussis has been increasing in infants, adolescents, and adults, but it has remained relatively stable for young children contrary to what is suggested in the introduction.
- How old were the infants that were too young to have started vaccination? I assume you are talking about those <2 months.
- The duration of immunity described is surprisingly short—3 years seems a little bit earlier than published studies suggest.

Methods:
- Data is relatively old from 1996-1999. Is there a reason more recent data was not included, particularly since the total number of reported cases of adolescent/adult disease has increased over the past 5 years?
- Why was the diagnosis of encephalopathy not included as a potential complication in pertussis, particularly in infants? Encephalopathy is included as a major complication in most published studies.
- Pulmonary hypertension may also have been a secondary complication of pertussis in infants, which may or may not have been included under the diagnostic code respiratory distress. Was the MA cost-to-charge ratio estimate used for all states? Why not use national estimates?
- Please describe the rationale for including these 4 states.
- Please describe the percent of hospitals included in this sample. (i.e. Were all hospitals in each state included in the sample? Or only 80% of hospitals? etc.)
- The source of pediatric utilization data is not clear in this manuscript. Are the cost sources for children different than the ones used for adults?

Discussion:
- The rate of complications is surprisingly high in this database compared to national estimates for hospitalized complications, suggesting that selection bias may play a role. Can the authors comment on this in their discussion?
- In order to assess potential threats to validity, it would be useful to obtain some assessment of the rate of coding errors in a random subset of their data.
- The authors discuss adolescent and adult disease at the end of the discussion section. They should make it clear that the potential to significantly impact the costs of hospitalizations due to pertussis will critically depend on the level of herd immunity that may or may not occur with an adolescent/adult vaccination program.
- Further discussion on the significant differences in the rates of hospitalization for pertussis should be included. Overall, the authors state that ¼ of pertussis cases are hospitalized suggesting that these costs are important. However, this may not be a fair assessment of the true burden of hospitalized disease or associated costs as Figure 2 suggests. In MA and WA, the number of reported cases is high, but the rate of pertussis hospitalization is low. This is presumably due to the number of cases of infant vs. adolescent/adult disease reported in each state. In contrast, the rate of pertussis hospitalization in FL is quite high, but the data suggest under diagnosis may be common since the number of overall reported cases is low.

Figure 3. Y axis has cases, but did they mean percent? Total N would be useful in caption or in the figure.

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Discretionary Revisions (which the author can choose to ignore)

**What next?:** Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No

**Declaration of competing interests:**

I declare that I have no competing interests.