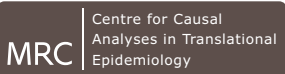


# Contour enhanced funnel plots for meta-analysis

Tom Palmer<sup>1</sup>, Jaime Peters<sup>2</sup>, Alex Sutton<sup>3</sup>, Santiago Moreno<sup>3</sup>

1. MRC Centre for Causal Analyses in Translational Epidemiology, Department of Social Medicine, University of Bristol
2. PenTAG/PenCLAHRC, Peninsula Medical School
3. Department of Health Sciences, University of Leicester

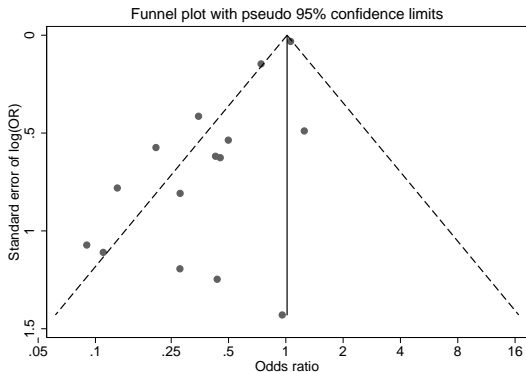
11 September 2009



# Outline

- ▶ Introduction to funnel plots & contour enhanced funnel plots
- ▶ Moreno, Sutton, Turner, et al., 2009 BMJ example
  - Use with other bias assessment methods
- ▶ `confunnel`: syntax and options
- ▶ Discussion

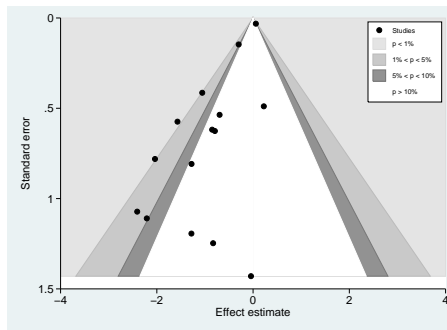
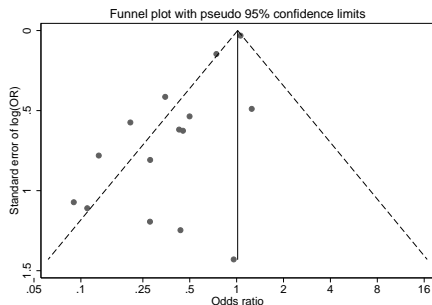
# Introduction to funnel plots



- ▶ Plot of std error ( $y$ -axis) versus effect estimate ( $x$ -axis)
- ▶ Help assess small study reporting bias/publication bias
- ▶ Sterne & Harbord, 2004; `metafunnel`, `funnel`
- ▶ Same metric as Egger's test (Egger, Davey Smith, Schneider, & Minder, 1997)

# Introduction to contour enhanced funnel plots

- ▶ Indicate regions of statistical significance on funnel plot
- ▶ Spiegelhalter, 2002, 2005; Peters, Sutton, Jones, Abrams, & Rushton, 2008

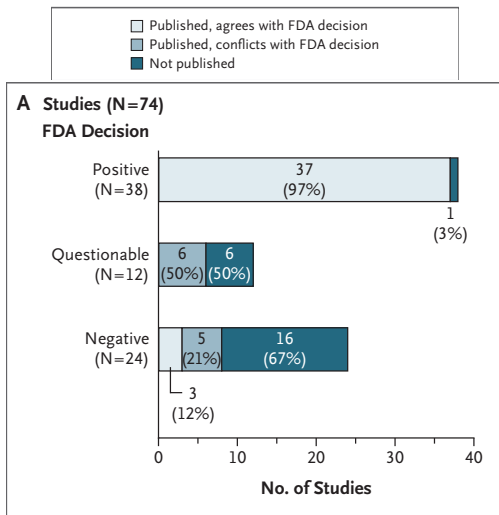


## Moreno, Sutton, Turner, et al., 2009, BMJ, example

- ▶ Re-analysis of Turner, Matthews, Linardatos, Tell, & Rosenthal, 2008, NEJM
- ▶ Results of 74 trials of 12 antidepressant drugs
- ▶ Compare FDA results versus journal results

# Moreno, Sutton, Turner, et al., 2009, BMJ, example

- ▶ Re-analysis of Turner et al., 2008, NEJM
- ▶ Results of 74 trials of 12 antidepressant drugs
- ▶ Compare FDA results versus journal results

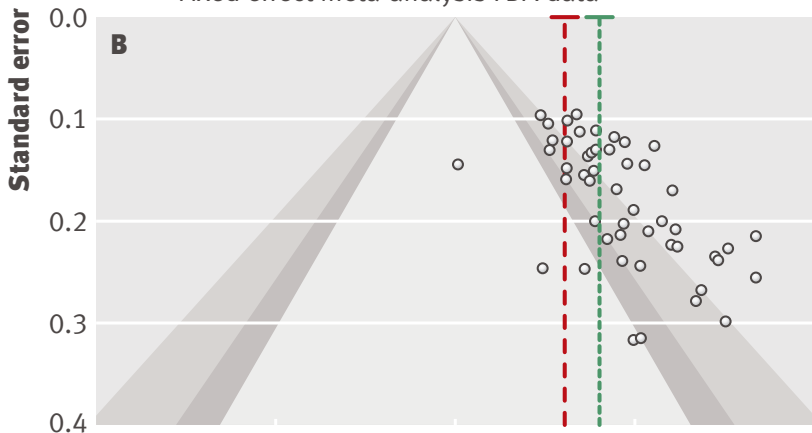


- Significance level <1%
- Significance level 1-5%
- Significance level 5-10%
- Significance level >10%

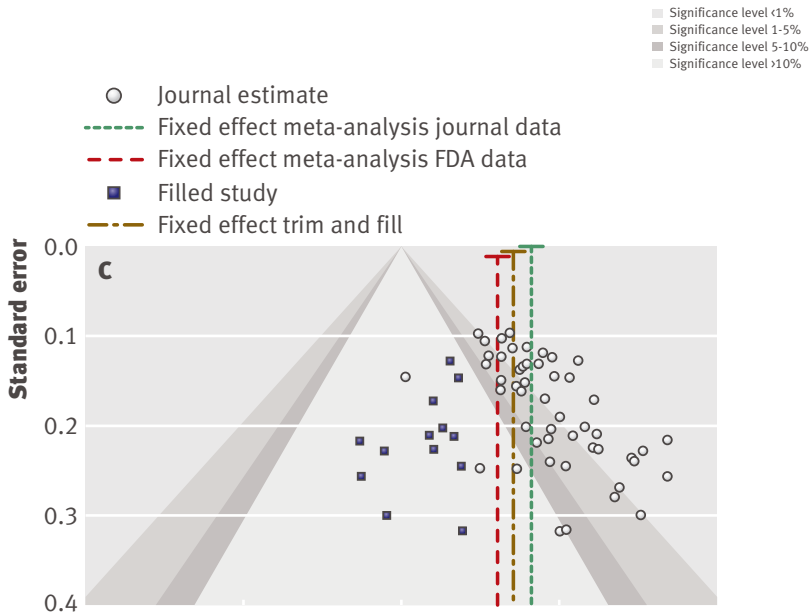
○ Journal estimate

--- Fixed effect meta-analysis journal data

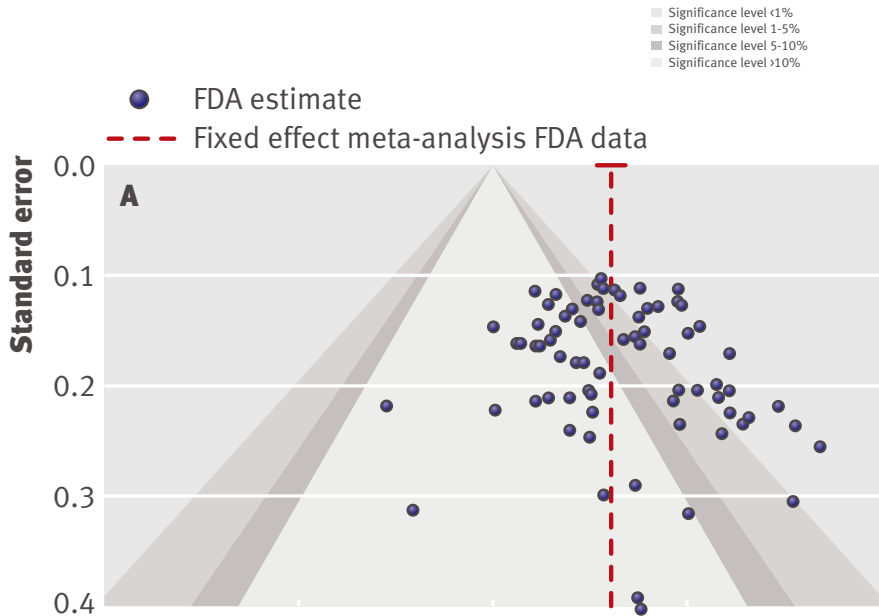
--- Fixed effect meta-analysis FDA data



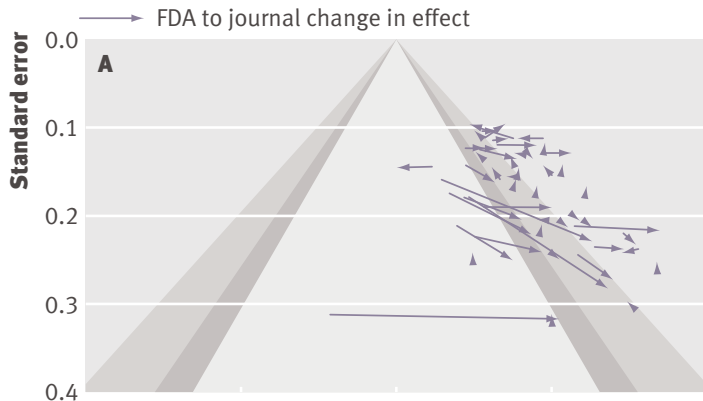
▶ Trim & fill: Duval & Tweedie, 2000b, 2000a

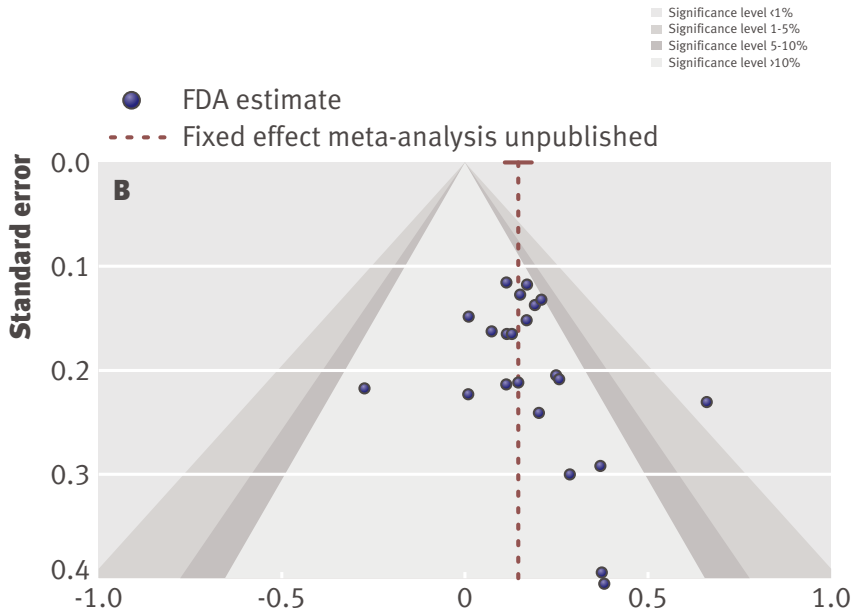






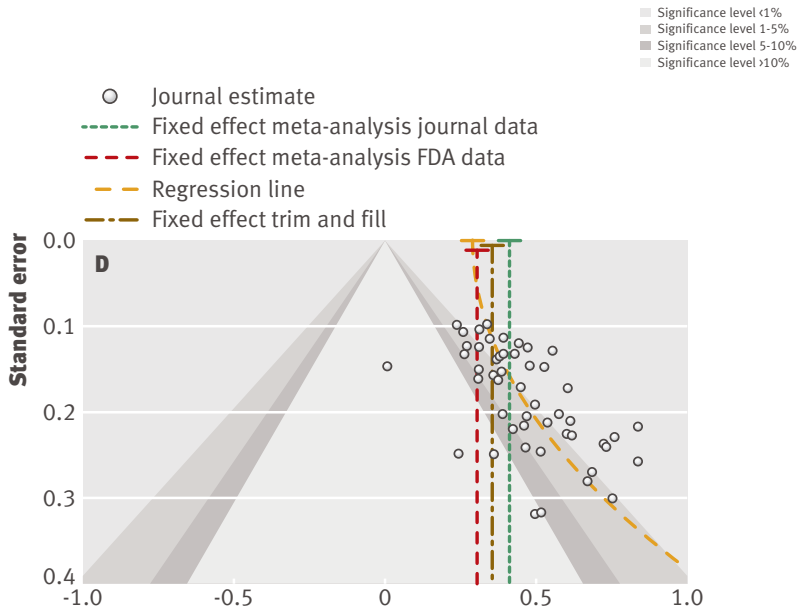
- Significance level <1%
- Significance level 1-5%
- Significance level 5-10%
- Significance level >10%





► Regression based bias adjustment methods:

Shang et al., 2005; Moreno, Sutton, Ades, et al., 2009



## The `confunnel` command

- ▶ Peters et al., 2008
  - investigation of 48 published Cochrane meta-analyses

## The `confunnel` command

- ▶ Peters et al., 2008
  - investigation of 48 published Cochrane meta-analyses
- ▶ Sterne et al., 2008, Cochrane Handbook, section 10.4.b

## The `confunnel` command

- ▶ Peters et al., 2008
  - investigation of 48 published Cochrane meta-analyses
- ▶ Sterne et al., 2008, Cochrane Handbook, section 10.4.b
- ▶ Palmer et al., 2008 (v1.0.4)
- ▶ Palmer et al., 2009 (v1.0.5)

# The confunnel command

- ▶ Peters et al., 2008
  - investigation of 48 published Cochrane meta-analyses
- ▶ Sterne et al., 2008, Cochrane Handbook, section 10.4.b
- ▶ Palmer et al., 2008 (v1.0.4)
- ▶ Palmer et al., 2009 (v1.0.5)





## confunnel: syntax and options

- ▶ Syntax:

```
confunnel logor selogor [, options]
```

## confunnel: syntax and options

- ▶ Syntax:

```
confunnel logor selogor [, options]
```

- ▶ Options:

- ▶ metric(*se|invse|var|invvar*): different y-axes: variance, standard error & their inverses (Sterne & Egger, 2001)
- ▶ onesided(*lower|upper*): one sided significance levels
- ▶ Other twoway options

## Contour enhanced funnel plots discussion

- ▶ Funnel plots should be used with care (Lau, Ioannidis, Terrin, Schmid, & Olkin, 2006)
- ▶ Aid assessment of reporting biases
- ▶ Put other bias assessment methods in a context
- ▶ `confunnel` can be used with `metan`, `metabias`, `metatrim`

# References I

- Duval, S., & Tweedie, R. L. (2000a). A nonparametric "trim and fill" method of accounting for publication bias in meta-analysis. *Journal of the American Statistical Society*, *95*, 89–98.
- Duval, S., & Tweedie, R. L. (2000b). Trim and fill: A simple funnel plot based method of testing and adjusting for publication bias in meta-analysis. *Biometrics*, *56*, 455–463.
- Egger, M., Davey Smith, G., Schneider, M., & Minder, C. (1997). Bias in meta-analysis detected by a simple, graphical test. *British Medical Journal*, *315*(7109), 629–634.
- Lau, J., Ioannidis, J., Terrin, N., Schmid, C. H., & Olkin, I. (2006). The case of the misleading funnel plot. *British Medical Journal*, *333*(7568), 597–600.
- Moreno, S. G., Sutton, A. J., Ades, A. E., Stanley, T. D., Abrams, K. R., Peters, J. L., et al. (2009). Assessment of regression-based methods to adjust for publication bias through a comprehensive simulation study. *BMC Medical Research Methodology*, *2*. (published online 12 January 2009)
- Moreno, S. G., Sutton, A. J., Turner, E. H., Abrams, K. R., Cooper, N. J., Palmer, T. M., et al. (2009). Novel methods to deal with publication biases: secondary analysis of antidepressant trials in the FDA trial registry database and related journal publications. *British Medical Journal*, *339*, 494–498. (b2981)
- Palmer, T. M., Peters, J. L., Sutton, A. J., & Moreno, S. G. (2008). Contour enhanced funnel plots for meta-analysis. *The Stata Journal*, *8*(2), 242–254. Available from <http://www.stata-journal.com/article.html?article=gr0033>

## References II

- Palmer, T. M., Peters, J. L., Sutton, A. J., & Moreno, S. G. (2009). Meta-Analysis in Stata: An Updated Collection from The Stata Journal. In J. A. C. Sterne (Ed.), (pp. 124–137). College Station, Texas: Stata Press. Available from <http://www.stata.com/bookstore/mais.html>
- Peters, J. L., Sutton, A. J., Jones, D. R., Abrams, K. R., & Rushton, L. (2008). Contour-enhanced meta-analysis funnel plots help distinguish publication bias from other causes of asymmetry. *Journal of Clinical Epidemiology*, *61*(10), 991–996.
- Shang, A., Huwiler-Müntener, K., Nartey, L., Jüni, P., Dörig, S., Sterne, J. A. C., et al. (2005). Are the clinical effects of homoeopathy placebo effects? Comparative study of placebo-controlled trials of homoeopathy and allopathy. *The Lancet*, *366*(9487), 726–732.
- Spiegelhalter, D. J. (2002). Funnel plots for institutional comparison. *Quality Safety in Health Care*, *11*(4), 390–391.
- Spiegelhalter, D. J. (2005). Funnel plots for comparing institutional performance. *Statistics in Medicine*, *24*(8), 1185–1202.
- Sterne, J. A. C., & Egger, M. (2001). Funnel plots for detecting bias in meta-analysis: Guidelines on choice of axis. *Journal of Clinical Epidemiology*, *54*(10), 1046–1055.

## References III

- Sterne, J. A. C., Egger, M., & Moher, D. (2008, September). Cochrane handbook for systematic reviews of interventions version 5.0.1. In J. P. T. Higgins & S. Green (Eds.), (chap. Chapter 10: Addressing reporting biases). The Cochrane Collaboration. Available from [http://www.mrc-bsu.cam.ac.uk/cochrane/handbook/chapter\\_10/figure\\_10\\_4\\_b\\_contour\\_enhanced\\_funnel\\_plots.htm](http://www.mrc-bsu.cam.ac.uk/cochrane/handbook/chapter_10/figure_10_4_b_contour_enhanced_funnel_plots.htm)
- Sterne, J. A. C., & Harbord, R. M. (2004). Funnel plots in meta-analysis. *The Stata Journal*, 4(2), 127–141.
- Turner, E. H., Matthews, A. M., Linardatos, E., Tell, R. A., & Rosenthal, R. (2008). Selective publication of antidepressant trials and its influence on apparent efficacy. *New England Journal of Medicine*, 358(3), 252–260.