Introduction to meta-analysis 2: Effect measures for dichotomous outcomes

Areti- Angeliki Veroniki
University of Ioannina, Greece
averonik@cc.uoi.gr

Dimitris Mavridis,
University of Ioannina, Greece
dmavridi@cc.uoi.gr
Acknowledgements

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Many slides were written by

* Julian Higgins (MRC Biostatistics Unit, Cambridge, UK)
* Georgia Salanti (University of Ioannina, Greece)
Effect Sizes for Dichotomous Data

Introduction to meta-analysis

Transformations from one effect size to another

Practical in RevMan
Results of experiments or observations

- Studies usually compare outcomes between intervention groups
  - The risk of TB with and without the vaccination
  - The mean weight loss with two different diets

- How can we compare the outcomes between the interventions?

  Using **Effect Sizes**

**Effect size**: a value reflecting the magnitude of the treatment effect
Dichotomous outcome data:

<table>
<thead>
<tr>
<th></th>
<th>TB+</th>
<th>TB-</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCG+</td>
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</tr>
<tr>
<td></td>
<td>24</td>
<td>176</td>
</tr>
</tbody>
</table>

Relative measures:

- **RR** = \( \frac{\frac{10}{100}}{\frac{14}{100}} = 0.71 = 71\% \)
- **OR** = \( \frac{\frac{90}{14}}{\frac{86}{100}} = 0.68 \)

Absolute measure:

- **RD** = \( \frac{\frac{10}{100} - \frac{14}{100}} = -4\% \)

Effect Sizes
Many studies addressing the same question

Does BCG vaccine prevent TB?

Forest Plot

<table>
<thead>
<tr>
<th>Study</th>
<th>Effect Measure</th>
<th>Scale (effect measure)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study 2</td>
<td></td>
<td>RR = 1.7 (0.4, 2.8)</td>
</tr>
<tr>
<td>Study 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study 4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study 5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Effect Measure (e.g. Risk Ratio)

Favours Vaccination ← → Favours Non-Vaccination

Direction of effect

Line of no effect
Graphical Display: Forest Plot

Does BCG vaccine prevent TB?

Forest Plot

Estimate and confidence interval for each study. Block sizes are proportional to weight.

Effect Measure (e.g. Risk Ratio)

Favours Vaccination ← → Favours Non-Vaccination

Direction of effect
Basic Principles of meta-analysis

- **Compare like with like**
  - participants in one study are not directly compared with those in another
  - each study is analysed separately
  - summary statistics are combined to give the meta-analysis

- **Weight studies according to the information they provide**
  - usually by precision (inverse variance)
  - *gives more weight to larger studies...*
  - ... so that larger studies have more influence on the summary estimate
To apply a meta-analysis

1. Require from each study
   • estimate of treatment effect
   • variance of estimate

   \[
   \text{weight of study} = \frac{1}{\text{variance}}
   \]

2. Combine these using a weighted average:

   \[
   \text{pooled estimate} = \frac{\text{sum of (estimate} \times \text{weight)}}{\text{sum of weights}}
   \]

   \[
   \text{with variance} = \frac{1}{\text{sum of weights}}
   \]
To increase **power** and **precision**

To quantify **effect sizes** and their **uncertainty**
To assess heterogeneity (generalizability) of results

- Conduct a meta-analysis…

![Risk difference estimates with 95% confidence intervals](image)

- Risk difference
  - Favours Treatment
  - Favours placebo

![Risk ratio estimates with 95% confidence intervals](image)

- Risk ratio
  - Favours Treatment
  - Favours placebo
1. Identify the data type for the outcome measurements.

2. Use an effect size to compare the outcomes between the interventions.
Effect measures for dichotomous data

We can compare the two groups in several ways

- Odds ratio \((OR)\)
- Risk ratio \((RR)\)
- Risk difference \((RD)\)
- Number needed to treat \((NNT)\)

*Risk and odds are just different ways of expressing how likely an event is*
Consider a single study:

<table>
<thead>
<tr>
<th></th>
<th>Event</th>
<th>No-Event</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment</td>
<td>a</td>
<td>b</td>
<td>m₁</td>
</tr>
<tr>
<td>Control</td>
<td>c</td>
<td>d</td>
<td>m₂</td>
</tr>
<tr>
<td>Total</td>
<td>N₁</td>
<td>N₂</td>
<td>N</td>
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</table>

Control Group Risk (CGR) = \( \frac{c}{m₂} \)
Borchgrevink 1966 RCT from Omega 3 fatty acids and mortality:

<table>
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<td>24</td>
<td>176</td>
<td>200</td>
</tr>
</tbody>
</table>
The chance or probability of having a specific event

\[
\text{risk} = \frac{\text{number of events of interest}}{\text{total number of observations}}
\]

- 20 people drink rum the night before the exams, 5 fail to pass
- risk of a failure
  \[
  = \frac{5 \text{ fail}}{20 \text{ who drank rum}}
  = \frac{5}{20} = \frac{1}{4} = 0.25 = 25\%
  \]
- The chance to fail is 25% if you drink rum the night before
Risk of having an event divided by the risk of not having it

\[
\text{odds} = \frac{\text{number of events}}{\text{number of no events}}
\]

• 20 people drink rum the night before the exams, 5 fail to pass
• odds of failure

\[
= \frac{5 \text{ fail}}{15 \text{ did not fail}} = \frac{5}{15} = \frac{1}{3} = 0.3
\]

○ the chances of failure when drinking rum are one third of the chances of passing
○ one person will fail for every three that will pass
○ the chances of failing are 3 to 1 against
Risk and Odds

\[
\text{Risk} = \frac{Odds}{1 + Odds} \quad \text{Odds} = \frac{Risk}{1 - Risk}
\]

The difference between risk and odds is small when the event is rare but can be large for common events.
Risk of TB with BCG: \[ \frac{10}{100} = 10\% \]

Odds of TB with BCG: \[ \frac{\frac{10}{90}}{100/100} = \frac{1}{9} \]

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</tr>
</tbody>
</table>

Risk: The probability with which an event will occur.

Odds: The ratio of the probability that a particular event will occur to the probability that it will not occur.
Risk Ratio and Odds Ratio

**Risk Ratio**

\[
\text{risk ratio} = \frac{\text{risk in treatment group}}{\text{risk in control group}} = \frac{a/(a+b)}{c/(c+d)}
\]

**Odds Ratio**

\[
\text{odds ratio} = \frac{\text{odds in treatment group}}{\text{odds in control group}} = \frac{a/b}{c/d}
\]

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<td>N</td>
</tr>
</tbody>
</table>
A risk ratio of 3 \((RR = 3)\) implies:
- Events are 3 times more likely in the treatment group
- The treatment *increases* the risk of events by 
  \[100 \times (RR - 1)\% = 200\%\]

A risk ratio of 0.25 \((RR = 0.25)\) implies:
- The probability of an event in the treatment group is 1/4 of the probability in the control group
- The treatment *reduces* the risk of events by 
  \[100 \times (1 - RR)\% = 75\%\]
• $RR = 1 \rightarrow$ there is *no difference* in risk of event ($OR = 1$) between the two groups

• $RR < 1 \rightarrow$ the *event rate is lower* in the group ($OR < 1$) in the nominator ($OR < RR$)

• $RR > 1 \rightarrow$ the *event rate is larger* in the group ($OR > 1$) in the nominator ($OR > RR$)
If some cells contain zeros, then add 0.5 correction to each cell

\[
\text{Risk Ratio} = \frac{\frac{a}{a+b}}{\frac{c}{c+d}} \quad \text{Odds Ratio} = \frac{\frac{a}{b}}{\frac{c}{d}}
\]

If \(a = c = 0\) or \(b = d = 0\) then OR and RR are not defined and it is valid to exclude the study from the analysis.
Example: Borchgrevink 1966 study

**Treatment group**: Food supplement with Omega 3 fatty acids

**Control group**: Food supplement with placebo

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<td>100</td>
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<td>200</td>
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\[
RR = \frac{10}{14} = 0.71 = 71\%
\]

\[
OR = \frac{90}{14} = 0.68
\]
## Risk Ratio of Adverse Events

<table>
<thead>
<tr>
<th></th>
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<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Treatment</strong></td>
<td>1</td>
<td>99</td>
<td>100</td>
</tr>
<tr>
<td><strong>Control</strong></td>
<td>10</td>
<td>90</td>
<td>100</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>11</td>
<td>189</td>
<td>200</td>
</tr>
</tbody>
</table>

**Risk Ratio of Event**

\[
RR_{Dead} = \frac{1}{\frac{100}{10}} = 0.1
\]

95% CI: (0.01, 0.80)

**Risk Ratio of No-Event**

\[
RR_{Alive} = \frac{99}{\frac{100}{90}} = 1.10
\]

95% CI: (0.74, 1.64)
Which is better? RR or OR

- They are both valid as long as they are not misinterpreted!
- OR is difficult to understand
- OR are used in case-control studies and can account for covariates
- RR may be very different if we switch the outcome

When the event rate is rare
- OR and RR will be similar

When the event rate is common
- OR and RR will differ

Risk to be or risk not to be?
Log-Risk Ratio (LogRR)

\[
\log RR = \log \frac{a + b}{c} = \log \left( \frac{a(c + d)}{c(a + b)} \right)
\]

\[
\text{var}(\log RR) = \frac{1}{a} + \frac{1}{a + b} + \frac{1}{c} + \frac{1}{c + d}
\]
Log-Risk Ratio (LogRR)

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Calculate Risk Ratio

\[ RR = \frac{10}{100} = \frac{10}{14} = 0.71 \]

Introduce in meta-analysis

\[ \log(RR) = \log(0.71) = -0.34 \]

and

\[ \text{var}(\log RR) = \frac{1}{10} + \frac{1}{100} + \frac{1}{14} + \frac{1}{100} = 0.194 \]

or

\[ \text{SE}(\log RR) = \sqrt{\text{var}(\log RR)} = \sqrt{0.19} = 0.44 \]

Calculate a 95% C.I. for \( \log RR \)

\[ 95\% \text{ CI for } \log RR: \log RR \pm 1.96 \times S.E(\log RR) = (-1.20, 0.52) \]

Back-calculate to the original scale

\[ 95\% \text{ CI for } RR: (e^{-1.20}, e^{0.52}) = (0.30, 1.68) \]
Log-Odds Ratio (LogOR)

\[
\text{logOR} = \log \frac{a}{b} = \log \left( \frac{a}{b} \right) - \log \left( \frac{c}{d} \right) = \log \left( \frac{ad}{bc} \right)
\]

\[
\text{var}(\text{logOR}) = \frac{1}{a} + \frac{1}{b} + \frac{1}{c} + \frac{1}{d}
\]
Log-Odds Ratio (LogOR)

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</table>

Calculate Odds Ratio

\[
OR = \frac{10}{90} = \frac{14}{86} = 0.68
\]

To apply a meta-analysis calculate

\[
\text{log}(OR) = \frac{1}{a} + \frac{1}{b} + \frac{1}{c} + \frac{1}{d}
\]

\[
\text{var}(\text{logOR}) = \frac{1}{a} + \frac{1}{b} + \frac{1}{c} + \frac{1}{d}
\]

\[
\text{SE}(\text{logOR}) = \sqrt{\text{var}(\text{logOR})}
\]

95% CI for logRR

\[
\text{logOR} \pm 1.96 \times \text{SE}(\text{logOR})
\]

<table>
<thead>
<tr>
<th>log(OR)</th>
<th>var(logOR)</th>
<th>SE(logOR)</th>
<th>95% CI for logRR</th>
</tr>
</thead>
<tbody>
<tr>
<td>-0.38</td>
<td>0.191</td>
<td>0.44</td>
<td>(-1.24, 0.48)</td>
</tr>
</tbody>
</table>

Back-calculate to the original scale

95% CI for OR : \((e^{-1.24}, e^{0.48}) = (0.29, 1.62)\)
Treatment effects on the log-scale: Why?

- **RR, OR are not symmetric**

  **Ex:** halving the odds (OR=0.5) and doubling the odds (OR=2) are not cancelling each other (average OR=1.25)

- **log(OR) and log(RR)**
  - Easier to compare positive with negative values
    - Log(OR) takes values in \((-\infty, \infty)\)
    - Log(RR) takes values in \((-\infty, \log(1/CGR))\)
  - no effect at zero (neutral value)
  - are symmetric
    - log(OR) follows the normal distribution
    - log(RR) has a better approximation with the normal distribution than RR
The *difference in the probability* between the treated and control groups

\[ RD = \frac{a}{a + b} - \frac{c}{c + d} \]

- A measure *easy to interpret* but clinical interpretation depends on context (RD is not a relative treatment effect)
  - A treatment reduces the probability of death RD= 2%
    - From 70% risk goes to 68% or from 3% to 1%?

- Gives *improbable values* if applied in different populations
  - RD of -10% applied to a population with 7% risk gives -3% risk
Risk Difference

\[ RD = \frac{a}{a + b} - \frac{c}{c + d} \]

\[ \text{var}(RD) = \frac{ab}{(a + b)^3} + \frac{cd}{(c + d)^3} \]
Number of people need to treat to prevent one event that would not have occurred on the control treatment.

- $RD = 0.76$ : For every 100 treated people 76 will benefit by using the intervention
- How many would we need to treat to help one person?
  \[ NNT = \frac{100}{76} = 1.3 \rightarrow 2 \text{ people} \]

- No useful variance formula
  - discontinuities at $RD = 0$
- Never used directly for meta-analysis
Number Needed to Treat

\[ \text{NNT} = \frac{1}{|\text{RD}|} \]

Gives misleading results if applied to populations with different CGR !!

**Example:**

CGR = 10%, treatment with RR=0.5 \( \Rightarrow \) RD = -5%

\[ \Rightarrow \text{NNT} = 20 \] to treat to heal one

If CGR = 0.5% , ( \( \Rightarrow \) RD=-0.25%) \( \Rightarrow \) NNT= 400!

*Use the RR to derive NNT!*

\[ \text{NNT} = \frac{1}{(1-\text{RR}) \times \text{CGR}} \]

*Smeeth et al., BMJ 318, 1548-1551*
Example: Borchgrevink 1966 study

$$RR = \frac{10}{14} \div \frac{100}{100} = 0.71 = 71\%$$

$$OR = \frac{90}{14} \div \frac{86}{100} = 0.68$$

$$RD = \frac{10}{100} - \frac{14}{100} = (-)4\%$$

$$NNT = 25$$
Choosing an effect measure

Which to pick? $OR$, $RR$ or $RD$?

Consider

* Homogeneity across studies
* Mathematical properties
* Interpretability

Deeks (2002)
## Heterogeneity

### Hypothetical trial:

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Control</th>
<th>RR</th>
<th>OR</th>
<th>RD</th>
</tr>
</thead>
<tbody>
<tr>
<td>100/1000</td>
<td>150/1000</td>
<td>0.67</td>
<td>0.63</td>
<td>-0.05</td>
</tr>
</tbody>
</table>

*Now double treatment group risk (TGR). To maintain consistent effect sizes…*

<table>
<thead>
<tr>
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<th>OR</th>
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<td>300/1000</td>
<td>0.67</td>
<td>0.58</td>
<td>-0.10</td>
</tr>
<tr>
<td>200/1000</td>
<td>284/1000</td>
<td>0.70</td>
<td>0.63</td>
<td>-0.08</td>
</tr>
<tr>
<td>200/1000</td>
<td>250/1000</td>
<td>0.80</td>
<td>0.75</td>
<td>-0.05</td>
</tr>
</tbody>
</table>

Homogeneity in one measure means heterogeneity in others (unless there is no effect, or no variation in event rate)
Empirical evidence suggests that

✓ Ratio measures \((RR\ and\ OR)\) exhibit considerably less heterogeneity than difference measures \((RD)\)

Deeks (2002)
Engels et al. (2000)
Heterogeneity

(OR vs RR)

(RD vs RR)
Mathematical Properties

* Risk difference \((RD = TGR - CGR)\)
  - can lead to impossible predictions (e.g. CGR = 0.8, RD = 0.3 \(\rightarrow TGR=1.1\))
  - normal approximation not great (RD must lie between -1 and 1)

* Risk ratios \((RR = TGR / CGR)\)
  - can lead to impossible predictions (e.g. CGR = 0.8, RR = 1.3 \(\rightarrow TGR=1.04\))
  - normal approximation not great
  - Swapping outcomes can have an important impact

* Odds ratio
  - no impossible predictions
  - normal approximation better than others
  - outcome of logistic regression
Risk difference
leads to NNT - clinicians are familiar with it

Risk ratio
well understood by non-statisticians

Odds ratio
poorly understood (often is interpreted as RR)
Summary

<table>
<thead>
<tr>
<th></th>
<th>OR</th>
<th>RR</th>
<th>RD</th>
</tr>
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<tbody>
<tr>
<td><strong>Homogeneity</strong></td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td><strong>Mathematics</strong></td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Interpretation</strong></td>
<td>-</td>
<td>+</td>
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- No measure is uniformly best
- Consider meta-analysing using one measure, and interpreting using another
Methods for meta-analysis of dichotomous data

- Inverse Variance Method (IV)
- Mantel-Haenszel (MH)
- Peto Odds Ratio
To apply a meta-analysis:

• Use the natural log scale for OR and RR, but **not** for RD

• Let’s call $y_i$ the effect size in any study $i$

• So what we have from each study is $y_i$ and SE of the effect size

• Summarize all $y_i$ to estimate the pooled $\Theta$ and $SE(\Theta)$. 

Inverse Variance

Woolf’s method

\[ \Theta_{IV} = \frac{\sum w_i y_i}{\sum w_i} \]

Where \( w_i \) is the inverse of the variance:

\[ w_i = \frac{1}{SE^2} \]

\[ SE(\Theta_{IV}) = \frac{1}{\sqrt{\sum w_i}} \]

* \( y_i \) can be either logOR or logRR or RD for dichotomous data and can be pooled if we know the SE.
Mantel-Haenszel (MH) method

Mantel and Haenszel (1959)

• Is more robust for
  • few events
  • sparse data (event rates being low or study size being small)

• In practice, meta-analysis follows the same logic as the inverse variance method, but now the weights are different
For each trial we define weights:

\[
\begin{align*}
w &= \frac{bc}{a+b+c+d} \quad \text{for OR} \\
&= \frac{c(a+b)}{a+b+c+d} \quad \text{for RR} \\
&= \frac{(a+b)(c+d)}{a+b+c+d} \quad \text{for RD}
\end{align*}
\]

Then Mantel-Haenszel odds ratio estimate is

\[
\theta_{MH} = \frac{\sum w_i y_i}{\sum w_i}
\]

- For \( SE(\theta_{MH}) \) look at the RevMan manual
Peto method
Yusuf et al. (1985)

• Developed for large trials with small treatment effects

• Biased when odds ratios are far from 1 (underestimates the effect) or sizes of groups being compared are very different

• May be best method for rare events ($\leq 1\%$) when group sizes are balanced

• No correction needed for zero cells
Peto Odds Ratio: calculation

- Based on comparing observed $O$ with expected $E$ number of events in treated group ($O$-$E$)

\[
O = a \\
E = (a + b) \times \frac{a + c}{(a + b + c + d)}
\]

\[
v = \frac{(a + b)(c + d)(a + c)(b + d)}{(a + b + c + d)^2 (a + b + c + d - 1)}
\]

\[
OR = \exp\left(\frac{O - E}{v}\right)
\]

\[
SE(\ln OR) = \frac{1}{\sqrt{v}}
\]

$E$ is the expected number of events in treated group according to event rate in the trial.
Summary: Meta-analysis for Dichotomous Data

- **Inverse-variance** weighted averages are fine for studies with large sample sizes
  - For both Fixed and Random effect

- **Mantel-Haenszel** offer an improvement for sparse data
  - For both Fixed and Random effect

- **Peto method** may be best for **rare** events
  - only exists for OR
  - Only for **Fixed** effects model
  - ✓ If numbers of subjects in each arm are reasonably balanced and the effect size is not too large
How to conduct a meta-analysis with dichotomous data in different format?

<table>
<thead>
<tr>
<th>Studies</th>
<th>Available Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study 1</td>
<td>$\ln OR$, $SE(\ln OR)$</td>
</tr>
<tr>
<td>Study 2</td>
<td>$a, b, c, d$ (2×2 table)</td>
</tr>
<tr>
<td>Study 3</td>
<td>$RD$, $SE(RD)$</td>
</tr>
<tr>
<td>Study 4</td>
<td>$a, b, c, d$ (2×2 table)</td>
</tr>
<tr>
<td>Study 5</td>
<td>$\ln RR$, $SE(\ln RR)$</td>
</tr>
</tbody>
</table>
### Possible Transformations between effect measures

- **RR $\rightarrow$ RD**
  \[ RD = CGR \cdot (RR - 1) \]

- **OR $\rightarrow$ RD**
  \[ RD = \frac{OR \cdot CGR}{1 - CGR + (OR \cdot CGR)} - CGR \]

- **OR $\rightarrow$ RR**
  \[ RR = \frac{OR}{1 - CGR(1 - OR)} \]

- **RR $\rightarrow$ OR**
  \[ OR = \frac{RR(1 - CGR)}{1 - CGR \cdot RR} \]

- **OR**
- **RR** $\rightarrow$ SE, sample sizes $\rightarrow$ 2x2 table (a,b,c,d)
- **RD**
Effect sizes to 2x2 tables

- **RR**, its *SE* and the $m_1$, $m_2$
- **OR**, its *SE* and the $m_1$, $m_2$
- **RD**, its *SE* and the $m_1$, $m_2$

<table>
<thead>
<tr>
<th></th>
<th>Event</th>
<th>No-Event</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Treatment</strong></td>
<td>a</td>
<td>b</td>
<td>$m_1$</td>
</tr>
<tr>
<td><strong>Control</strong></td>
<td>c</td>
<td>d</td>
<td>$m_2$</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>$N_1$</td>
<td>$N_2$</td>
<td>N</td>
</tr>
</tbody>
</table>

CGR
If $RR$, its $SE$ and the $m_1$, $m_2$ are available then calculate:

\[
c = \frac{m_2 + RRm_1}{RRm_1(SE^2 + \frac{m_2 + m_1}{m_1m_2})}
\]

\[
a = c \frac{RRm_1}{m_2}
\]

\[
b = m_1 - a
\]

\[
d = m_2 - c
\]
Odds Ratio and Risk Difference → 2x2 table

**OR, }m_1, m_2 and the SE**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Event</th>
<th>No-Event</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment</td>
<td>a</td>
<td>b</td>
<td>m_1</td>
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</tr>
<tr>
<td>Total</td>
<td>N_1</td>
<td>N_2</td>
<td>N</td>
</tr>
</tbody>
</table>

Control group risk

\[
\alpha = (1 - OR)^2 + ORm_1SE^2(Ln(OR)),
\beta = -m_2[2(1 - OR) + m_1 \times OR \times SE^2(Ln(OR))],
\gamma = m_2(m_2 + ORm_1)
\]

Pietrantonj (2006)

\[
c = \frac{-\beta \pm \sqrt{\beta^2 - 4\alpha\gamma}}{2\alpha} = \begin{cases} c_1 \\ c_2 \end{cases}
\]

\[
\alpha = m_1^2m_2 + m_1^3,
\beta = -m_2(m_1^2m_2 + m_1^3) + 2RDm_1^2m_2^2,
\gamma = -m_1^2m_2^3(\text{RD}(1 - \text{RD}) + -m_1^3m_2^3SE^2)
\]
Review Manager (RevMan) is The Cochrane Collaboration’s software for preparing and maintaining Cochrane reviews.

RevMan Practical

Meta-analysis using
- Inverse Variance
- Mantel-Haenszel methods
- Peto

It needs:

1. The 2×2 table (a,b,c,d) [data entry as dichotomous outcome]
2. A treatment effect (e.g. lnOR, lnRR) and its standard error (SE) [data entry as generic inverse variance outcome]
RevMan Calculator can:

- RevMan can transform OR to RR or RD and vice versa.
- RevMan can transform OR or RR or RD to $2 \times 2$ table and vice versa.
# Acupuncture for depression

*CA Smith and PPJ Hay*

<table>
<thead>
<tr>
<th>Study</th>
<th>Acupuncture</th>
<th></th>
<th>Control</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Luo 1985</td>
<td>Improvement</td>
<td>24</td>
<td>Total</td>
<td>127</td>
</tr>
<tr>
<td>Luo 1988</td>
<td></td>
<td>10</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>Roschke 2000</td>
<td></td>
<td>45</td>
<td>182</td>
<td></td>
</tr>
<tr>
<td>Xiujuan 1994</td>
<td></td>
<td>14</td>
<td>97</td>
<td></td>
</tr>
</tbody>
</table>
Practical in RevMan
Resources

• **Cochrane Handbook for Systematic Reviews of Interventions**
  - Higgins and Green (eds); Wiley 2008, updated online

• **RevMan Tutorial and User Guide**
  - www.cc-ims.net/RevMan/documentation.htm

• **Introduction to Meta-analysis**
  - Borenstein, Hedge, Higgins and Rothwell; Wiley 2009
  - for meta-analysis methods (basic)

• **Meta-Analysis of Controlled Clinical Trials**
  - Whitehead; Wiley 2002
  - for meta-analysis methods (more technical)

• **Handbook of Research Synthesis and Meta-analysis**
  - Cooper, Hedges and Valentine; Sage 2009
  - all issues, quite technical in places