

# Tools for Identifying Missing Outcome Data in Systematic Reviews

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## BACKGROUND

Systematic reviews of clinical trials aim to include all relevant studies conducted on a particular topic and to provide an unbiased summary of their results, producing the best evidence on the benefits and harms of medical treatments. Recommendations made by the National Institute for Health and Clinical Excellence (NICE), who issue guidance on the use of treatments and procedures within the NHS, are based largely on systematic reviews. To be considered a reliable source of evidence about healthcare practice, systematic reviewers should explicitly address the issue of missing outcome data at the study level. Systematic reviewers should be encouraged to obtain any missing outcome data from trialists, failing this it is recommended that reviewers present missing outcome data from their reviews in a transparent way. Outcome reporting bias (ORB) as a result of missing outcome data is one of the many problems that has been shown to affect the validity of a review meta-analysis [1].

## OUTCOME MATRIX GENERATOR

The outcome matrix generator application has been set up as a tool for identifying missing outcome data at the study level in a review. Using the outcome matrix generator, we propose a five step approach for investigating missing outcome data in a review and subsequently using the matrix as a tool to assess for ORB.

GO TO MATRIX GENERATOR APPLICATION:

<http://mcrcctu.org.uk/orbit/>

## A FIVE STEP APPROACH FOR ADDRESSING MISSING OUTCOME DATA IN REVIEWS

### Step 1 - Exclusion Criteria

The first step is to ensure that no potentially eligible studies are excluded from the review for the sole reason of not reporting on any review outcomes of interest. If a study report does not give results for, or mention, certain outcomes this does not necessarily mean that they were not measured or analysed. For this reason, studies MUST NOT be excluded if they do not report on any of the relevant review outcomes.

### Step 2 - Constructing the Outcome Matrix from study reports

The outcome matrix is constructed by listing all the eligible studies as rows and all the review outcomes of interest as columns in the matrix. Outcomes can be distinguished in terms of review primary and secondary outcomes. Outcomes that are not of interest in the review but are reported in the reports for eligible trials are also listed. Our [Matrix Generator](#) will automatically create your blank matrix.

### Step 3 - Completing the Outcome Matrix

Once the outcome matrix has been constructed, the outcome matrix can be filled in using the [Matrix Generator](#). For each study, a reviewer should indicate which outcomes were reported and differentiate between 'full reporting', 'partial reporting', 'not reported – not clear whether measured or not' and 'not measured'. Guidelines for filling in the matrix can be found on our website ([http://www.liv.ac.uk/nwhtmr/orbit/outcome\\_matrix.htm](http://www.liv.ac.uk/nwhtmr/orbit/outcome_matrix.htm))

### Step 4 - Contacting Trialists

After the outcome matrix has been completed, reviewers should make an attempt to contact the trialists from the studies included in the review that partially reported the review outcomes of interest or where it was not clear whether the outcome was measured or not. The purpose of this contact is to try and obtain missing outcome data to include in the review analysis or to confirm that the outcomes of interest were not measured. The matrix should be updated accordingly.

### Step 5 - Assessment of ORB

Once the outcome matrix is complete and trialists have been contacted for missing data, a reviewer may then want to assess the potential risk of outcome reporting bias as a result of outcomes being partially reported or measured but not reported. A tutorial for assessing the potential for outcome reporting bias in a review, using the ORB classification system (Kirkham et al, 2010) [1] is provided in Dwan et al (2010)[2].

## AN EXAMPLE OF THE MATRIX GENERATOR

### ORBIT Matrix Generator

#### Step 1: Add list of review primary and secondary outcomes

##### Review primary outcomes

Enter a review primary outcome and then click add. Repeat this process until all review primary outcomes have been entered.

##### Review secondary outcomes

Enter a review secondary outcome and then click add. Repeat this process until all review secondary outcomes have been entered.

#### Step 2: Add a list of the names of included studies and all other study outcomes

##### Add study

Enter a study name and click add. Repeat this process until all included studies have been entered.

##### Other study outcomes

Enter a study outcome that was reported in an included study but not listed as a review outcome. Repeat this process until all other study outcomes have been entered.



Study ID (author, date of publication)	Review primary outcomes	Review secondary outcomes					Other study outcomes	
	Overall Survival	Event Free Survival	Overall Remission Rate	Relapse Rate	Adverse Events	Quality of Life	Relapse Site	Time to Relapse
Anderson 1983	✗	✗	✗	✗	✗	✗	✗	✗
Brecher 1997	✓	✓	✓	✗	✓	✗	✗	✗
Cairo 2003	✗	○	✗	✗	✗	✗	✗	✗
Magrath 1973	✗	✗	✗	✓	✗	✗	✗	✓
Magrath 1976	✓	✗	✗	✓	✗	✗	✓	✓
Neequaye 1990	✓	✗	✗	✓	✗	✗	✗	✓
Otweny 1976	✓	✗	✓	✓	✗	✗	✗	✗
Otweny 1977	✓	✗	✗	✓	✓	✗	✗	✗
Patte 1991	✓	✓	○	✗	✓	✗	✗	✗
Sullivan 1991	✗	✓	✗	✗	✗	✗	✗	✗
Ziegler 1971	✗	✗	✗	✓	✗	✗	✗	✗
Ziegler 1972	✓	✗	✗	✓	✗	✗	○	○

The default setting (✗) is that the study did not report the outcome but it is not clear whether the outcome was measured or not. You change the setting to either full reporting (✓), partial reporting (○) or not measured (✗), by clicking on the cross once for full reporting, twice for partial reporting and three times for not measured. Clicking on it again, reverts to not reported (✗).

## CONCLUSIONS

Our outcome matrix generator has thus far received positive feedback from Cochrane reviewers and the Cochrane handbook editors. We encourage all review authors to use the outcome matrix generator as a tool to transparently report missing study data from their reviews. The matrix generator has a built-in facility to easily copy and paste the matrix into their reviews. We also encourage reviewers to assess the potential risk of outcome reporting bias as a result of missing outcome data. Collaborations are ongoing with regards to including the outcome matrix as a standard tool for reporting missing study data in all Cochrane reviews.

## REFERENCES

- [1] Kirkham JJ, Dwan KM, Altman DG, Gamble C, Dodd S, Smyth R, Williamson PR. The impact of outcome reporting bias in randomised controlled trials on a cohort of systematic reviews. *BMJ* (2010); 340:c356.
- [2] Dwan K, Gamble C, Kolamunnage-Dona R, Mohammed S, Powell C, Williamson PR. Assessing the potential for outcome reporting bias in a review: A tutorial. *Trials* (2010); 11:52.