Network analysis of possible anaphylaxis cases reported to the US Vaccine Adverse Event Reporting System after H1N1 influenza vaccine

Taxiarchis Botsis\textsuperscript{1,2} & Robert Ball\textsuperscript{1}

\textsuperscript{1}Center for Biologics Evaluation and Research (CBER), U.S. Food and Drug Administration
\textsuperscript{2}Department of Computer Science, University of Tromsø, Tromsø, Norway

MIE 2011
Oslo, Norway
Vaccine Adverse Event Reporting System (VAERS)

- VAERS stores adverse events (AEs) reported by:
  - health care providers
  - vaccine recipients
  - manufacturers

- Well-trained nurses code these reports:
  - using the Medical Dictionary for Regulatory Activities (MedDRA) and
  - assign preferred terms (PTs) that represent the AEs described in the narratives.
Study hypothesis

- Identify patterns and
- Detect safety signals

by applying **Network Analysis** to VAERS
Methods: Dataset

- 6034 VAERS reports for H1N1 vaccine (November 22, 2009-January 31, 2010)
- 237 possible anaphylaxis reports
- Anaphylaxis: acute allergic reaction after vaccination
- Dataset of 237 reports used to identify patterns of PTs related to anaphylaxis
Methods: Network Analysis

Report_1= [VAX1 VAX2 PT1 PT2 PT3]

decomposed to combinations of:

VAX1-PT1, VAX1-PT2, VAX1-PT3,

VAX2- PT1, VAX2- PT2, VAX2- PT3

And

VAX1-VAX2

And

PT1- PT2, PT1- PT3, PT2-PT3

<table>
<thead>
<tr>
<th></th>
<th>PT1</th>
<th>PT2</th>
<th>PT3</th>
<th>VAX1</th>
<th>VAX2</th>
</tr>
</thead>
<tbody>
<tr>
<td>VAX1</td>
<td>16</td>
<td>33</td>
<td>5</td>
<td>0</td>
<td>50</td>
</tr>
<tr>
<td>VAX2</td>
<td>4</td>
<td>10</td>
<td>5</td>
<td>50</td>
<td>0</td>
</tr>
<tr>
<td>PT1</td>
<td>0</td>
<td>12</td>
<td>10</td>
<td>16</td>
<td>4</td>
</tr>
<tr>
<td>PT2</td>
<td>12</td>
<td>0</td>
<td>9</td>
<td>33</td>
<td>10</td>
</tr>
<tr>
<td>PT3</td>
<td>10</td>
<td>9</td>
<td>0</td>
<td>5</td>
<td>5</td>
</tr>
</tbody>
</table>

VAX1, VAX2: Vaccines
PT1, PT2, PT3: MedDRA Preferred Terms (PT) representing adverse events
Methods: Network construction

- **Nodes** the PTs and vaccines
- **Edges** their interconnections
- **Edge weight** the number of occurrences for each tie
Methods: Network reduction

Application of the ‘islands’ algorithm* to anaphylaxis network:
- identifies all the maximal islands within a predefined node interval for an edge weight threshold
And combine it with:
- triangular weight – TW (= number of triangles each edge of the original network is contained).
- TWs emphasize multiple interactions, filter out weak connections and reveal the patterns.

Results: Anaphylaxis network

N=301 nodes

What a mess!
Results: Reduced network

N=30 nodes

Brighton Collaboration Criteria
Summary

- Network analysis identifies patterns related to adverse events after vaccination\(^1\)

- Limitations:
  - Statistical framework of network analysis
  - Retrospectively collected dataset

- Future goals:
  - Evaluation of other approaches for network reduction and
  - Application to prospectively collected data for prediction purposes.

---

\(^1\)R. Ball and T. Botsis, Can network analysis improve pattern recognition among adverse events following immunization reported to VAERS? *Clinical Pharmacology & Therapeutics*. 2011 Aug;90(2):271-8.
Acknowledgements

- We thank the Medical Officers at FDA who evaluated the reports and those who reported them.
- Research Participation Program, Center for Biologics Evaluation and Research, Oak Ridge Institute for Science and Education.