Confounding in influenza VE studies in seniors, and possible solutions

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Outline

• Focus is on “non-specific” outcomes (e.g. community-acquired pneumonia, all-cause mortality)

• The problem: administrative data do not identify confounders in influenza VE studies among seniors

• Possible solutions:
  – Collect better data
  – Model the confounding and subtract it out
Part I: Important confounders are not captured by administrative data

<table>
<thead>
<tr>
<th>Percent “not diseased” by ICD codes:</th>
<th>Dementia</th>
<th>Live in non-home setting</th>
<th>Need help with ambulation</th>
<th>Need help with bathing</th>
<th>Use home health care services</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases (N=34)</td>
<td>32%</td>
<td>44%</td>
<td>56%</td>
<td>32%</td>
<td>32%</td>
</tr>
<tr>
<td>Controls (N=203)</td>
<td>3%</td>
<td>8%</td>
<td>12%</td>
<td>3%</td>
<td>8%</td>
</tr>
</tbody>
</table>

Jackson LA et al; Int J Epidem 2006; 35:345-52
Adjustment for administrative data does not reduce confounding

• Cohort study of influenza VE against pneumonia among seniors
• 2000/01 through 2002/03 influenza years
• Detailed administrative data (ICD codes, pharmacy prescriptions, laboratory test results, claims for home health services, and more)
• Defined several common risk adjustment indices

Jackson ML et al; Pharmacepi Drug Safety 2011; 20:858-65
Estimates of the association between influenza vaccination and pneumonia risk

Expected true association
How well do administrative data predict pneumonia and vaccination?

C-statistic

- Poor
- Fair
- Good
- Excellent

Predict pneumonia
Predict influenza vaccination
Hypothetical good propensity score

![Graph showing the distribution of propensity scores for exposed and unexposed subjects. The x-axis represents the propensity score ranging from 0.05 to 1.00, and the y-axis represents the number of subjects ranging from 0 to 30,000. The graph is divided into two sections: Unexposed (blue) and Exposed (cyan). The distribution is skewed, with a higher concentration of unexposed subjects in the lower propensity score ranges.](image-url)
Distribution of vaccination propensity scores between vaccinated and unvaccinated
Summary

- Seniors who choose flu vaccine are different from seniors who do not
- These differences are not captured in administrative health care databases, because existing data do not contain predictors of vaccination
- Estimates of flu VE in seniors using these databases will have strong uncontrolled confounding
Part II: Ways forward

• Collect better data
  – Detailed data on functional status, disease severity from medical records can remove confounding

• Model the confounding and subtract it out (ratio-of-ratios approach)
  – Flu VE = (Apparent VE when flu circulates / apparent VE when flu does not circulate)
  – Confounding in both estimates cancels out
Collecting better data works

- A case-control study of influenza VE against community-acquired pneumonia
- 1,173 cases and 2,346 age- and sex-matched controls
- Detailed administrative data (ICD codes, prescriptions, laboratory test results, use of home health services, claims for medical equipment)
- Detailed medical record review (severity of comorbidities, smoking, alcohol use, functional status, lung function measures)

Jackson et al; Lancet 2008; 372:398-405
Pre-influenza associations between influenza vaccination and risk of pneumonia

<table>
<thead>
<tr>
<th>Adjustment</th>
<th>Odds ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age and sex</td>
<td>0.60</td>
<td>0.38–0.95</td>
</tr>
<tr>
<td>Administrative data</td>
<td>0.82</td>
<td>0.48–1.41</td>
</tr>
<tr>
<td>Medical record + administrative data</td>
<td><strong>1.01</strong></td>
<td>0.58–1.76</td>
</tr>
</tbody>
</table>

Adjusted odds ratio during influenza season: **0.92** (95% CI 0.77–1.10)

Jackson et al; Lancet 2008; 372:398-405
"Ratio of ratios" method: weeks when influenza did not circulate

Adapted from: Baxter R et al; Vaccine 2010; 28:7267-72
“Ratio of ratios” method: weeks when influenza did circulate

Adapted from: Baxter R et al; Vaccine 2010; 28:7267-72
“Ratio of ratios” method

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Challenges

• Ratio-of-ratios approach requires multiple influenza seasons and many observations (68,000 outcomes and 10 million person-years in the Baxter study)
  – Not suited for a single season
• Collecting additional data on confounders is expensive
Summary

• Existing methods can remove confounding in estimates of influenza VE in seniors
• However, these methods have practical limitations
Thank you!

Questions?