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| Risk of Bias for Randomized Controlled Trials  |
| Study ID | Domains of Bias  |
| Randomization process | Deviations from intended interventions | Missing outcome data | Measurement of the outcome | Selection of the reported result | Overall Bias |
| Griffiths 2016 | Low | Low | Some Concerns | High | High | High |
| Ross 2016 | Low  | Low | Low | Some Concerns | High | High |
| Davis 2020 | High | Low | Low | Low | High | High |
| Grob 2011 | Low | Some Concerns | Low | High | High | High |
| Gasser 2014 (Phase 1) | Some Concerns | Some Concerns | Low  | Low | High | High |
| Palhano-Fontes 2019 | High | Low | Low | High | High | High |
| **Supplemental Table 1**: *Risk of Bias Assessment using the Cochrane Risk of Bias 2 (RoB 2) Tool*. Assessments across the domains of bias for randomized controlled trials are shown for the included trials fitting that description used in the meta-analysis. Note, for most included studies bias was largely the result of either multiple assessment scales used for the same outcome (i.e. depression & anxiety) in the selection of the reported result domain, and from failure of blinding procedures due to subjects and monitors often correctly determining which patients received the experimental drugs versus placebo. In the case of Palhano-Fontes et al. a high assessment of bias was made in the randomization domain, due to the statistically significant differences in baseline measures of depression for both the HAM-D & MADRS indices in favor of lower scores in the control group (Palhano-Fontes et al., 2019). Although this does indicate problematic randomization, the bias is in the direction of favoring the null hypothesis. |