GP encounter data to assess vaccine safety

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NCIRS
Background

- In April 2011, TGA issued interim advice to not administer subsequent doses of Pneumovax following an increase in reporting of severe injection site reactions + recall of a batch of the vaccine

- Questions for investigators
  - Increase in incidence or reporting?
  - Due to a vaccine batch?
  - Due to an increase in 2\textsuperscript{nd} doses?
  - Something else?
Background, cont.

- Available data sources limited:
  - AEFI reports to TGA
    - Stimulated reporting
  - Denominators
    - “vaccinated within 5 years” from infrequent CATI surveys
    - Requests to GPs
    - Nothing on dose number
Strategic Solutions

The General Practice Research Network (GPRN) is a national network of Australian clinicians participating in quality assurance and research activities through Medical Director. Each week the panel of participating GPs' supply de-identified data that is used to support research and development in general practice. With more than 1,600 GPs contributing to prescribing data to create a longitudinal patient-based database containing over 30 million scripts, in excess of 32 million unique encounters for more than 3 million patients.

HCN has an experienced analytical team dedicated to producing concise reports from data collected. GPRN provides the highest quality health information to government, academia and industry, helping to support market planning and monitoring, product strategy development, product positioning, targeting and forecasting.

Some of the key features include:
- Monitoring behavioural trends in General Practitioners prescribing patterns
- Provide in depth market segmentation tools
- Deliver virtually "live to market" information
- Weekly monitoring report where growth in prescribing can be followed week by week

Over 70 data fields are collected including...
Health Communication Network

- Developer of Medical Director practice software

- General Practice Research Network (GPRN):
  - Sample of MD users contribute weekly de-identified unit records
  - Primarily used to provide data on prescribing patterns
  - 1,100 GPs in 400 practices
Study aims

- Post hoc evaluation of a data source (GPRN) to:
  - Detect AEFI signals
  - Evaluate signals

- Advantages:
  - Independent of stimulated reporting
  - Denominators
  - Dose numbers
  - Potential rapid availability

- Unknowns:
  - Data validity
  - Data completeness

- Trial AEFI event - 23vPPV 2011
- Control vaccine - influenza
Methods

- GPRN unit records purchased by DoH
- All patients with a recorded pneumococcal or influenza vaccination
- 2002 – 2012
RELATIONSHIP DIAGRAM

PROJECT: The provision of General Practice Research Network Data relating to adverse events following administration of Pnuemovax 23R vaccine in older Australians.
Methods, cont.

- Merge dataset
- Clean, remove duplicates
- Assess for data quality/plausibility
  - Patient age, dose number, dose spacing, etc.
- Analyse for known characteristics of vaccines
  - Reaction rate 23vPPV > influenza
  - 23vPPV local reactions 2\(^{nd}\) dose > 1\(^{st}\) dose
- Examine for 2011 23vPPV signal
Results

- Pneumovax
  - 96,000 doses
  - 86,000 patient IDs
  - mean age 72 years

- Flu
  - 684,000 doses
  - 275,000 patient IDs
  - Mean age 67 years

- 75,000 duplicate records
- 7,000 patient IDs missing DOB or gender
23vPPV vaccination rate, aged ≥65 years

![Graph showing vaccination rates and coverage](image-url)

- **Rate - Victoria**
- **Rate - Other jurisdictions**
- **Coverage - Victoria**
- **Coverage - Other jurisdictions**

**National funding**

**Year**

- 2002
- 2003
- 2004
- 2005
- 2006
- 2007
- 2008
- 2009
- 2010
- 2011

**Vaccination per 100,000 encounters**

- 0
- 500
- 1,000
- 1,500
- 2,000
- 2,500

**Vaccinated within previous 5 years**

- 0
- 0.1
- 0.2
- 0.3
- 0.4
- 0.5
- 0.6
- 0.7
- 0.8
- 0.9
- 1
Seasonality of vaccinations

- Pneumovax
- Flu
Local reactions, first vs subsequent doses

<table>
<thead>
<tr>
<th></th>
<th>PNEUMOVAX</th>
<th></th>
<th>INFLUENZA</th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Vaccinations</td>
<td>Reactions</td>
<td>Rate*</td>
<td>Vaccinations</td>
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<tr>
<td>First dose</td>
<td>9,228</td>
<td>4</td>
<td>43</td>
<td>146,518</td>
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<tr>
<td>Subsequent doses</td>
<td>9,416</td>
<td>45</td>
<td>478</td>
<td>408,557</td>
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<tr>
<td>Total</td>
<td>18,644</td>
<td>49</td>
<td>263</td>
<td>555,075</td>
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</table>

* Vaccinations per 100,000 doses
Interval between pneumovax doses

Interval between influenza doses
Signal in 2011?

- 2010, n=18
  - Jan-Mar n=5
- 2011, n=14
  - Jan-Mar n=3

Reaction rate per 100,000 vaccinations

- Pneumovax
- Influenza

Year:
Discussion

- Data appeared broadly consistent with expectations:
  - Dose spacing, number, seasonality, age, reaction rate
  - Data cleaning required

- Good source of data on
  - Reaction rates
  - Denominators (vaccinations)
  - Revaccination
  - More independent of stimulated reporting

- More sensitive than passive reports (per 100,000 doses):
  - RCTs – 5,000
  - GPRN – 240
  - TGA – 80
Discussion cont.

- Pneumovax local reaction numbers too low to detect this signal
  - 200 participating practices in 2011
  - Total local reactions Jan-Mar 2011
    - GPRN – 3
    - TGA – 40

- General practice datasets of sufficient size have potential for AEFI signal detection and assessment
Acknowledgements

- Data purchased by the Australian Government Department of Health
## Interval between doses

<table>
<thead>
<tr>
<th>Interval between vaccinations</th>
<th>PNEUMOVAX</th>
<th></th>
<th></th>
<th>INFLUENZA</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Vaccinations</td>
<td>Reactions</td>
<td>Rate*</td>
<td>Vaccinations</td>
<td>Reactions</td>
<td>Rate*</td>
</tr>
<tr>
<td>6 months–&lt;5 years</td>
<td>3,456</td>
<td>14</td>
<td>405</td>
<td>401,448</td>
<td>196</td>
<td>49</td>
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<tr>
<td>≥5 years</td>
<td>5,960</td>
<td>31</td>
<td>520</td>
<td>3,508</td>
<td>4</td>
<td>114</td>
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</table>

* Vaccinations per 100,000 doses
Definitions of reactions

- Local reactions at the site of injection within 35 days: redness, swelling, tenderness, soreness, rash, limitation of arm movement, cellulitis/abscess of the upper limb, and shoulder region problem (e.g. “sore at injection site”)
  - Severe local reactions: Local reactions that were severe and occurred within 7 days (e.g. “extreme arm swelling”, “bad local redness”, “cellulitis”, “swollen arm”, “huge local reaction”, “inflamed arm”, “local erythema++”)
- Non-local reactions within 35 days: nausea, headache, dermatitis, myalgia, joint pain, fatigue and fever
Data quality

- Data consistent with expectations:
  - 23vPPV doses reduced sharply from April 2011
  - Seasonality and age distribution of doses, 1\textsuperscript{st} vs 2\textsuperscript{nd} doses and revaccination interval = recommendations
  - Immunization data consistent with reason for visit

- Data limitations
  - Duplicates (6.1%)
  - Missing data. e.g. 84% for dose number
  - Limited data to classify some potential reactions (e.g. classifying “rash” as local or non-local reaction)
Definitions of reactions (continued)

- Any reaction within 35 days: local, non-local and indeterminate (e.g. “rash”)
- Visit to GP within 35 days for any reason
- History of reaction to vaccine, classified into above categories, no time limit
## Reaction rates

<table>
<thead>
<tr>
<th></th>
<th>PNEUMOVAX</th>
<th>INFLUENZA VACCINES</th>
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<tbody>
<tr>
<td></td>
<td>Number</td>
<td>Rate per 100,000 doses</td>
</tr>
<tr>
<td>Severe local reactions</td>
<td>40</td>
<td>42</td>
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<tr>
<td>Local reactions</td>
<td>233</td>
<td>243</td>
</tr>
<tr>
<td>Non-local reactions</td>
<td>215</td>
<td>225</td>
</tr>
<tr>
<td>Any reactions</td>
<td>823</td>
<td>859</td>
</tr>
<tr>
<td>Visit to GPs</td>
<td>45,835</td>
<td>47,864</td>
</tr>
</tbody>
</table>

- TGA data 2011: 63.4 per 100,000 doses for age group 18-64 years and 90.7 per 100,000 doses for age group 65 years and older
## Local reactions by gender and age

<table>
<thead>
<tr>
<th></th>
<th>Pneumovax</th>
<th>Flu</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Vaccinations</td>
<td>Reaction</td>
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<tr>
<td><strong>Gender</strong></td>
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</tr>
<tr>
<td>Female</td>
<td>50,893</td>
<td>169</td>
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<tr>
<td>Male</td>
<td>44,757</td>
<td>64</td>
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<tr>
<td>Missing</td>
<td>110</td>
<td>0</td>
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<tr>
<td>Total</td>
<td>95,760</td>
<td>233</td>
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<tr>
<td><strong>Age group</strong></td>
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<tr>
<td>18-&lt;40</td>
<td>1,792</td>
<td>5</td>
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<td>&gt;=40-&lt;50</td>
<td>2,361</td>
<td>6</td>
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<tr>
<td>&gt;=50-&lt;65</td>
<td>13,151</td>
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<tr>
<td>&gt;=65-&lt;70</td>
<td>23,924</td>
<td>59</td>
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<tr>
<td>&gt;=70</td>
<td>54,532</td>
<td>143</td>
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<tr>
<td>Total</td>
<td>95,760</td>
<td>233</td>
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