**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, 20083  Russell, 20084  Arnold, 20055  Arnold, 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 blinding  input RCTs: High risk of bias (all 4 studies) |
| Bradley, 201025 | Chappell, 20083  Russell, 20084  Arnold, 20055  Arnold, 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 blinding  input RCTs: High risk of bias (all 4 studies) |
| Arnold, 200926 | Chappell, 20083  Russell, 20084  Arnold, 20055  Arnold, 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 blinding  input RCTs: High risk of bias (all 4 studies) |
| ***Milnacipran*** |  |  |  |
| Arnold, 201227 | Subgroup analysis:  Arnold, 201028  Mease, 200929  Clauw, 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 group  Used optimal individual patient data (IPD) pooled analytic technique (Fischer et al. 2011)44 study blinding  input RCTs: High risk of bias (all 3 input studies) |
| Geisser, 201131 | Mease, 200929  Clauw, 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 analyses  Used optimal individual patient data (IPD) pooled analytic technique (Fischer et al. 2011)44 study blinding  input RCTs: High risk of bias (both input studies) |
| ***Pregabalin*** |  |  |  |
| Arnold, 201032 | Arnold, 200833  Mease, 200834  Crofford, 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 reported  Used optimal individual patient data (IPD) pooled analytic technique (Fischer et al. 2011)44 study blinding  input RCTs: High risk of bias (all) |
| Bhadra, 201036 | Arnold, 200833  Mease, 200834  Crofford, 200535  Pauer, 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 without  Used optimal individual patient data (IPD) pooled analytic technique (Fischer et al. 2011)44, study blinding  input RCTs: High risk of bias (3 of 4 studies, 4th study unable to determine; Pauer et al. is an abstract only) |
| Byon, 201038 | Arnold, 200833  Mease, 200834  Crofford, 200535  Pauer 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 subgroups  input 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) |