Adjusting for publication bias:

a multiple imputation approach

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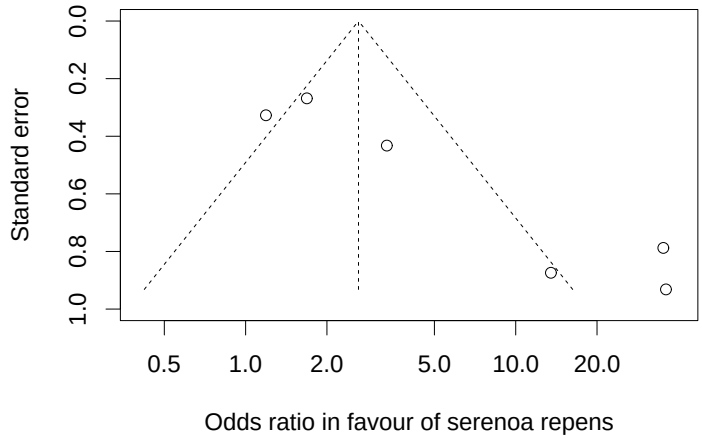
Outline

1. Possible publication bias: *serenoa repens* meta-analysis
2. Logistic selection model for publication bias
3. Estimation using MI
4. Application to example
5. Discussion

Example

Funnel plot: serenoa repens for benign enlarged prostate



Dotted lines show the overall (fixed effects) estimate of treatment $\pm$ 2 standard errors. P-value from arcsine test: 0.006. Random effects OR: 5.3, $p < 0.0001$

Selection model

For trial i, let

$$\texttt{logit}\,\Pr(\text{success in placebo group}) = \beta_{0i}$$
$$\texttt{logit}\,\Pr(\text{success in intervention group}) = \beta_{0i} + \beta_{1i}$$
$$\begin{pmatrix}\beta_{0i}\\ \beta_{1i}\end{pmatrix} \sim N\left[\begin{pmatrix}\beta_0\\ \beta_1\end{pmatrix}, \begin{pmatrix}\sigma_0^2 & \\ \sigma_{01} & \sigma_1^2\end{pmatrix}\right]$$
$$\texttt{logit}\,\Pr(\text{observe trial } i) = \alpha + \delta \log(\text{odds ratio trial})_i$$

Analyst chooses:

- $\tilde{n}$, the number of missing trials
- δ, the increase in the log-odds ratio of observing trial i with each unit increase in the log-odds in favour of treatment found in trial i

For each choice of δ fit the model, and calculate the publication bias test using the observed trial data and posterior imputed trial data

If $(\delta, \tilde{n})$ are plausible, the test for publication bias will not be significant.

Approximate model fitting via MI

For simplicity, let $\tilde{n} = 1$.

With $\delta = 0$, simulate M trials from the random effects meta-analysis model above.

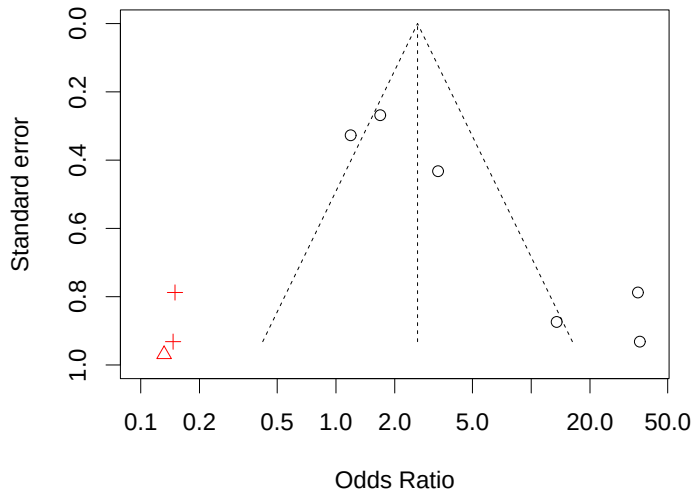
Thus create M imputed meta-analysis data sets, each with (i) the observed trials and (ii) one of the imputed studies.

If we analyse each of these imputed datasets, and combine the results using Rubin's MI rules, we get the same estimate and standard error as from the original data.

Re-weight estimates to represent increasing selection (Carpenter *et al* 2007) [1].

Weights depend only on δ.

Results



With $\delta = 1.24$ the model suggests the extra trial shown '△'; the odds ratio in favour of treatment is 3.6 ($p = 0.02$); cf the results of trim and fill (extra studies shown '+', OR 2.5 ($p = 0.07$))

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Summary: method

More work needed to check out the behaviour of this fitting approach [1].

- Nevertheless, fitting selection models in this way is fast and not subject to numerical problems;
- The results can be shown on the funnel plot, and
- Can be used with a range of models and tests for publication bias.

Our choice of selection model enables sensitivity to be explored in terms of relatively accessible parameters.

One could use this approach to understand the selection mechanisms implicit in 'Trim & Fill'.

See poster in statistical methodology session.

References

[1] James R Carpenter, Michael G Kenward, and Ian R White. Sensitivity analysis after multiple imputation under missing at random — a weighting approach. *Statistical Methods in Medical Research*, 16:259–275, 2007.