Intent-to-treat analysis in observational studies

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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?

$T =$

Response	Positive	Negative
Treatment 1	70	30
Treatment 2	60	40

$T =$

Response	Positive	Negative
Treatment 1	70	30
Treatment 2	600	400

$T =$

Response	Positive	Negative
Treatment 1	70	30
Treatment 2	6000	4000

The usual way of choosing the better treatment is not sensitive to allocation

Odds ratio or cross product ratio (cpr)

$$\frac{f_{11}/f_{12}}{f_{21}/f_{22}} = \frac{f_{11}f_{22}}{f_{12}f_{21}}$$

Relative risk or risk ratio

$$\frac{\frac{f_{11}}{f_{11}+f_{12}}}{\frac{f_{21}}{f_{21}+f_{22}}}$$

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 *sgn log* of cpr or csr

$$\gamma\left(\begin{array}{|c|c|}\hline a & a \\ \hline b & b \\ \hline\end{array}\right) = 0$$

$$\gamma\left(\begin{array}{|c|c|}\hline a & b \\ \hline a & b \\ \hline\end{array}\right) = 0$$

$$\gamma\left(\begin{array}{|c|c|}\hline a & b \\ \hline c & d \\ \hline\end{array}\right) = -\gamma\left(\begin{array}{|c|c|}\hline c & d \\ \hline a & b \\ \hline\end{array}\right)$$

$$\gamma\left(\begin{array}{|c|c|}\hline a & b \\ \hline c & d \\ \hline\end{array}\right) = -\gamma\left(\begin{array}{|c|c|}\hline b & a \\ \hline d & c \\ \hline\end{array}\right)$$

$$a > b,\ c \le d \Rightarrow \gamma\left(\begin{array}{|c|c|}\hline a & b \\ \hline c & d \\ \hline\end{array}\right) = 1$$

$$a > c,\ d = b \Rightarrow \gamma\left(\begin{array}{|c|c|}\hline a & b \\ \hline c & d \\ \hline\end{array}\right) = 1$$

Consistency

$$\text{if } \gamma(T_1) = \gamma(T_2), \text{ then } \gamma(T_1 + T_2) = \gamma(T_1).$$

(No Simpson's paradox!)

Indifference

$$\text{If } \gamma(T) = 0 \text{ by Properties 1 or 2, then}$$

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

Invariance against changes in allocation

$$\gamma\left(\begin{array}{|c|c|}\hline a & b \\ \hline c & d \\ \hline\end{array}\right) = \gamma\left(\begin{array}{|c|c|}\hline ta & tb \\ \hline uc & ud \\ \hline\end{array}\right)$$

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) γ is consistent

(b) γ is indifferent

(c) $\gamma = CSR$.

Can we / do we want to learn to conclude that Treatment 1 is better?

$T =$

Response	Positive	Negative
Treatment 1	50	30
Treatment 2	20	10

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

Response	Died	Survived
Penicillin	22	83
No penicillin	2	45

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

Response	Died	Survived
Penicillin	22	83
No penicillin	81	262

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