Appendix 1

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# Definition of covariates

## Severity score of participants at baseline

To make the mean baseline severity scores of participants comparable across studies that used different rating scales we used the transformation tables provided online at [http://www.ids-qids.org/index2.html - table1](http://www.ids-qids.org/index2.html#table1) (tables 3, 4). We converted all values into HAMD17 scale. We excluded studies that used HAMD29, HAMD31 or other scales that we could not transform into HAMD17 using this online tool. We included studies that reported the use of a HAMD scale without specifying which HAMD scale was used by assuming that such studies used the HAMD17 scale.

## Comparison of published versus unpublished reports and recording of the response rate.

For all studies we sought information about the response to treatment from published and unpublished data. The flowchart below presents the followed hierarchy when extracting response rates from published and unpublished reports of trials.

Studies can be classified into the following 6 categories. These categories are grouped into forming the variables “Response rate presented in published report” and “Unpublished report available and presents adequate response data” as shown in the following table.

|  |  |  |  |
| --- | --- | --- | --- |
| **Trial category** | Number of trials (arms) | *Variable “*Response rate presented in published report” | Variable “Unpublished report available and presents adequate response data” |
| No response rates were reported in in the published or the unpublished study reports | 35(56) | *Excluded from the analysis of response* | NO |
| No response data presented in the published report. Response rate is presented in the unpublished report (and recorded).  | 73(123) | NO | YES |
| The published report presents some information about response but the numerical data reported is not sufficient to estimate response rates. Response rate is recorded from unpublished reports. | 22(43) |
| Response rates are presented both in published and unpublished reports but figures do not match. We recorded response rates from the unpublished reports.  | 26(36) | YES |
| Response rates imputed from other relevant information presented in the published reports (e.g. from continuous outcomes). There is no unpublished study report or the unpublished report presents insufficient data to calculate response rates.  | 51(78) | NO |
| Response rates are presented in published report. There is no unpublished study report or the unpublished report presents insufficient data to calculate response rates. | 164(277) |
| Response rates are presented both in published and unpublished reports and figures do match.  | 50 (93) | YES |

## Risk of bias in the included studies

Blinding: Because of the pre-specified inclusions we had only those studies that were reported to be double-blinded, and hence the blinding of the outcome assessor take values «Stated but not tested» and «Unclear risk of bias» when it was not clear whether the outcome assessors were blinded.

Generation of sequence or allocation concealment: Studies that were at high risk of bias for generation of sequence or allocation concealment were excluded, consequently we had only «low» and «unclear» risk of bias for these two components.

Sponsorship bias was considered first at the trial level by recording whether the trial was sponsored by industry (high risk of sponsorship bias) versus an academic, governmental or non-for-profit organization (low risk of sponsorship bias). Studies for which the source of sponsoring was unclear were considered at high risk of bias. Studies for which it was clear that they receive no funding at all were considered at low risk of bias.

Sponsorship bias was also considered at the arm level. Arms in trials sponsored by an academic, governmental or non-for-profit organization were considered to be at low risk of bias. In trials that received finding by industry we considered the arm examining the drug manufactured by the company to be at high risk of bias whereas the comparator arm not associated with the company to be at low risk of bias. Arms in studies with unclear sponsoring were considered at high risk of bias.

Attrition bias: We recorded what the authors did to address missing outcome data. We recorded how often the response was estimated using the ‘Last observation carried forward’ (LOCF) approach or analyzed using incomplete data analysis such as an ‘available cases analysis’. In these two cases we assumed high risk of attrition bias. When the response was estimated using valid models such as Multiple Imputations or Mixed-Effect Model Repeated Measure (MMRM) model or when dropout rate was less than 1% we assumed the study had low risk of bias. If we were unable to tell what the authors used and or when no data was presented on the main outcomes we classified the study (and arm) as pertaining to unclear risk of bias.