The use of data-driven vs. clinical based propensity score in COVID-19 vaccine safety research:

Association between thrombosis with thrombocytopenia syndrome (TTS) or thromboembolic events (TE), and COVID-19 vaccines

PRESENTER: Xintong Li

INTRO
- Propensity score (PS) have been widely used in observational studies to reduce confounding by indication
- Clinical knowledge based vs. data-driven PS

METHODS
Data source: OMOPed data from 5 European counties: France, Germany, Netherlands, Spain, and the United Kingdom) and two from the United States.

Cohort study:
- Target: adenovirus-based
- Comparator: mRNA
- Analysis:
  - miniPS: clinically-driven
  - Large-scale PS: data-driven, L1 regularized logistic regression
- 1-to-4 matching

Diagnostics:
1. Measured confounding: Covariate balance after propensity score matching (SMD < 0.1)
2. Power: minimal detectable relative risk in the matched cohorts
3. Systematic error: using negative control outcomes

RESULTS
- PS distribution
- Before and after matching SMD
- Systematic error using negative control outcomes

CONCLUSIONS
- Index month and age have high impact for both clinical based and data-driven propensity scores.
- Clinical-based PS: balanced on selected variables, but not other covariates
- Large-scale PS: all covariates were well-balanced after matching
- Performance on controlling systematic errors were similar
- Cons of large-scale: computing time (30mins vs. 6 hours on a 250,000 down sampling cohort)

Table 1. Summary of the covariate balance for both propensity scores.

<table>
<thead>
<tr>
<th>Database</th>
<th>Target</th>
<th>Comparator</th>
<th>No SMD &gt; 0.1 after matching</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK CPRD AURUM</td>
<td>Vaxzevria 1st</td>
<td>Comirnaty 1st</td>
<td>✓</td>
</tr>
<tr>
<td>UK CPRD AURUM</td>
<td>Vaxzevria 2nd</td>
<td>Comirnaty 2nd</td>
<td>✓</td>
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<td>janssen</td>
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<td>✓</td>
</tr>
<tr>
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<td>Vaxzevria 1st</td>
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<td>✓</td>
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<tr>
<td>15 OpenClaims</td>
<td>Spikevax 1st</td>
<td>✓</td>
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</tr>
</tbody>
</table>

*CPRD AURUM: Clinical Practice Research Datalink (CPRD) AURUM, United Kingdom; IPCI: Integrated Primary Care Information (IPCI), The Netherlands; DA Germany: IQVIA Disease Analyser (DA) Germany; 15 OpenClaims: Medical and Institutional Claims (Dx and Hx); SMD: standardized mean difference

Figure 1. Propensity score distribution covariates with top 6 absolute values of Beta, 2nd dose Vaxzevria and Comirnaty cohorts, UK CPRD data.

Figure 2. Before and after matching SMD, 2nd dose Vaxzevria and Comirnaty cohorts, UK CPRD data.

Figure 3. Systematic errors before and after calibration, 2nd dose Vaxzevria and Comirnaty cohorts, UK CPRD data.