**Appendix Table E12. Quality issues and risk of bias summary for pooled analyses of patient-level randomized clinical trial data on fibromyalgia subgroups**

| **Study** | **Pooled RCTs** | **Overall Risk of Bias Assessment** | **Rationale** |
| --- | --- | --- | --- |
| **Pharmacologic** (all) |  |  |  |
| **Duloxetine** |  |  |  |
| Bennett, 201224 | Chappell, 20083Russell, 20084Arnold, 20055Arnold, 20046 | RCT inputs: High Pooled: issues detailed in rationale | Pooled: No a priori hypothesis of direction of treatment effect in subgroups, outcome measure is subscale of common tool but subscale has not been formally validated, study power not discussed, no adjustments made for multiple comparisons and less stringent statistical criteria used to evaluate treatment-by-subgroup interaction, attrition not discussed despite high attrition in input RCTs, small sample size in certain subgroup strata (e.g., extreme obesity)Used optimal individual patient data (IPD) pooled analytic technique (Fischer et al. 2011)44 study blindinginput RCTs: High risk of bias (all 4 studies) |
| Bradley, 201025 | Chappell, 20083Russell, 20084Arnold, 20055Arnold, 20046 | RCT inputs: High Pooled: issues detailed in rationale | Pooled: No a priori hypothesis of direction of treatment effect in subgroups, study power not discussed, no adjustments for multiple comparisons and less stringent statistical criteria used to evaluate treatment-by-subgroup interactions, attrition not discussed despite high attrition in input RCTs, some selective reporting in results presentation, small sample size in certain subgroup strata (e.g., FIQ tiredness, mile group), different duloxetine doses combined analysis (with rationale)Used optimal individual patient data (IPD) pooled analytic technique (Fischer et al. 2011)44 study blindinginput RCTs: High risk of bias (all 4 studies) |
| Arnold, 200926 | Chappell, 20083Russell, 20084Arnold, 20055Arnold, 20046 | RCT inputs: High Pooled: issues detailed in rationale  | Pooled:No a priori hypothesis of direction of treatment effect in subgroups, study power not discussed, no adjustments for multiple comparisons and less stringent statistical criteria used to evaluate treatment-by-subgroup interactions, attrition not discussed despite high attrition in input RCTs, some selective reporting in results presentation, different duloxetine doses combined analysis (with rationale)Used optimal individual patient data (IPD) pooled analytic technique (Fischer et al. 2011)44 study blindinginput RCTs: High risk of bias (all 4 studies) |
| ***Milnacipran*** |  |  |  |
| Arnold, 201227 | Subgroup analysis:Arnold, 201028Mease, 200929Clauw, 200830 | RCT inputs: High Pooled: issues detailed in rationale  | Pooled:No a priori hypothesis of direction of treatment effect in subgroups, study power not discussed, no adjustments for multiple comparisons, attrition not discussed despite high attrition in input RCTs, unable to determine subgroup sample size within each treatment groupUsed optimal individual patient data (IPD) pooled analytic technique (Fischer et al. 2011)44 study blindinginput RCTs: High risk of bias (all 3 input studies) |
| Geisser, 201131 | Mease, 200929Clauw, 200830 | RCT inputs: High Pooled: issues detailed in rationale | Pooled:No a priori hypothesis of direction of treatment effect in subgroups, study power not discussed, no adjustments for multiple comparisons, attrition not discussed despite high attrition in input RCTs, unable to determine subgroup sample size, only patients classified as responders included in subgroup analysesUsed optimal individual patient data (IPD) pooled analytic technique (Fischer et al. 2011)44 study blindinginput RCTs: High risk of bias (both input studies) |
| ***Pregabalin*** |  |  |  |
| Arnold, 201032 | Arnold, 200833Mease, 200834Crofford, 200535 | RCT inputs: High Pooled: issues detailed in rationale | Pooled: No a priori hypothesis of direction of treatment effect in subgroups, study power not discussed, no adjustments made for multiple comparisons, outcome assessment timing varies by study, attrition not discussed despite high attrition in input RCTs, unable to determine effect of treatment in subgroups as reportedUsed optimal individual patient data (IPD) pooled analytic technique (Fischer et al. 2011)44 study blindinginput RCTs: High risk of bias (all) |
| Bhadra, 201036 | Arnold, 200833Mease, 200834Crofford, 200535Pauer, 200837 | RCT inputs: High Pooled: issues detailed in rationale | Pooled: No a priori hypothesis of direction of treatment effect in subgroups, study power not discussed, no adjustments made for multiple comparisons, outcome assessment timing varies by study, attrition not discussed despite high attrition in input RCTs, only those with given co-morbid medical condition are shown in results and not those withoutUsed optimal individual patient data (IPD) pooled analytic technique (Fischer et al. 2011)44, study blindinginput RCTs: High risk of bias (3 of 4 studies, 4th study unable to determine; Pauer et al. is an abstract only) |
| Byon, 201038 | Arnold, 200833Mease, 200834Crofford, 200535Pauer 200837 | RCT inputs: High Pooled: issues detailed in rationale | Pooled: No a priori hypothesis of direction of treatment effect in subgroups, study power not discussed, outcome assessment timing varies by study, attrition not discussed despite high attrition in input RCTs, insufficient information on actual (vs. predicted) clinical values to evaluate changes from baseline in subgroupsinput RCTs: High risk of bias (3 of 4 studies, 4th study unable to determine; Pauer et al. is an abstract only – unable to assess quality) |