#### Item 22: RISK OF BIAS ACROSS STUDIES.

Present results of any assessment of risk of bias across studies (see Item 15).

**Examples.** “Strong evidence of heterogeneity (I2 = 79%, P<0.001) was observed. To explore this heterogeneity, a funnel plot was drawn. The funnel plot in [Figure 4](http://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1000100#pmed-1000100-g004) shows evidence of considerable asymmetry.”

“Specifically, four sertraline trials involving 486 participants and one citalopram trial involving 274 participants were reported as having failed to achieve a statistically significant drug effect, without reporting mean HRSD [Hamilton Rating Scale for Depression] scores. We were unable to find data from these trials on pharmaceutical company Web sites or through our search of the published literature. These omissions represent 38% of patients in sertraline trials and 23% of patients in citalopram trials. Analyses with and without inclusion of these trials found no differences in the patterns of results; similarly, the revealed patterns do not interact with drug type. The purpose of using the data obtained from the FDA was to avoid publication bias, by including unpublished as well as published trials. Inclusion of only those sertraline and citalopram trials for which means were reported to the FDA would constitute a form of reporting bias similar to publication bias and would lead to overestimation of drug–placebo differences for these drug types. Therefore, we present analyses only on data for medications for which complete clinical trials' change was reported.”

#### Explanation.

Authors should present the results of any assessments of risk of bias across studies. If a funnel plot is reported, authors should specify the effect estimate and measure of precision used, presented typically on the x-axis and y-axis, respectively. Authors should describe if and how they have tested the statistical significance of any possible asymmetry (see Item 15). Results of any investigations of selective reporting of outcomes within studies (as discussed in Item 15) should also be reported. Also, we advise authors to tell readers if any pre-specified analyses for assessing risk of bias across studies were not completed and the reasons (e.g., too few included studies).