Intent-to-treat analysis in observational studies

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European Association of Methodology
Society for Multivariate Analysis in the Behavioural Sciences
Outline

Intent to treat analysis
Informative allocation
How do we choose the better treatment?
Axiomatic discussion of decision functions
The cross sum ratio
The meningococcal disease debate
Intent to treat analysis

Effect of the decision to
- apply a treatment (designed experiment)
- to make the treatment available (observational study)

Analysis
- as allocated, disregarding compliance (d. e.)
- not only effect on those who choose but also how many choose the treatment (o. s.)

Examples
Which smoking cessation aid is more useful? Patch or gum? Does it matter how many choose each?

Which candidate has a larger chance to win? The one liked in larger proportion? Or does it matter how many know each candidate?

In observational studies the allocation into treatment categories is informative
Which treatment is better?

<table>
<thead>
<tr>
<th></th>
<th>Response</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment 1</td>
<td></td>
<td>70</td>
<td>30</td>
</tr>
<tr>
<td>Treatment 2</td>
<td></td>
<td>60</td>
<td>40</td>
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The usual way of choosing the better treatment is not sensitive to allocation

Odds ratio or cross product ratio (cpr)

\[
\frac{f_{11}}{f_{12}} \cdot \frac{f_{22}}{f_{21}} = \frac{f_{11}f_{22}}{f_{12}f_{21}}
\]

Relative risk or risk ratio

\[
\frac{f_{11}}{f_{11} + f_{12}} \cdot \frac{f_{21}}{f_{21} + f_{22}}
\]

Something new:

Cross sum ratio (csr)

\[
\frac{f_{11} + f_{22}}{f_{12} + f_{21}}
\]
Decision functions tell which treatment is better (-1, 0, 1)

Take \( \text{sgn log} \) of cpr or csr

\[
\gamma \left( \begin{array}{cc}
a & a \\
b & b \\
\end{array} \right) = 0
\]

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a & b \\
a & b \\
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\]

\[
\gamma \left( \begin{array}{cc}
a & b \\
c & d \\
\end{array} \right) = -\gamma \left( \begin{array}{cc}
c & d \\
a & b \\
\end{array} \right)
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c & d \\
\end{array} \right) = -\gamma \left( \begin{array}{cc}
b & a \\
d & c \\
\end{array} \right)
\]

\[
a > b, \ c \leq d \Rightarrow \gamma \left( \begin{array}{cc}
a & b \\
c & d \\
\end{array} \right) = 1
\]

\[
a > c, \ d = b \Rightarrow \gamma \left( \begin{array}{cc}
a & b \\
c & d \\
\end{array} \right) = 1
\]
Consistency

if \( \gamma(T_1) = \gamma(T_2) \), then \( \gamma(T_1 + T_2) = \gamma(T_1) \).

(No Simpson’s paradox!)

Indifference

If \( \gamma(T) = 0 \) by Properties 1 or 2, then

\[ \gamma(T_1 + T) = \gamma(T_1), \text{ for all } T_1. \]

Invariance against changes in allocation

\[ \gamma \left( \begin{array}{cc} a & b \\ c & d \end{array} \right) = \gamma \left( \begin{array}{cc} ta & tb \\ uc & ud \end{array} \right) \]

for every table \( T \) and all positive \( t \) and \( u \).

\( CPR \) is not consistent and not indifferent but is invariant against changes in allocation

\( CSR \) is consistent and indifferent but is not invariant against changes in allocation.
Some results

If a decision function is invariant against changes in allocation, then it is equal to the CPR (and Simpson’s paradox may occur).

The following three statements are equivalent

(a) $\gamma$ is consistent
(b) $\gamma$ is indifferent
(c) $\gamma = CSR$.
Can we / do we want to learn to conclude that Treatment 1 is better?

\[ T = \begin{array}{c|c|c}
\text{Response} & \text{Positive} & \text{Negative} \\
\hline
\text{Treatment 1} & 50 & 30 \\
\text{Treatment 2} & 20 & 10 \\
\end{array} \]

How much do you think allocation is informative?

How much do you want to avoid Simpson’s paradox?
The meningococcal disease debate (BMJ 2006)

If diagnosed with MC, the GP administers penicillin

Is this practice 'good'?
Patients with meningococcal disease diagnosed before hospital admission

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<th>Survived</th>
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</thead>
<tbody>
<tr>
<td>Penicillin</td>
<td>22</td>
<td>83</td>
</tr>
<tr>
<td>No penicillin</td>
<td>2</td>
<td>45</td>
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$CPR=1$ ($cpr=5.96$) – penicillin is bad

Authors: perhaps those diagnosed were in a more advanced state of the illness

Editorial: administering penicillin may be harmful

Readers: continue administering penicillin

Statistician: the CPR depends strongly on whether all children or only those diagnosed with MC are taken into account

All patients with meningococcal disease

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<td>22</td>
<td>83</td>
</tr>
<tr>
<td>No penicillin</td>
<td>81</td>
<td>262</td>
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$CPR=-1$ ($cpr=0.86$) – penicillin is good

Diagnosed: $CSR=-1$ ($csr=0.79$) – penicillin is good

All children: $CSR=1$ ($csr=1.73$) – penicillin is bad