**Additional file 6: GRADE appraisal of the certainty of the evidence**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Outcome** | **Estimate of effect (95% CI)** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Publication Bias** | **Evidence Certainty \*** |
| Cheng 2019 [1] | Fibromyalgia impact questionnaire 12-16 wks (4 RCTs) | SMD -0.61 (-0.90 to -0.31) | serious | not serious | not serious | not serious | not serious | MODERATE |
| FIQ 24-32 wks (2 RCTs) | SMD -0.49 (-1.56 to 0.58) | serious | serious | not serious | very serious | not serious | VERY LOW |
| Pain PROMs (3 RCTs) | SMD -0.88 (-1.58 to -0.18) | serious | serious | not serious | serious | not serious | VERY LOW |
| Choo 2020 [2] | QoL - physical PROMs (6 RCTs) | SMD 0.46 (0.13 to 0.80) | serious | not serious | not serious | not serious | not serious | MODERATE |
| QoL - mental health PROMs (6 RCTs) | SMD 0.21 (0.03 to 0.39) | serious | not serious | not serious | not serious | not serious | MODERATE |
|  | Depressive symptoms (5 RCTs) | SMD -0.42 (-0.84 to -0.01) | serious | serious | not serious | not serious | not serious | LOW |
|  | Time up and go (5 RCTs) | MD -0.2 (-0.66 to 0.26) | serious | not serious | not serious | not serious | not serious | MODERATE |
| Cui 2019 [3] | Serious adverse events - AE (TC vs active interventions) (15 RCTs) | RD 0.0 (-0.02 to 0.02) | not serious | not serious | not serious | very serious | not serious | LOW |
|  | Non-serious AE (TC vs active interventions) (15 RCTs) | RD 0.01 (-0.01 to 0.03) | not serious | not serious | not serious | serious | not serious | MODERATE |
|  | TC related AE (TC vs active interventions) (15 RCTs) | RD 0.0 (-0.01 to 0.02) | not serious | not serious | not serious | serious | not serious | MODERATE |
|  | Serious AE (TC vs inactive interventions) (9 RCTs) | RD -0.03 (-0.06 to 0.00) | not serious | not serious | not serious | serious | not serious | MODERATE |
|  | Non-serious AE (TC vs inactive interventions) (9 RCTs) | RD 0.03 (-0.00 to 0.07) | not serious | not serious | not serious | serious | not serious | MODERATE |
|  | TC related AE (TC vs inactive interventions) (9 RCTs) | RD 0.0 (-0.01 to 0.02) | not serious | not serious | not serious | serious | not serious | MODERATE |
| Gu 2017 [4] | 6-minute walk test (10 RCTs) | MD 51 (30.49 to 71.5) | very serious | serious | not serious | not serious | not serious | VERY LOW |
|  | Minnesota Living with Heart Failure Questionnaire - MLHFQ (8 RCTs) | MD -10.4 (-14.4 to -6.3) | very serious | serious | not serious | not serious | not serious | VERY LOW |
|  | Left ventricular ejection fraction (7 RCTs) | MD 7.7 (3.6 to 11.9) | very serious | serious | not serious | not serious | not serious | VERY LOW |
| Guo 2020 [5] | Forced expiratory volume in 1 second - FEV1 (3 RCTs) | MD 0.13 (0.06 to 0.20) | serious | not serious | not serious | not serious | not serious | MODERATE |
| FEV1 (5 RCTs) | MD 0.06 (-0.01 to 0.14) | serious | not serious | not serious | serious | not serious | LOW |
| 6-minute walk time - 6-MWT (TC vs control) (6 RCTs) | MD 24.3 (6.3 to 42.3) | serious | serious | not serious | not serious | not serious | LOW |
|  | 6MWT (TC vs exercise) (6 RCTs) | MD 7.5 (2.1 to 12.3) | serious | not serious | not serious | not serious | not serious | MODERATE |
|  | St George Respiratory Questionnaire - SGRQ (TC vs control) (3 RCTs) | MD -8.7 (-14.6 to -2.7) | serious | not serious | not serious | not serious | not serious | MODERATE |
|  | SGRQ (TC vs exercise) (4 RCTs) | MD -1.9 (-4.6 to 0.7) | serious | not serious | not serious | not serious | not serious | MODERATE |
| Hall 2017 [6] | Pain SF-36 15 wks (1 RCTs) | SMD -1.85 (-2.73 to -0.97) | very serious | not serious | not serious | very serious | not serious | VERY LOW |
| Hu 2020 [7] | Western Ontario and McMaster Universities Arthritis Index - WOMAC pain (14 RCTs) | SMD -0.69 (-0.95 to -0.44) | serious | not serious | not serious | not serious | not serious | MODERATE |
|  | WOMAC stiffness (12 RCTs) | SMD -0.65 (-0.98 to -0.33) | serious | serious | not serious | not serious | not serious | LOW |
|  | WOMAC physical function (13 RCTs) | SMD -0.92 (-1.16 to -0.69) | serious | not serious | not serious | not serious | not serious | MODERATE |
|  | QoL mental health, SF-36 (5 RCTs) | SMD 0.26 (0.06 to 0.45) | serious | not serious | not serious | not serious | not serious | MODERATE |
|  | QoL physical, SF-36 (5 RCTs) | SMD 0.48 (0.28 to 0.68) | serious | not serious | not serious | not serious | not serious | MODERATE |
|  | Arthritis self-efficacy scale (4 RCTs) | SMD 0.27 (0.06 to 0.48) | serious | not serious | not serious | not serious | not serious | MODERATE |
| Huang 2017 [8] | Rate of people who fell (no. of fallers) (16 RCTs) | RR 0.80 (0.72 to 0.88) | not serious | not serious | not serious | not serious | serious | MODERATE |
| Incidence of falls (no. falls) (15 RCTs) | RR 0.69 (0.60 to 0.80) | not serious | not serious | not serious | not serious | serious | MODERATE |
| Huang 2020 [9] | Single Leg Stance (8 RCTs) | MD 5.8 (0.62 to 10.90) | serious | very serious | not serious | not serious | not serious | VERY LOW |
| Berg balance scale (4 RCTs) | MD 1.0 (0.2 to 1.9) | serious | not serious | not serious | not serious | not serious | MODERATE |
|  | Time up and go (6 RCTs) | MD -0.71 (-0.88 to -0.54) | serious | not serious | not serious | not serious | not serious | MODERATE |
| Jiang 2018 [10] | VO2max (4 RCTs) | SMD 2.2 (0.81 to 3.63) | very serious | serious | not serious | not serious | not serious | VERY LOW |
| Kruisbrink 2020 [11] | Fear of falling (5 RCTs) | SMD -1.05 (-1.60 to -0.50) | very serious | serious | not serious | not serious | serious | VERY LOW |
| Luo 2020 [12] | Pain, 3 wks (2 RCTs) | SMD 0.25 (-0.02 to 0.51) | serious | not serious | not serious | serious | not serious | LOW |
| Pain, 12 wks (4 RCTs) | SMD 0.3 (0.08 to 0.51) | serious | not serious | not serious | not serious | not serious | MODERATE |
| Liu LZ 2020 [13] | Fatigue (TC vs control) 3 mths (2 RCTs) | MD -0.46 (-1.09 to 0.17) | serious | not serious | not serious | serious | not serious | LOW |
| Fatigue (TC vs control) 6 mths (2 RCTs) | MD -0.16 (-0.98 to 0.67) | serious | not serious | not serious | serious | not serious | LOW |
|  | Fatigue (TC+Ucare/Rehab vs Ucare/Rehab) 3 mths (2 RCTs) | SMD -0.91 (-1.30 to -0.53) | serious | not serious | not serious | serious | not serious | LOW |
| Lyu 2018 [15] | Activities of daily living - Barther Index (2 RCTs) | MD 9.9 (6.8 to 13.0) | serious | not serious | not serious | serious | not serious | LOW |
| Fugl-Meyer Assessment FMA - lower extremity (3 RCTs) | MD 2.8 (0.95 to 4.56) | serious | serious | not serious | serious | not serious | VERY LOW |
| FMA - upper extremity (2 RCTs) | MD 8.3 (4.7 to 11.8) | serious | not serious | not serious | serious | not serious | LOW |
|  | FMA - all four limb (2 RCTs) | MD 4.5 (1.9 to 7.1) | serious | not serious | not serious | serious | not serious | LOW |
|  | Berg Balance Scale (2 RCTs) | MD 5.2 (3.4 to 7.1) | serious | not serious | not serious | serious | not serious | LOW |
|  | Time up and go (4 RCTs) | MD 2.6 (1.8 to 3.4) | serious | not serious | not serious | serious | not serious | LOW |
| Lyu 2020 [16] | Depression (6 RCTs) | SMD 0.36 (0.10 to 0.61) | very serious | not serious | not serious | not serious | not serious | LOW |
| Mudano 2019 [17] | Pain, Visual Analog Scale, 12 wks (2 RCTs) | SMD -0.95 (-1.41 to -0.49) | very serious | not serious | not serious | very serious | not serious | VERY LOW |
| Disease activity, DAS-28-ESR, 12 wks (1 RCTs) | MD -0.40 (-1.10 to 0.30) | very serious | not serious | not serious | very serious | not serious | VERY LOW |
|  | Function, Health Assessment Questionnaire - HAQ, 12 wks (2 RCTs) | MD -0.33 (-0.79 to 0.12) | very serious | serious | not serious | very serious | not serious | VERY LOW |
| Ni 2019 [18] | QoL physical domain (9 RCTs) | SMD 0.34 (0.09 to 0.59) | very serious | not serious | not serious | not serious | not serious | LOW |
|  | QoL psychological Domain (9 RCTs) | SMD 0.60 (0.12 to 1.08) | very serious | serious | not serious | not serious | not serious | VERY LOW |
|  | QoL social relationship domain (8 RCTs) | SMD 0.26 (0.25 to 0.77) | very serious | serious | not serious | not serious | not serious | VERY LOW |
|  | Sleep quality (3 RCTs) | SMD 0.26 (-0.02 to 0.53) | very serious | serious | not serious | serious | not serious | VERY LOW |
| Pan 2016 [19] | Total Cholesterol (6 RCTs) | MD -7.7 (-17.3 to 1.4) | serious | serious | not serious | serious | not serious | VERY LOW |
| Triglycerides (6 RCTs) | MD -16.8 (-31.3 to -2.4) | serious | not serious | not serious | not serious | not serious | MODERATE |
| High-density lipoprotein cholesterol (5 RCTs) | MD 0.46 (-0.71 to 1.64) | serious | not serious | not serious | not serious | not serious | MODERATE |
|  | Low density lipoprotein cholesterol (4 RCTs) | MD -1.61 (-16.25 to 13.02) | serious | very serious | not serious | serious | not serious | VERY LOW |
| Qin 2019 [20] | Pain VAS 1-10 scale (TC vs control) (3 RCTs) | MD -1.2 (-2.3 to -1.1) | serious | serious | not serious | not serious | not serious | LOW |
| Pain VAS 1-10 scale (TC + usual care vs usual care) (5 RCTs) | MD -1.1 (-1.3 to -0.9) | serious | not serious | not serious | not serious | not serious | MODERATE |
| Si 2020 [21] | Pittsburgh Sleep Quality Index - PSQI, healthy (10 RCTs) | SMD -0.68 (-1.06 to -0.31) | serious | serious | not serious | not serious | not serious | LOW |
|  | PSQI, chronic disease (15 RCTs) | SMD -0.39 (-0.74 to -0.05) | serious | serious | not serious | not serious | not serious | LOW |
| Song 2018 [22] | Cancer related fatigue, lung cancer <8wks (2 RCTs) | SMD -0.5 (-0.83 to -0.18) | very serious | not serious | not serious | serious | not serious | VERY LOW |
| Cancer related fatigue, prostate cancer <8wks (1 RCTs) | SMD 0.01 (-0.51 to 0.52) | very serious | not serious | not serious | very serious | not serious | VERY LOW |
| Su 2020 [23] | knee extensor muscle strength (60°/sec) (2 RCTs) | MD 17.5 (-12.0 to 47.0) | serious | serious | not serious | very serious | not serious | VERY LOW |
|  | Knee flexor muscle strength (60°/sec) (2 RCTs) | MD 22.1 (1.1 to 43.2) | serious | not serious | not serious | very serious | not serious | VERY LOW |
|  | Knee flexor muscle strength 1-RM (2 RCTs) | MD 3.3 (2.1 to 4.4) | serious | not serious | not serious | serious | not serious | LOW |
|  | Knee extensor muscle strength 1-RM (4 RCTs) | MD 0.90 (0.34 to 1.45) | serious | not serious | not serious | not serious | not serious | MODERATE |
| Taylor-Piliae 2020 [24] | QoL mental health PROMs, hypertension (3 RCTs) | SMD 0.13 (NI) | not serious | not serious | not serious | serious | not serious | MODERATE |
| QoL physical PROMs, hypertensive (3 RCTs) | SMD 0.47 (NI) | not serious | not serious | not serious | not serious | not serious | HIGH |
|  | Psychological distress, chronic heart failure (2 RCTs) | SMD -0.58 (-0.95 to -0.22) | not serious | not serious | not serious | serious | not serious | MODERATE |
| Wang 2020 [25] | QoL general, PROMs (6 RCTs) | SMD 1.23 (0.56 to 1.89) | serious | serious | not serious | not serious | not serious | LOW |
| QoL physical, SF-36 (3 RCTs) | MD 5.9 (1.1 to 10.8) | serious | serious | not serious | not serious | not serious | LOW |
| QoL psychological, SF-36 (3 RCTs) | MD 2.2 (-1.2 to 5.6) | serious | not serious | not serious | serious | not serious | LOW |
| Wang 2010 [26] | Stress PROMs (4 RCTs) | SMD 0.97 (0.06 to 1.87) | very serious | very serious | not serious | not serious | not serious | VERY LOW |
| Mood / affect PROMs (2 RCTs) | SMD 0.25 (-0.04 to 0.53) | very serious | not serious | not serious | serious | not serious | VERY LOW |
| Wayne 2014 [27] | Executive function (Tai Chi vs inactive control) (4 RCTs) | SMD 0.90 (0.03 to 1.78) | not serious | serious | not serious | not serious | not serious | MODERATE |
| Executive function (TC vs excerise) (2 RCTs) | SMD 0.51 (0.17 to 0.85) | not serious | not serious | not serious | serious | not serious | MODERATE |
| Wang 2017 [28] | Physical function SF-36 (4 RCTs) | MD -1.8 (-5.2 to 1.6) | serious | not serious | not serious | serious | not serious | LOW |
| Bodily pain SF-36 (3 RCTs) | MD -3.6 (-6.6 to -0.6) | serious | not serious | not serious | not serious | not serious | MODERATE |
|  | General health SF-36 (3 RCTs) | MD -5.1 (-7.6 to -2.6) | serious | not serious | not serious | not serious | not serious | MODERATE |
|  | Vitality SF-36 (3 RCTs) | MD -5.7 (-8.5 to -2.8) | serious | not serious | not serious | not serious | not serious | MODERATE |
|  | Mental health SF-36 (4 RCTs) | MD -2.5 (-4.8 to -0.2) | serious | not serious | not serious | not serious | not serious | MODERATE |
|  | Social function SF-36 (3 RCTs) | MD -2.2 (-5.0 to 0.6) | serious | not serious | not serious | serious | not serious | LOW |
| Wu 2020 [29] | 6-minute walk time (5 RCTs) | SMD 1.3 (0.50 to 2.11) | serious | serious | not serious | not serious | not serious | LOW |
| Left ventricular ejection fraction (5 RCTs) | SMD 1.0 (0.43 to 1.57) | serious | serious | not serious | not serious | not serious | LOW |
| Xiang 2017 [30] | Fatigue PROMs (10 RCTs) | SMD -0.45 (-0.70 to -0.20) | serious | not serious | not serious | not serious | not serious | MODERATE |
| Vitality PROMs (4 RCTs) | SMD 0.63 (0.20 to 1.07) | very serious | not serious | not serious | not serious | not serious | LOW |
|  | Sleep PROMs (3 RCTs) | SMD -0.32 (-0.61 to -0.04) | very serious | not serious | not serious | not serious | not serious | LOW |
|  | Depression PROMs (7 RCTs) | SMD -0.58 (-1.04 to -0.11) | very serious | serious | not serious | not serious | not serious | VERY LOW |
| Yin 2014 [31] | Depression scales (25 RCTs) | SMD 0.36 (0.19 to 0.53) | not serious | not serious | not serious | not serious | not serious | HIGH |
| Anxiety scales (11 RCTs) | SMD 0.34 (0.02 to 0.66) | not serious | serious | not serious | not serious | not serious | MODERATE |
| Yu 2018 [32] | Unified Parkinson's Disease Rating III: Motor (8 RCTs) | MD -3.7 (-5.7 to -1.7) | not serious | serious | not serious | not serious | not serious | MODERATE |
| Time up and go (7 RCTs) | SMD -0.5 (-0.88 to -0.11) | not serious | not serious | not serious | not serious | not serious | HIGH |
| Berg balance scale (6 RCTs) | SMD 0.85 (0.44 to 1.27) | not serious | not serious | not serious | not serious | not serious | HIGH |
|  | Parkinson's Disease Questionnaire (3 RCTs) | SMD -0.75 (-1.45 to -0.04) | not serious | not serious | not serious | not serious | not serious | HIGH |
| Zhang 2019 [33] | Spine bone mineral density - BMD (6 RCTs) | MD 0.04 g/cm2 (0.02 to 0.06) | serious | not serious | not serious | not serious | not serious | MODERATE |
| Femur BMD (3 RCTs) | MD 0.04 g/cm2 (0.01 to 0.06) | serious | not serious | not serious | serious | not serious | LOW |
| Spine BMD (2 RCTs) | MD 0.16 g/cm2 (0.09 to 0.23) | serious | not serious | not serious | serious | not serious | LOW |
|  | Femur BMD (2 RCTs) | MD 0.16 g/cm2 (0.04 to 0.29) | serious | serious | not serious | serious | not serious | VERY LOW |
| Zhang 2020 [34] | Global cognitive function (5 RCTs) | MD 0.29 (-0.61 to 0.74) | not serious | not serious | not serious | not serious | not serious | HIGH |
| Memory - Delayed Recall Test (4 RCTs) | MD 0.37 (0.13 to 0.61) | not serious | not serious | not serious | not serious | not serious | HIGH |
| Performance - Digit Span Test (4 RCTs) | MD 0.03 (-0.16 to 0.22) | not serious | not serious | not serious | not serious | not serious | HIGH |
| Zheng 2015 [35] | Incidence of nonfatal stroke over 1 - 2 yrs (2 RCTs) | RR 0.11 (0.01 to 0.85) | serious | not serious | not serious | serious | not serious | LOW |
| Incidence of fatal stroke over 1 - 2 yrs (2 RCTs) | RR 0.33 (0.05 to 2.05) | serious | not serious | not serious | serious | not serious | LOW |
| Zheng 2016 [36] | Negative symptoms - Positive and Negative Syndrome Scale and Scale - PANSS (6 RCTs) | SMD -0.87 (-1.51 to -0.24) | serious | serious | not serious | not serious | not serious | LOW |
|  | Positive symptoms - PANSS (5 RCTs) | SMD -0.09 (-0.44 to 0.26) | serious | not serious | not serious | not serious | not serious | MODERATE |
|  | Discontinuation rate (4 RCTs) | RR 0.06 (0.23 to 1.40) | serious | not serious | not serious | very serious | not serious | VERY LOW |
| Zhou 2019 [37] | Glycosylated haemoglobin - HbA1c % (14 RCTs) | MD -0.88 (-1.45 to -0.31) | serious | serious | not serious | not serious | not serious | LOW |
| Systolic blood pressure (5 RCTs) | MD -10.0 mmHg (-15.8 to -4.3) | serious | not serious | not serious | not serious | not serious | MODERATE |
| Diastolic blood pressure (5 RCTs) | MD -4.9 mmHg (-8.2 to -1.5) | serious | not serious | not serious | not serious | not serious | MODERATE |
| QoL physical function (5 RCTs) | MD 7.1 (0.79 to 13.4) | serious | serious | not serious | not serious | not serious | LOW |
| QoL bodily pain (5 RCTs) | MD 4.3 (0.8 to 7.8) | serious | not serious | not serious | not serious | not serious | MODERATE |
| Zhong 2020 [38] | Systolic blood pressure - SBP (TC vs inactive control) (9 RCTs) | MD -14.8 (-19.6 to -10.0) | serious | serious | not serious | not serious | not serious | LOW |
| Diastolic blood pressure - DBP (TC vs inactive control) (9 RCTs) | MD -7.0 (-9.1 to -5.0) | serious | not serious | not serious | not serious | not serious | MODERATE |
| SBP (TC vs exercise) (5 RCTs) | MD -7.9 (-14.2 to -1.7) | serious | serious | not serious | not serious | not serious | LOW |
| DBP (TC vs exercise) (5 RCTs) | MD -3.9 (-6.5 to -1.2) | serious | not serious | not serious | not serious | not serious | MODERATE |
| SBP (medication) 15 RCTs) | MD -9.1 (-14.0 to -4.1) | serious | serious | not serious | not serious | not serious | LOW |
|  | DBP (medication) (15 RCTs) | MD -5.6 (-14.0 to -4.1) | serious | serious | not serious | not serious | not serious | LOW |

**TC:** Tai Chi; **RCTs:** Randomized controlled trials, **QoL:** Quality of Life

**\* GRADE RUBRIC**

**Risk of bias (RoB)**

**Overall assessment of RoB: Low RoB:** ≥75% RCTs were assessed as low RoB in all three categories - randomisation, assessor blinding, and missing data; OR if no information (NI) about the categories, ≥75% RCTs were rated overall as low RoB; **Moderate RoB:** ≥75% RCTs were assessed as low RoB in one or two categories - randomisation, assessor blinding, and missing data; OR if NI about categories, ≥75% RCTs were rated overall as moderate RoB; **High RoB:** <75% RCTs were assessed overall as low RoB in all three categories - randomisation, assessor blinding, and missing data; OR if NI about categories <75% RCTs were rated overall as low or moderate RoB.

Very serious: high RoB & no sensitivity analysis or the effect estimate is unstable with sensitivity analysis.

Serious: high RoB, however, the effect estimate stable with sensitivity analysis when high RoB of RCTs excluded or only low RoB RCTs included; OR moderate RoB & no sensitivity analysis or the effect estimate is unstable with sensitivity analysis.

Not serious: low RoB; OR moderate RoB, however, the effect estimate is stable with sensitivity analysis when only low RoB of RCTs included.

NOTE: cut-off of 75% and the most important RoB categories - randomisation, assessor blinding - were informed by algorithm developed by Pollock et al.[39]

**Inconsistency**

Very serious: very high heterogeneity (*I2* ≥90%) & mixed direction of results, +/- appreciable non-overlap in CIs (confirm with visual inspection of Forest plot) or NI.

Serious: considerable heterogeneity *I2*between 76% to 89%; OR I2>90%, however, all RCTs favour one direction & CIs mostly overlap & if subgroup/sensitivity analysis is indicated then reduces (*I2*≤ 75%) and estimate of effect is stable.

Not serious: no heterogeneity; OR acceptable heterogeneity (*I2*≤ 75%).

NOTE: heterogeneity cut off set at *I2* ≤ 75% as per algorithm developed by Pollock et al.[39]; subgroup analysis deemed unreliable or not indicated if <10 RCTs, and ‘one-out’ study sensitivity analysis unreliable if <6 RCTs.

**Indirectness**

NOTE: all estimates of effect were assessed as ‘not serious’ as all participants, interventions and outcomes were directly relevant to the research question.

**Imprecision**

**Optimum information size (OIS):** is met if trial sequential analysis conducted and information size is reached; otherwise for continuous data OIS is met if no. participants in meta-analysis ≥ 200; for relative/absolute risk OIS is met if >4,000 participants & no. events >100, alternatively calculate OIS (α = 0.05; β = 0.02; 25% RRR) or use Fig.4/5 in GRADE guidelines 5.2.4. to estimate OIS [40].

**Important benefit and harm included:** SMD ±0.5; MD ±minimal clinically important difference (MCID); OR/RR/HR <0.75 and >1.25; ARR treatment outcomes and non-serious AEs ±0.1; ARR serious AEs ±0.01

Very serious: no. participants in meta-analysis of continuous data <100; OR OIS is not met & 95%CI includes no effect and both important benefit and harm included

Serious: OIS is not met & 95% CI excludes no effect; OR OIS is met, however, 95% CI includes no effect & important benefit or harm included

Not serious: OIS is met & 95% CI excludes no effect; OR OIS is met, however, 95% CI includes no effect & important benefit and harm excluded.

NOTE: OIS cut offs of 100 and 200 for continuous data as per algorithm developed by Pollock et al.[39]

**Publication bias**

Serious: assessed as ‘strongly suspected’ based on funnel plot and/or statistical test; OR not assessed, however, assessed as ‘strongly suspected’ for another meta-analysis in the same systematic review; OR not assessed despite >10 studies in the meta-analysis and at least half of the studies have a sample size <100.

Not serious: not assessable <10 studies in the meta-analysis; OR assessed as not present or probably not present.

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