Distance to health services modifies the effect of an 11-valent pneumococcal vaccine (PCV) on pneumonia risk among children less than 2 years of age in Bohol, Philippines

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INTRODUCTION

• Lower respiratory infections (LRIs) are responsible for approximately 900,000 deaths among children <5 years of age each year.
• The World Health Organization recommends that pneumococcal conjugate vaccines (PCVs) be included in childhood immunization programs worldwide.
• The cost of PCV is daunting to many low-middle-income countries given limited economic resources and significant competing health and programmatic priorities (e.g., HIV/AIDS, diarrheal disease).
• Targeted vaccination strategies may ultimately be more sustainable until financing is available for universal roll-out.
• Decisions regarding targeted strategies require data for the burden of vaccine-preventable disease and the demographic, socioeconomic, and geographic factors contributing to higher disease risk in a population.

STUDY AIMS

1. Examine the major risk factors for pneumonia and the effect of the PCV11 on risk of infection from birth to 2 years of age.
2. Explore how geographic data collection and spatial analysis can be used to develop targeted vaccine strategies.

Figure 1: Study Area, Bohol, Philippines

METHODS

Sample
• Reanalysis of a randomized, placebo-controlled, double-blind trial which examined the efficacy of an 11-valent pneumococcal conjugate vaccine (11PCV) in children <2 years of age in Bohol, Philippines.
• The geographic location of each child’s household of residence was collected using handheld GPS and linked to study data in a Geographic Information System (GIS).
• 12,194 children randomized; final sample was 11,729 children with GPS data in the per-protocol population.
• Study endpoints included: radiographic pneumonia and clinical pneumonia classified using WHO definitions (nonsevere, severe/very severe).

Statistical Analysis
• Observed variation in pneumonia and pneumonia case-rates over space and time necessitated a spatio-temporal approach to modeling (Figure 2).
• Monthly covariates at 3 spatial scales – 500m, 1000m, and 2000m – were developed using ArcGIS and Python scripting:
  - Vaccine coverage, pneumonia rate, population density
  - Cox’s proportional hazard models with spatio-temporally varying covariates estimated the risk of pneumonia infection between 3rd dose and 24 months.

Figure 2: Pneumonia Rate by Study Endpoint

RESULTS

• Increased pneumonia risk was observed among children with lower weight-for-age z-scores, maternal education, larger households, and closer proximity to Bohol Regional Hospital [BRH] (Table 1).
• A significant interaction effect between distance from BRH and vaccination with 11PCV indicated a reduction in risk for vaccinees living further from health services (Figure 3).
  - Radiographic pneumonia: 40% reduction in risk for children 10km away from BRH.
  - Severe/very severe pneumonia: 25% reduction in risk for children >10km.
  - No significant interaction effect among children with non-severe pneumonia.
• Significant increase in risk (~24%) of severe/very severe pneumonia for children living <1km from BRH.

DISCUSSION

• Children living a greater distance from health services derive greater benefit from vaccination with 11PCV.
• Barriers to healthcare in rural areas lead families to wait until children develop more severe disease before seeking formal care, resulting in higher rates of severe ALRI/radiographic pneumonia in the placebo group.
• Increased risk of severe pneumonia in children <1km from BRH may be due to higher rates of RSV in vaccinees.

Table 1: Multivariate Cox Regression Models by Study Endpoint, Per Protocol Population

<table>
<thead>
<tr>
<th>Individual Child Variables</th>
<th>Non-Severe Pneumonia</th>
<th>Severe/Very Severe Pneumonia</th>
<th>Radiographic Pneumonia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Received Vaccine</td>
<td>0.809</td>
<td>0.001</td>
<td>0.008</td>
</tr>
<tr>
<td>Female</td>
<td>0.84 (0.75-0.93)</td>
<td>0.001</td>
<td>0.71 (0.61-0.83)</td>
</tr>
<tr>
<td>Weight-for-Age z-score</td>
<td>0.97 (0.92-1.02)</td>
<td>0.202</td>
<td>0.93 (0.86-1.00)</td>
</tr>
<tr>
<td>Mother’s Education</td>
<td>0.95 (0.93-0.96)</td>
<td>0.001</td>
<td>0.94 (0.92-0.97)</td>
</tr>
<tr>
<td>No. Children in the household</td>
<td>1.07 (1.03-1.10)</td>
<td>0.001</td>
<td>1.11 (1.07-1.15)</td>
</tr>
<tr>
<td>Log(Distance) From BRH</td>
<td>0.001</td>
<td>0.160</td>
<td>1.14 (1.10-1.23)</td>
</tr>
<tr>
<td>Received Vaccine * Log(Distance)</td>
<td>0.988</td>
<td>0.001</td>
<td>-</td>
</tr>
<tr>
<td>Area-Level Variables</td>
<td>-</td>
<td>-</td>
<td>1.03 (1.02-1.04)</td>
</tr>
</tbody>
</table>

CONCLUSIONS

• This study provides important information that can be used for targeting public health interventions in the Philippines, and perhaps other similar settings.
• Findings support recommendations to strengthen surveillance systems and burden of disease data both before and after vaccine introduction.

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