**Background Rates of Neonatal Outcomes in a Maternal Vaccine Clinical Trial**

Gabriel Gomide, Vagelos College of Physicians and Surgeons | Class of 2023;
Mentors: Eileen Farnon, MD; Negar Aliabadi, MD; Iona Munjal, MD
Pfizer, Vaccine Clinical Research and Development

Research Question: What are the background rates of the neonatal outcomes measured in a maternal vaccine clinical trial?

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**Background**

Maternal immunization presents a unique opportunity to diminish infant mortality caused by infectious diseases. Clinical trials for maternal vaccines require careful monitoring of adverse events that may arise during pregnancy, birth, and the neonatal period to assess whether the incidence of these events increases after vaccine administration.

Understanding the expected background rates of neonatal adverse events is necessary to determine the safety of maternal vaccines.

**PFIZER’S RSV MATERNAL VACCINATION CLINICAL TRIAL**

Respiratory Syncytial Virus (RSV) causes 33 million cases of lower respiratory tract infections (LRTIs) in children under 5, globally. Particularly affected are children aged less than 1 year. While a monoclonal antibody for RSV (Palivizumab, brand name Synagis) is available, its high price excludes administration to all but the highest risk newborns in developed countries. Maternal vaccination presents an opportunity to provide infants with antibodies needed to prevent major infections. A vaccine administered to women during pregnancy may boost the concentration of maternal antibodies transferred across the placenta.

Pfizer is conducting a Phase 3, multicenter, placebo-controlled trial to test the safety, efficacy, and immunogenicity of a RSV maternal vaccine candidate. Along with the outcomes related to vaccine efficacy (incidence of severe LRTI), they are also measuring the incidences of serious adverse events and newly diagnosed chronic medical conditions in infants born to vaccinated mothers during the study.

**METHODS**

**Literature review**

- To identify estimates for four neonatal outcomes in the 17 countries included in Pfizer’s maternal RSV vaccine trial

**Outcomes Included:**

- Neonatal mortality
- Preterm birth
- Low birthweight
- Congenital anomalies

**Quality criteria measured:**

- Recency of data (within 5 years)
- Clearly defined population
- Clearly defined outcome
- Design of study (surveillance research)
- Representativeness of study (national database or survey)

While published estimates for the 4 outcomes have been found for the 17 countries, there were variabilities in the quality of data available.

**RESULTS**

- We identified 57 sources for review and determined the best estimates for the 4 neonatal outcomes per country

**Table. Best Estimates of 4 Selected Neonatal Outcomes by Quality of Source**

<table>
<thead>
<tr>
<th>Outcomes Included</th>
<th>North America</th>
<th>Europe</th>
<th>Latin America</th>
<th>Africa</th>
<th>Asia/Pacific</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>US</td>
<td>Canada</td>
<td>Mexico</td>
<td>Finland</td>
<td>NL</td>
</tr>
<tr>
<td>Neonatal death</td>
<td>3.85</td>
<td>3.5</td>
<td>10.29</td>
<td>3.2</td>
<td>1.0</td>
</tr>
<tr>
<td>(per 10,000 live births)</td>
<td>Preterm birth (% of live births)</td>
<td>&lt;37 weeks</td>
<td>10.23</td>
<td>8.0</td>
<td>7.0</td>
</tr>
<tr>
<td></td>
<td>&lt;34 weeks</td>
<td>2.77</td>
<td>2.1*</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td></td>
<td>&lt;28 weeks</td>
<td>0.66</td>
<td>0.5*</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Low birthweight</td>
<td>3.28</td>
<td>5.5*</td>
<td>7.9</td>
<td>4.3</td>
<td>5.8*</td>
</tr>
<tr>
<td>(% of live births)</td>
<td>&lt;3000 g</td>
<td>1.38</td>
<td>1.0*</td>
<td>---</td>
<td>0.7</td>
</tr>
<tr>
<td></td>
<td>&lt;1500 g</td>
<td>0.64</td>
<td>0.5*</td>
<td>---</td>
<td>0.3</td>
</tr>
<tr>
<td>Congenital Anomalies (% of live births)</td>
<td>&lt;35%</td>
<td>371.1</td>
<td>77.8</td>
<td>592</td>
<td>213.2</td>
</tr>
</tbody>
</table>

**DISCUSSION**

Countries with robust vital statistics systems tend to have high quality, nationally representative data available, allowing for the examination of outcomes by specific regions, maternal age groups, and other variables. While neonatal mortality, preterm birth, and low birth weight were generally similarly defined across countries, congenital anomalies were variably defined among nations. While most based their definitions on ICD-10 codes, different countries included different birth defects within their overall incidence calculations. Maternal immunization programs would benefit from improved and consistent surveillance methods worldwide for neonatal outcomes.

**REFERENCES**


A full list of included studies is available on request: gag2154@cumc.columbia.edu

Funded in collaboration with Pfizer, Inc. and Columbia University