Interpreting randomized trial data

Different ways of reporting differences
(absolute, relative, etc.)

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Conflicts of interest

• None to declare
Relative differences sells newspapers!
Reporting differences

**INDEPENDENT**

Vitamin D can prevent asthma attacks, study finds

Taking oral vitamin D supplements can reduce the risk of severe asthma attacks by 3 per cent, according to research.

Vitamin supplements, new research

Taking oral vitamin D tablets can reduce the likelihood of bouts requiring hospital admission or emergency department attendance from 6 per cent to 3 per cent, analysts at medical research group Cochrane concluded.

http://www.independent.co.uk/news/science/vitamin-d-asthma-attacks-prevent-study-cochrane-a7226756.html

**the guardian**

Vitamin D supplements could halve risk of serious asthma attacks

Major research review suggests that people who take vitamin D have fewer attacks requiring hospital treatment than those who do not.

Vitamin D pills can halve the risk of serious asthma attacks according to a major review of research into the impact the supplements have on the condition.

People with mild or moderate asthma who took the vitamin with their normal medicine had fewer attacks that required hospital treatment than those who went without, scientists found.

The risk of severe attacks fell from 6% to 3% in patients who had a vitamin D boost for six months to a year. The supplements cut the frequency of attacks too, with cases needing steroid treatment falling from one per person every two or so years, to one every four years.

https://www.theguardian.com/society/2016/sep/05/vitamin-d-supplements-could-halve-risk-of-serious-asthma-attacks

**Absolute difference**

**Relative difference**
Randomization
\[ N = 200 \]

Treatment
\[ n = 100 \]
Dead at 30-days
\[ n = 30 \]
Alive at 30-days
\[ n = 70 \]

Control
\[ n = 100 \]
Dead at 30-days
\[ n = 40 \]
Alive at 30-days
\[ n = 60 \]
### Example

A 2x2 contingency table + marginal totals

<table>
<thead>
<tr>
<th></th>
<th>Treatment</th>
<th>Control</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Died within 30-days</td>
<td>30</td>
<td>40</td>
<td>70</td>
</tr>
<tr>
<td>Alive at 30-days</td>
<td>70</td>
<td>60</td>
<td>130</td>
</tr>
</tbody>
</table>
| Total                | 100       | 100     | \(N = 200\)
<table>
<thead>
<tr>
<th></th>
<th>Treatment</th>
<th>Control</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Died within 30-days</td>
<td>$a$</td>
<td>$b$</td>
<td>$a + b$</td>
</tr>
<tr>
<td>Alive at 30-days</td>
<td>$c$</td>
<td>$d$</td>
<td>$c + d$</td>
</tr>
<tr>
<td>Total</td>
<td>$a + c$</td>
<td>$b + d$</td>
<td>$N = a + b + c + d$</td>
</tr>
</tbody>
</table>

A 2x2 contingency table + marginal totals
## Absolute risk reduction

<table>
<thead>
<tr>
<th>Measure</th>
<th>Formula</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absolute risk in treatment group ($AR_{treat}$) =</td>
<td>$\frac{a}{a + c}$</td>
<td>$\frac{30}{100} = 0.3$</td>
</tr>
<tr>
<td>Absolute risk in control group ($AR_{control}$) =</td>
<td>$\frac{b}{b + d}$</td>
<td>$\frac{40}{100} = 0.4$</td>
</tr>
<tr>
<td>Absolute risk reduction (ARR) =</td>
<td>$AR_{control} - AR_{treat}$</td>
<td>$0.4 - 0.3 = 0.1$</td>
</tr>
</tbody>
</table>
# Absolute risk reduction

<table>
<thead>
<tr>
<th>Measure</th>
<th>Formula</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absolute risk in treatment group ($AR_{treat}$) =</td>
<td>$\frac{a}{a + c}$</td>
<td>$\frac{30}{100} = 30%$</td>
</tr>
<tr>
<td>Absolute risk in control group ($AR_{control}$) =</td>
<td>$\frac{b}{b + d}$</td>
<td>$\frac{40}{100} = 40%$</td>
</tr>
<tr>
<td>Absolute risk reduction (ARR) =</td>
<td>$AR_{control} - AR_{treat}$</td>
<td>$0.4 - 0.3 = 10%$</td>
</tr>
</tbody>
</table>
# Number needed to treat

<table>
<thead>
<tr>
<th>Measure</th>
<th>Formula</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number needed to treat (NNT)</td>
<td>( \frac{1}{ARR} )</td>
<td>( \frac{1}{0.1} = 10 )</td>
</tr>
</tbody>
</table>

Equivalent to the average number of patients who need to be treated to prevent one additional event.
### Relative risk (reduction)

<table>
<thead>
<tr>
<th>Measure</th>
<th>Formula</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relative risk (RR)</td>
<td>$\frac{AR_{treat}}{AR_{control}}$</td>
<td>$\frac{0.3}{0.4} = 0.75$</td>
</tr>
<tr>
<td>Relative risk reduction (RRR)</td>
<td>$1 - RR$</td>
<td>$1 - 0.75 = 0.25$</td>
</tr>
</tbody>
</table>
Results from 3 hypothetical RCTs of the same treatment

- **High risk**
  - ARR = 0.1 (or 10%)
  - NNT = 10
  - RRR = 0.25 (or 25%)

- **Intermediate risk**
  - ARR = 0.05 (or 5%)
  - NNT = 20
  - RRR = 0.25 (or 25%)

- **Low risk**
  - ARR = 0.01 (or 1%)
  - NNT = 100
  - RRR = 0.25 (or 25%)
Relative vs. absolute differences

- Ratios more robust to baseline risk
  - better for meta-analysis
  - not as useful for patients and clinicians
  - inappropriate to extrapolate ARR from one population to another if baseline risk is different
Odds ratio vs. relative risk

<table>
<thead>
<tr>
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<th>Formula</th>
<th>Example</th>
</tr>
</thead>
</table>
| Relative risk (RR) | \[
\frac{a(b + d)}{b(a + c)}
\]                          | = 0.75      |
| Odds ratio (OR)    | \[
\frac{\text{odds}_{\text{treat}}}{\text{odds}_{\text{control}}} = \frac{ad}{bc}
\] | 18/28 = 0.64 |
Are they ever equivalent?

- OR \approx RR \text{ for low baseline risk}
  - High risk trial (event rate = 0.30; RR = 0.75 vs. OR = 0.64)
  - Intermediate risk trial (event rate = 0.15; RR = 0.75 vs. OR = 0.71)
  - Low risk trial (event rate = 0.04; RR = 0.75 vs. OR = 0.74)
- But ORs exaggerate reduction effect otherwise
- ORs are easily confused with RRs!

\[
RR = \frac{OR}{1 - AR_{control} + (1 - AR_{control})OR}
\]

An interpretative disadvantage

• What if we think of ‘survival at 30-days’ as the outcome rather than ‘death at 30-days’?

\[
\text{OR}_{\text{survival}} = \frac{28}{18} = 1.56 = \frac{1}{\text{OR}_{\text{death}}}
\]

\[
\text{RR}_{\text{survival}} = \frac{0.7}{0.6} = 1.17 \neq \frac{1}{\text{RR}_{\text{death}}}
\]
Time-to-event outcomes

Relative effect:
HR = 0.55

• HR uses all data at each time point
• Not robust to departures from proportionality

Absolute effect:
ARR(12-months) = 20.0%
30.7% in the TAVI group
50.7% in the standard therapy group
NNT(12-months) = 5

Conclusions

- Preferable to report **both** absolute and relative effects

<table>
<thead>
<tr>
<th>Outcomes and estimation</th>
<th>17a</th>
<th>For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>17b</td>
<td>For binary outcomes, presentation of both absolute and relative effect sizes is recommended</td>
</tr>
</tbody>
</table>

- Evidence suggests reporting choice affects interpretation*
- If presented with a relative risk, always ask ‘relative to what?’
- The uncertainty about effect sizes should always be reported

THINGS GOT REALLY INTERESTING WHEN THE STATISTICIAN STARTED DOING WARD ROUNDS.