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The PneumoNIA Study Group

Measuring the impact of 10-valent pneumococcal conjugate vaccine on pneumonia, meningitis, and sepsis hospitalizations in Nepal: proposed methods

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INTRODUCTION

- In August 2015, the 10-valent pneumococcal conjugate vaccine (PCV10) was introduced in the Kathmandu valley using a 2+1 schedule, with immunization at 6 weeks, 10 weeks, and 9 months of age. Children less than 1 year old at the time of introduction were recommended to receive 1-3 doses whenever possible.
- Data on the impact of PCV on disease endpoints in children under 5 years of age are lacking from Asia.
- The introduction of PCV10 in Nepal provides an opportunity to measure the impact of this vaccine on pneumonia, meningitis, and sepsis hospitalizations using administrative data from a low-income country in Asia. To inform analytical approaches for measuring vaccine impact on these endpoints, we studied hospitalizations for several syndromes in the period prior to PCV10 introduction.

METHODS

- The Paediatrics Department at Patan Hospital has rigorously maintained electronic records of admissions since 2005.
- We extracted clinical discharge diagnoses for children less than 5 years for the period August 2012 to July 2015 from the daily admissions log and invasive bacterial disease surveillance database at Patan Hospital.
- We used pre-specified inclusion criteria (see Table 1) to categorize patients as cases (i.e., pneumonia, meningitis or sepsis) and controls (i.e., diarrhea).
- We used various exploratory time series methods to identify trends and seasonal signatures during the three years prior to the introduction of PCV10 in Nepal.

TABLE 1
Inclusion criteria for case and control conditions

Syndrome	Inclusion	
Pneumonia	✓ Pneumonia anywhere in the diagnosis ✓ Acute respiratory infection ✓ Acute lower respiratory infection ✓ Lower respiratory tract infection ✓ Bronchiolitis	✓ Bronchitis ✓ Pleural effusion, pleurisy, or empyema; not tubercular ✓ Acute respiratory distress syndrome ✓ Respiratory distress of infectious origin
Meningitis	✓ Meningitis anywhere in the diagnosis; including viral meningitis ✓ Encephalitis	✓ Meningoencephalitis ✓ Central nervous system infection
Sepsis	✓ Sepsis / Septicemia anywhere in the diagnosis, including acute cardiac arrest with sepsis ✓ Severe febrile illness ✓ Septic shock ✓ Bacteremia ✓ Multiple organ dysfunction syndrome	✓ Systemic inflammatory response syndrome ✓ Disseminated intravascular coagulation ✓ Osteomyelitis ✓ Septic arthritis
Diarrhea	✓ Diarrhea	✓ Acute gastroenteritis

FIGURE 1
Time plots of case and control syndromes prior to PCV introduction

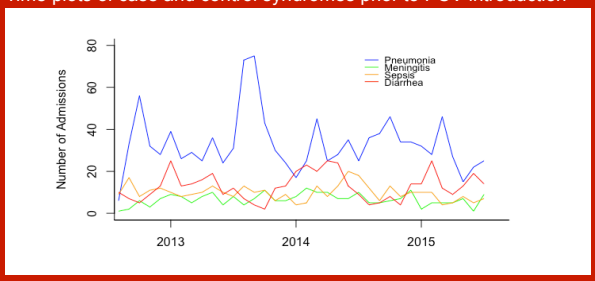
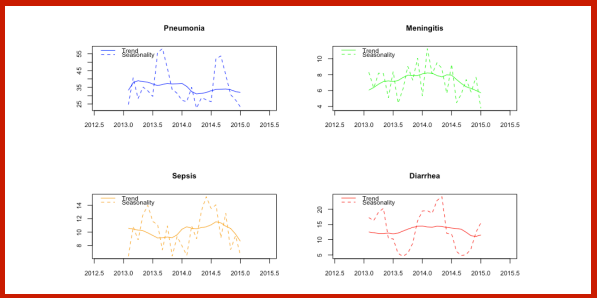


FIGURE 2
Estimates of trends and seasonality for case and control syndromes



RESULTS

- Pneumonia, meningitis, sepsis, and diarrhea accounted for 1193, 237, 353, and 465 hospital admissions, respectively, at Patan Hospital in the three years prior to the introduction of PCV10.
- The annual number of hospitalizations for each syndrome increased from year one to year two, then decreased in year three (Figure 1).
- Seasonality was observed most clearly for pneumonia and diarrhea.
  - On average, there were 47.2% more pneumonia admissions in September and 20.5% fewer admissions in May compared with other months in the same year (Figure 2).
  - The highest number of diarrhea admissions were observed between February and May. The fewest number of diarrhea admissions were observed in September and October (Figure 2).

CONCLUSIONS

- During the pre-PCV period, counts of hospitalizations for pneumonia, meningitis, and sepsis increased after the first year and then decreased following the second year.
- Diarrhea followed the same annual trends observed for the case conditions. Diarrhea could possibly be used as a control condition to improve our ability to measure the impact of PCV on pneumonia by controlling for confounding by access to hospital.
- Data from other hospitals in Kathmandu could help to refine our estimates of hospitalization trends and seasonality.
- We will explore the use of log-linear regression models conditioned on control condition counts, corrected for over-dispersion, and of change-point analyses to estimate the impact of PCV10 in Nepal.

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