	Sequence generation		Allocation concealment		Blinding of participants, personnel, and outcome assessors		Incomplete outcome data		Selective outcome reporting		Other sources of bias		OVERALL risk of bias for study as a whole
Author Year	**Describe method**	**Was it adequate? Yes/No/ Unclear**	**Describe method**	**Was it adequate? Yes/No/ Unclear**	**Describe all measures used, if any, to blind study participants and personnel from knowledge of which intervention participant received. Provide any information relating to whether intended blinding was effective.**	**Was knowledge of allocated intervention adequately prevented during study? Yes/No/ Unclear**	**Describe completeness of outcome data for each main outcome, including attrition and exclusions from analysis. State whether attrition and exclusions were reported, numbers in each intervention group (compared with total randomized participants), reasons for attrition/exclusions where reported and any re-inclusions in analyses performed by review authors.**	**Were incomplete outcome data adequately addressed? Yes/No/ Unclear**	**State how possibility of selective outcome reporting was examined by review authors and what was found.**	**Are reports of study free of suggestion of selective outcome reporting? Yes/No/ Unclear**	**State any important concerns about bias not addressed in other domains in tool. If particular questions/ entries were pre-specified in review's protocol, responses should be provided for each question/ entry.**	**Was study appar-ently free of other problems that could put it at high risk of bias? Yes/No/ Unclear**	**Low/Unclear/ High**
Berman 2007[29]	Method not described	Unclear	Method not described	Unclear	Described as double-blind, but no information about appearance or whether outcome assessors were blinded.	Unclear	For safety analyses, Intention-to-treat (ITT) using Last Observation Carried Forward (LOCF) of all who received double-blind treatment (99%); overall attrition=10%; placebo=9.1% vs aripiprazole=12.1%.	Yes	Protocol available on clinicaltrials. gov, but minimal detail about outcomes provided.	Unclear	No important concerns.	Yes	Unclear
Brent 2009[26]	"Subjects were randomly assigned to one of four conditions in a 2-by-2 factorial design… Subjects were assigned to treatment using a variation of Efron's biased coin toss, balancing both across and within sites."	Yes	No information provided	Unclear	"The intent was for study participants, clinicians, and independent evaluators to be blinded to medication treatment assignment, and for independent evaluators to be blinded to CBT assignment." Use of triple-dummy. "The pharmacotherapists' accuracy in guessing medication assignment was less accurate than chance (44.2%; 2=4.57; P=.03), whereas the independent evaluators guessed CBT assignment at a rate slightly higher than chance (58.3%; 2=5.14; P=.02). In 64 cases, the blinding of the independent evaluator was compromised, most commonly because of participant disclosure of receiving CBT." Study was designed to compare the relative efficacy of well-matched treatment alternatives and, therefore, even though patients may have been aware of the type of treatment they were receiving, all treatments were likely perceived as effective treatment methods.	Participants=yes to meds, no for CBT Personnel=yes for meds, no for CBT Assessors=unclear	Missing data, attritions, and exclusions adequately reported. Rates of treatment completion were reported with respect to primary outcomes. ITT using LOCF; attrition: overall=31%, venlafaxine alone=27%, venlafaxine with CBT=36%, SSRI alone=29%, SSRI with CBT=30%.	Yes	Protocol available on clinicaltrials.gov; but planned outcomes were not provided, and all expected suicide-related outcomes were reported.	Yes	Midway through the study, the paroxetine treatment option in the SSRI group was changed to citalopram due to safety concerns about paroxetine. Also, midway through the method for monitoring, self-harm was changed from spontaneous report to proactive assessment. No information is provided re: possible nested (e.g., therapist) effects.	Unclear	Unclear

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Calabrese 2005[28]	Insufficient information.	Unclear	Random assignment was achieved in a non-center-specific manner with an interactive voice-response central randomization service.	Yes	Described as double-blind and use of identically-appearing tablets is considered sufficient for blindings of study personnel and patient, but no information about blinding of outcome assessor. Also noted that "moderate rates of sedation or somnolence were observed in both quetiapine groups, which might have compromised the integrity of the double-blind design;" but lower likelihood that suicide assessment was influenced by inadequate blinding.	Unclear	No missing outcome data.	Yes	No omissions of any expected suicide-related outcomes.	Yes	The study appears to be free of other sources of bias.	Yes	Low
DeRubeis 2005[23]	Not described.	Unclear	Not described.	Unclear	Outcome assessors were blinded to all treatment conditions. Patients and pharmacotherapists were blinded to pharmacotherapy during first 8 weeks; patients and therapists were not blinded to cognitive therapy assignment.	Outcome assessors= yes. Patients/ therapists in pharmacotherapy groups= unclear. Patients/ therapists in cognitive therapy group=no.	ITT with LOCF; attrition was reasonable (13% in first 8 weeks; 5% in second 8 weeks); numbers and reasons were balanced across groups.	Yes	Protocol not available.	Unclear	None noted.	Yes	Unclear
Emslie 2006 (TADS)[19]	Computerized randomization.	Yes	No information provided.	Unclear	"Participants and all study staff remained masked in the pills-only conditions (FLX and PBO) until the end of stage I (week 12). Patients and treatment providers in COMB and CBT were aware of treatment assignment." "The primary dependent measures rated blindly by an independent evaluator are the Children's Depression Rating Scale and, for responder analysis, a dichotomized Clinical Global Impressions-Improvement score." Notably, the study was designed to compare the relative efficacy of well-matched treatment alternatives and, therefore, even though patients may have been aware of the type of treatment they were receiving, all treatments were likely perceived as effective treatment methods.	Unclear	Well-described ITT analysis and pre-treatment group comparisons included in article. No missing outcome data reported. Attritions and exclusions adequately documented, and subject flowchart included in article.	Yes	No omissions of any expected suicide-related outcomes.	Yes	The study appears to be free of other sources of bias. Well-described statistical accounting for potential nested data effects through the use of random effects modeling.	Yes	Unclear

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Emslie 2006[18]	Computer generated.	Yes	No information provided.	Unclear	Described as double-blind, but no details provided about appearance of treatments or blinding of outcome assessors.	Unclear	ITT using LOCF; overall attrition=18%, numbers and reasons balanced across groups.	Yes	Protocol available on clinicaltrials.gov. Primary outcome was consistent and reported; but only one secondary outcome was listed in protocol and many others were reported in publication.	Unclear	No concerns.	Yes	Unclear
Emslie 2009[20]	No information provided.	Unclear	No information provided.	Unclear	Described as double-blind, but no explicit statement about who was blinded. No information about appearance of tablets.	Unclear	ITT using LOCF; safety analyses included all patients who received ≥ 1 dose of study medication (99%); efficacy analyses included all patients in safety analyses who had ≥ 1 post-baseline assessment. Attrition: overall=18% in 8-week study; placebo=16%, escitalopram=20%.	Yes	Protocol available on clinicaltrials.gov, and primary and secondary outcomes match, and were reported.	Yes	Free of other sources of bias.	Yes	Unclear
Goodyer 2008[27]	Stochastic minimization used to ensure balance (so probably computer-generated).	Unclear	Central allocation, controlled by independent center.	Yes	Participants and treating clinicians: not blinded. Outcome assessment done by independent evaluators blind to treatment assignment. Participants, parents and treating clinicians instructed not to disclose treatment assignments. Adequacy of blinding tested by asking evaluators to guess treatment assignment, but results of testing NR.	Participants and treating clinicians=no. Outcome assessors= unclear.	ITT; overall attrition=15%, numbers balanced between groups. Reasons were not separated by group, but predictors of missing data were included as covariates in the statistical analyses.	Yes	Protocol not available.	Unclear	None noted.	Yes	Unclear
Grunebaum 2011[24]	Computer-generated.	Yes	Sequence generated by a pharmacist separate from research team.	Unclear (probably yes)	Patients, psychiatrists and assessors were blinded to treatment. Pills were identically over-encapsulated so patients were blinded. After 8 weeks, the 16-week continuation phase remained blinded if patient had a satisfactory response; otherwise they were switched to open treatment.	Yes for acute phase; no for those switched to open-label treatment in continuation phase.	Modified ITT, excluded 5% (3/78 due to ineligibility discovered after randomization, 1/78 lost to follow-up after randomization visit); high attrition (68%), but balanced across groups in numbers and reasons.	Unclear	Protocol not available.	Unclear	Only 27% completed 24 weeks on assigned medication.	Yes	Unclear

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Hallahan 2007[35]	Computer-generated list.	Yes	Dispensed by an independent colleague; code only revealed once data collection was complete.	Yes	Identical capsules, ensured equality of "fishy breath".	Yes	ITT using LOCF; attrition: overall=20%, placebo=26%, omega-3 fatty acid=14%.	Yes	Protocol not available. All expected suicide-related outcomes were reported.	Yes	Free of other sources of bias.	Yes	Low
Khan 2011[33]	Computer program.	Yes	Central allocation, controlled by independent pharmacist.	Yes	Double-blind: Patients and key study personnel. Blinding ensured by use of "closely matching" placebo and matching prescription bottles. Not explicitly stated that clinician was blinded.	Unclear for all	ITT using LOCF; Attrition=20%; numbers and reasons balanced across groups	Yes	Protocol not available.	Unclear	None noted.	Yes	Low
Lauterbach 2008[34 a]	Computerized randomization sequence.	Yes	Not described.	Unclear	Double-blinded assessment was conducted, although in some cases this procedure could not be maintained because of emergencies in relation to suicidal acts or insufficient drug compliance.	No	56/84 (67%) lithium and 59/83 (71%) placebo lost to follow-up by 12 months. Did ITT analysis. Recruitment was only 36% of that estimated required for adequate power 167/468. 7 patients in treatment group and 10 in control group with suicide or suicide attempts were counted as lost to follow-up.	No; although ITT analysis was done, loss to follow-up was very high.	Primary outcome was a composite of suicide and suicide attempts; suicidal acts were determined by self-report only. Did a post hoc analysis of deaths by suicides (showing 3 in placebo group vs 0 in lithium group) and this finding is highlighted even though there was no significant difference found on the primary outcome.	No	Differences between groups at baseline on important prognostic factors: more patients in the lithium group had personality disorders (53% vs 31%; P=0.12); more in the lithium group had multiple prior suicide attempts (57% vs 31%; P=0.001); and patients in the lithium group had higher scores on the suicide intent scale at their index attempt (P=0.046).	No	High

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Marcus 2008[30]	Method not described.	Unclear	Method not described.	Unclear	Described as double-blind, but no information about appearance or whether outcome assessors were blinded.	Unclear	For safety analyses, ITT using LOCF of all who received double-blind treatment (100%); overall attrition=15%; placebo=14.7% vs aripiprazole=15.2%.	Yes	No protocol available.	Unclear	No important concerns.	Yes	Unclear
Oquendo 2011[32]	Not described.	Unclear	Not described.	Unclear	"Patients, study psychiatrists, and assessors were blind to treatment assignment." Double-dummy approach used. Lithium levels monitored by nontreating physician.	Yes	46/48 lithium and 48/49 valpoate included in analysis. Used ITT analysis, but high loss to follow-up and those lost to follow-up had more previous psychiatric hospitalizations and were more likely to report a history of childhood abuse.	Unclear	Unclear if study protocol is available. No clinicaltrials.gov number provided, but reported all expected outcomes.	Unclear	1) 6 patients were eligible but not randomzed reason for not enolling notrepote 2) Power-analysis enrollment target not met. "However, the power analysis was based on an attempt rate much lower than that observed in this study."	Unclear	Unclear
Wagner 2006[22]	Computer-generated random-ization schedule.	Yes	No information provided.	Unclear	Described as double-blind and use of identically-appearing tablets. No information about blinding of outcome assessor.	Participants/ personnel: yes. Outcome assessor: unclear.	ITT using LOCF; attrition: overall=19%, numbers and reasons balanced across groups.	Yes	Protocol not available.	Unclear	No other concerns.	Yes	Unclear
Zisook 2011[25]	Web-based random-ization system (reference is from STAR*D).	Yes	Not described.	Unclear	Participants: only blind to second medication. Study personnel: not blinded.	Participants: no to first medication, yes to second medication. Study personnel: no.	ITT; attrition: acute phase=23%, continuation phase=12%; reasons for attrition not reported.	Unclear	Protocol available at clinicaltrials.gov, but explicit identification of specific scales planned to measure primary and secondary outcomes was lacking.	Unclear	2 of 4 suicide attempts occurred during the continuation phase; it is possible those who did not continue differed from those who did.	Unclear	Unclear

[a] This study was excluded due to the country in which it was conducted; it is included in this table as a background article for comparison and discussion purposes only.