

1 Treating depression with physical activity in 2 adolescents and young adults: a systematic review 3 and meta-analysis of randomised controlled trials

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10 We aimed to establish the treatment effect of physical activity for depression in young people through meta-analysis.
11 Four databases were searched to September 2016 for randomised controlled trials of physical activity interventions
12 for adolescents and young adults, 12–25 years, experiencing a diagnosis or threshold symptoms of depression.
13 Random-effects meta-analysis was used to estimate the standardised mean difference (SMD) between physical activity
14 and control conditions. Subgroup analysis and meta-regression investigated potential treatment effect modifiers.
15 Acceptability was estimated using dropout. Trials were assessed against risk of bias domains and overall quality of
16 evidence was assessed using GRADE criteria. Seventeen trials were eligible and 16 provided data from 771 participants
17 showing a large effect of physical activity on depression symptoms compared to controls (SMD = -0.82, 95% CI = -1.02
18 to -0.61, $p < 0.05$, $I^2 = 38\%$). The effect remained robust in trials with clinical samples ($k = 5$, SMD = -0.72, 95% CI = -1.15
19 to -0.30), and in trials using attention/activity placebo controls ($k = 7$, SMD = -0.82, 95% CI = -1.05 to -0.59). Dropout
20 was 11% across physical activity arms and equivalent in controls ($k = 12$, RD = -0.01, 95% CI = -0.04 to 0.03, $p = 0.70$).
21 However, the quality of RCT-level evidence contributing to the primary analysis was downgraded two levels to LOW
22 (trial-level risk of bias, suspected publication bias), suggesting uncertainty in the size of effect and caution in its inter-
23 pretation. While physical activity appears to be a promising and acceptable intervention for adolescents and young
24 adults experiencing depression, robust clinical effectiveness trials that minimise risk of bias are required to increase confi-
25 dence in the current finding. The specific intervention characteristics required to improve depression remain unclear,
26 however best candidates given current evidence may include, but are not limited to, supervised, aerobic-based activity
27 of moderate-to-vigorous intensity, engaged in multiple times per week over eight or more weeks. Further research is
28 needed. (Registration: PROSPERO-CRD 42015024388).

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30 **Key words:** Adolescent, depression, exercise, meta-analysis, physical activity, randomised controlled trial, systematic
31 review, young adult.

32 Introduction

33 Depression affects an estimated one in five people over
34 the lifetime with most cases beginning during the ado-
35 lescent to young adult period (Kessler *et al.* 2005, 2007).
36 It is often a chronic and recurring condition (Wilson
37 *et al.* 2015) associated with high levels of psychological
38 distress, impairments in functioning and poor physical
39 health (Lewinsohn *et al.* 1998, 2003; Brent & Birmaher,
40 2002; Thapar *et al.* 2012), and is the leading contributor
41 to the global burden of disease in young people under
42 the age of 25 (Gore *et al.* 2011).

Established, guideline recommended treatments for 43
depression such as cognitive behavioural therapy 44
(CBT) and antidepressants (e.g., fluoxetine) are at 45
best only modestly effective (Weersing & Brent, 2006; 46
Weisz *et al.* 2006; Hetrick *et al.* 2012; Cipriani *et al.* 47
2016), with significant proportions of recipients either 48
non-responsive or continuing to experience symptoms 49
(Andrews *et al.* 2000; March *et al.* 2004; TADS Team, 50
2007). Alternative interventions are therefore indicated 51
to support full recovery, either as stand-alone or 52
adjunct treatment strategies. Lifestyle medicine is one 53
such alternative strategy increasingly implicated in 54
the management of mental ill-health, particularly the 55
use of physical activity to treat depression (Sarris 56
et al. 2014). 57

The mechanisms through which physical activity 58
exerts influence on depression are largely understudied, 59

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60 however they are likely complex and multifaceted,
 61 involving synergies of neurobiological and psychosocial
 62 factors. These may include processes that are both dis-
 63 rupted or dysregulated in depression and potentially
 64 modulated by physical activity including inflammatory
 65 and oxidative stress responses, neurogenesis, modula-
 66 tion of monoamines (e.g., serotonin), and HPA axis
 67 regulation, among others (see Deslandes *et al.* (2009);
 68 Wegner *et al.* (2014); Schuch *et al.* (2016a) for review).

69 In terms of proposed psychosocial processes, physical
 70 activity may have a general behavioural activation effect
 71 though activity scheduling and positive reinforcement,
 72 and may provide opportunities for mastery or achieve-
 73 ment, thus improving self-efficacy. It may also afford
 74 opportunities for social interaction and potentially pro-
 75 vide distraction from negative thoughts, mood states
 76 or ruminative cognitions (Salmon, 2001; Craft & Perna,
 77 2004; Veale, 2008).

78 Recent meta-analytic reviews of adult trials have
 79 demonstrated that physical activity interventions can
 80 reduce depression symptoms, with moderate to large
 81 effects (Cooney *et al.* 2013; Stubbs *et al.* 2016a; Kvam
 82 *et al.* 2016; Schuch *et al.* 2016b). Meta-analyses of
 83 child and adolescent trials have identified small to
 84 moderate effects on mental health outcomes, including
 85 reducing depression (Larun *et al.* 2006; Brown *et al.*
 86 2013; Carter *et al.* 2016). However, these analyses
 87 have relied upon trials where physical activity was deliv-
 88 ered either to healthy samples, samples with primary
 89 conditions other than depression (e.g., anxiety, obesity,
 90 autism), or to children (under 12 years). The efficacy of
 91 physical activity for young people (aged 12–25) who
 92 are experiencing depression, particularly at clinical
 93 levels, is yet to be established.

94 We performed a meta-analysis on all available
 95 randomised controlled trials (RCT) where physical
 96 activity was delivered as an intervention to partici-
 97 pants aged 12–25 years, experiencing a diagnosis or
 98 symptoms of depression. The primary aim was to esti-
 99 mate the effect of physical activity on depression
 100 symptoms, with secondary aims to examine interven-
 101 tion acceptability using dropout as a proxy, and
 102 whether trial-level characteristics such as age group,
 103 diagnostic status, depression severity, clinical *v.* non-
 104 clinical samples and type of control group, modified
 105 the treatment effect. We also aimed to investigate the
 106 effect of different physical activity intervention charac-
 107 teristics on depression symptoms.

108 Method

109 The methods described in the Cochrane Handbook of
 110 Systematic Reviews (Higgins & Green, 2011a) were used
 111 and reporting is according to the PRISMA guidelines

(Moher *et al.* 2009, 2015). The review was prospectively
 registered with PROSPERO (CRD42015024388).

Trial eligibility criteria

Types of studies

RCTs were eligible. Only published, peer-reviewed
 English-language trials were considered.

Types of participants

Trials recruiting adolescents and/or young adults
 (mean age ≥ 12 and < 26 years) experiencing depres-
 sion as determined by (a) meeting diagnostic criteria
 according to established nosology or (b) an explicitly
 stated minimum threshold (defined by trial authors)
 on a self-report or observer-rated symptom measure
 indicating presence of depression symptoms. Trials
 that recruited participants without depression or
 where depression was secondary to another disorder
 or health condition were excluded.

Types of interventions

All physical activity interventions were eligible. We
 used the American College of Sports Medicine defini-
 tion of physical activity, which is 'any bodily move-
 ment produced by skeletal muscles that results in
 energy expenditure above resting levels' (Garber *et al.*
 2011).

Types of control/comparison groups

Control groups included no-treatment (NT), wait-list
 (WL) and attention/activity placebo (AP) conditions.
 AP was defined as a condition that could reasonably
 be considered to control for non-specific intervention
 group factors and was not an established treatment
 for depression (Lindheimer *et al.* 2015). Comparison
 treatments could include psychological therapy,
 medication and treatment as usual (TAU).

Outcome measures

The primary outcome was depression symptoms as
 assessed with a validated symptom scale at the post-
 intervention time-point. Where a trial reported more
 than one depression outcome, the following hierarchy
 was used: (1) Observer-rated depression, (2) Self-report
 depression.

Search strategy

Electronic database searches were conducted for the
 period January 1980 to September 2016 using
 PsycINFO, Medline, Embase and the Cochrane
 Central Register of Controlled Trials. Search terms for

157 depression, physical activity/exercise and controlled
 158 trials are available in Supplementary Material. This
 159 strategy was supplemented by an ancestry search of
 160 the included trials and recently published systematic
 161 reviews (Larun *et al.* 2006; Rethorst *et al.* 2009; Brown
 162 *et al.* 2013; Cooney *et al.* 2013; Rosenbaum *et al.* 2014;
 163 Wegner *et al.* 2014; Nyström *et al.* 2015). A two-stage
 164 screening process was conducted using the eligibility
 165 criteria defined above. One author conducted first
 166 stage screening based on title and abstract. A second
 167 author screened 10% of these references to ensure
 168 consistency. Independent second stage screening was
 169 conducted on the full-text of all references identified
 170 in the first stage. Discrepancies were resolved by dis-
 171 cussion of full-text.

172 *Data extraction*

173 Data were extracted using a previously piloted, stan-
 174 dardised extraction template and targets included sam-
 175 ple, intervention (e.g., type, frequency, duration and
 176 intensity of physical activity) and control/comparison
 177 group characteristics, and outcome data at post-
 178 intervention and follow-up. Where outcome data
 179 were reported in graphical format, trial authors were
 180 contacted requesting numeric data. Where it could
 181 not be obtained, the WebPlotDigitizer application
 182 (Rohatgi, 2013; Tsafnat *et al.* 2014) was used to convert
 183 graphical to numeric data. This process was used to
 184 reduce potential bias in the meta-analysis if these trials
 185 were excluded (Higgins & Green, 2011a; Vučić *et al.*
 186 2015). A second author independently extracted
 187 outcome data for meta-analysis. Discrepancies were
 188 discussed and checked against the trial publication.

189 *Risk of bias and GRADE*

190 Bias within trials was assessed using the Cochrane
 191 Collaboration's risk of bias tool (Higgins *et al.* 2011b).
 192 We examined selection bias (random sequence
 193 generation, allocation concealment), performance bias
 194 (blinding of participant and personnel), detection
 195 bias (outcome assessor blinding), attrition bias (hand-
 196 ling of incomplete outcome data), and other bias
 197 including baseline imbalance on the primary outcome
 198 and selective reporting. Risk of bias assessments were
 199 rated independently by two authors. Discrepancies
 200 were resolved in consultation with a third author.
 201 The GRADE criteria were used to rate overall quality
 202 of the evidence contributing to the primary
 203 meta-analysis (Balshem *et al.* 2011; Schünemann *et al.*
 204 2013). GRADE criteria included limitations of study
 205 design (risk of bias across trials), indirectness of evi-
 206 dence, inconsistency of results, imprecision of results
 207 and probability of significant publication bias.

Data analysis

209 The primary outcome was depression symptoms at
 210 post-intervention. Data were entered in RevMan®
 211 (The Cochrane Collaboration, 2014) as mean, standard
 212 deviation and number of participants for both inter-
 213 vention and control groups, and pooled for
 214 meta-analysis using a random-effects model due to
 215 expected between-trial heterogeneity (as trials likely
 216 employed different physical activity interventions).
 217 The effect was estimated as standardised mean differ-
 218 ence (SMD) using Hedges' *g* (adjusted for small sample
 219 size bias) with 95% Confidence Intervals (CI) to allow
 220 pooling of data from different depression symptom
 221 scales. The magnitude of estimated SMD was
 222 categorised as small (0.2), medium (0.5) or large (0.8)
 223 (Cohen, 1988). Heterogeneity was assessed using
 224 standard I^2 statistic parameters (Higgins *et al.* 2011a).
 225 Publication bias was assessed by funnel plot inspec-
 226 tion, use of the trim-and-fill method to adjust the
 227 pooled effect (Duval & Tweedie, 2000) and estimation
 228 of the fail-safe *N* (Rosenthal, 1979).

229 Sensitivity analyses were based on the primary
 230 meta-analysis and targets included risk of bias
 231 domains (sequence generation, allocation concealment,
 232 outcome assessor blinding and incomplete outcome
 233 data were selected as these have been shown to bias
 234 effect estimates towards the intervention (Schulz *et al.*
 235 1995; Wood *et al.* 2008; Bell *et al.* 2013)), source of
 236 depression symptom rating, and review-level decisions
 237 including pooling of activity arms and inclusion of
 238 potentially heterogeneous forms of activity interven-
 239 tion or control.

240 The secondary outcome was intervention acceptabil-
 241 ity, which was assessed using dropout rates. Where
 242 dropout and missing data could not be distinguished,
 243 missing data at post-treatment was used. These data
 244 were pooled for meta-analysis and the risk difference
 245 (RD) with 95% CI was estimated using the Mantel-
 246 Haenszel method with random-effects.

247 Observational subgroup analysis was used to inves-
 248 tigate whether the effect of physical activity on depres-
 249 sion was modified by certain factors. Pre-specified
 250 targets for subgrouping were type of control group
 251 (WL/NT *v.* AP), trial sample characteristics including
 252 age group (<18 *v.* ≥18 years), depression severity
 253 (mild, moderate, severe), diagnostic criteria (diagnosis
 254 *v.* threshold symptoms), sample recruitment (clinical
 255 *v.* non-clinical) and physical activity intervention
 256 characteristics including intensity (light, moderate,
 257 vigorous) and activity type (aerobic *v.* resistance).
 258 Meta-regression was used to examine whether con-
 259 tinuous variables (mean age and mean baseline
 260 depression symptom severity) were associated with
 261 effect size.

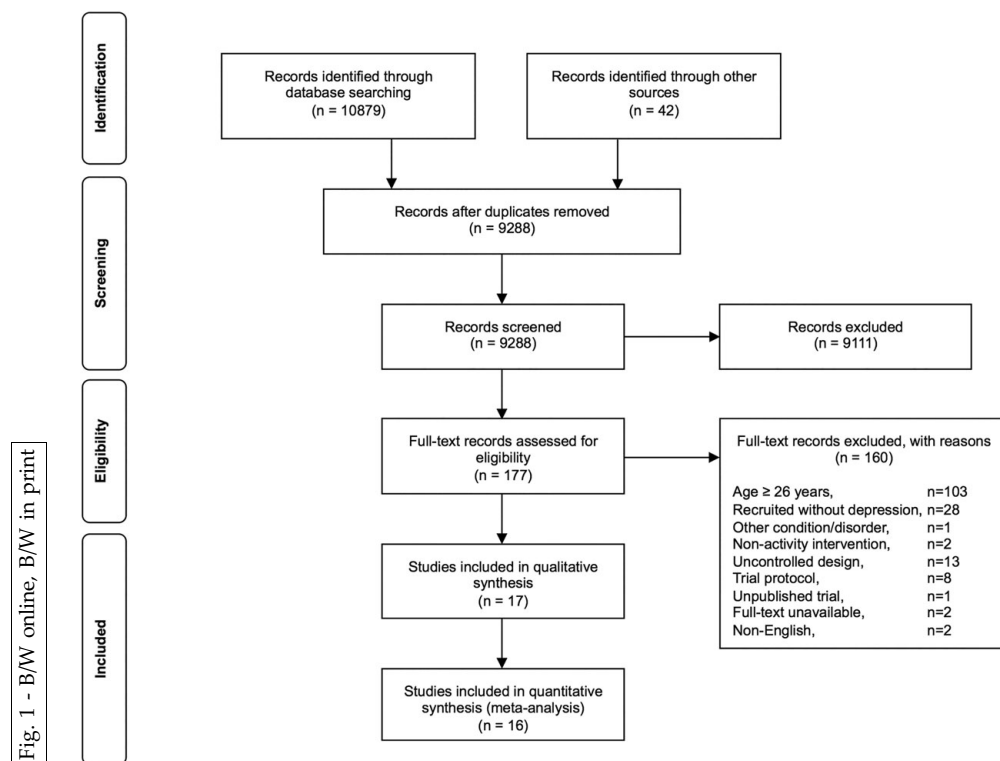


Fig. 1. PRISMA flow diagram of studies retrieved and screened.

262 **Unit of analysis issues**

263 Where a trial used a cross-over design, outcome from
 264 the first phase prior to cross-over was selected.
 265 Where a trial reported more than one physical activity
 266 arm compared with a control condition, the physical
 267 activity arms were pooled. This was done to avoid
 268 data loss and potential unit of analysis problems
 269 (Higgins *et al.* 2011a). Where a trial utilised more
 270 than one control arm (e.g., WL and AP), the more
 271 rigorous control was selected (see Lindheimer *et al.*
 272 2015). These approaches were taken to ensure the
 273 treatment effect was not inflated.

274 **Results**

275 We retrieved 9288 unique publications (see Fig. 1), of
 276 which 17 trials were eligible for inclusion (McCann &
 277 Holmes, 1984; Woolery *et al.* 2004; Jeong *et al.* 2005;
 278 Nabkasorn *et al.* 2006; Yavari, 2008; Chu *et al.* 2009;
 279 Mohammadi, 2011; Roshan *et al.* 2011; Hemat-Far
 280 *et al.* 2012; Moghaddam *et al.* 2012; Hughes *et al.*
 281 2013; Noorbakhsh & Alijani, 2013; Legrand, 2014;
 282 Carter *et al.* 2015; Cecchini-Estrada *et al.* 2015; Balchin
 283 *et al.* 2016; Sadeghi *et al.* 2016). Of these, 16 trials pro-
 284 vided data for the primary meta-analysis. The charac-
 285 teristics of the included trials are presented in Table 1
 286 and briefly summarised below.

Characteristics of included trials**Participants**

287
 288
 289 Trial sample sizes ranged from 20 to 106 participants
 290 (median = 47, IQR = 41). Mean age ranged from 15.4
 291 to 25.8 years. Eight trials were conducted with female
 292 participants only. Five trials recruited clinical samples
 293 (from inpatient/outpatient treatment services or having
 294 a clinician confirmed diagnosis) and 12 trials recruited
 295 non-clinical samples. Most trials recruited participants
 296 with elevated depression symptoms above a specified
 297 threshold (n = 13), while four used a clinician con-
 298 firmed diagnosis of depression. Baseline depression
 299 severity ranged from mild (n = 4) to moderate (n = 10)
 300 to severe (n = 2) (see Supplementary Material for
 301 categories). Ten trials recruited an inactive sample,
 302 while seven did not report baseline activity level.

Interventions and controls

303
 304 The characteristics of the physical activity interven-
 305 tions delivered in each trial are summarised in
 306 Table 2. Most trials used aerobic-based physical activ-
 307 ity (n = 12), and there was considerable variation in the
 308 type of activity. The intensity of activity was estimated
 309 by converting reported activity type or intensity into
 310 metabolic equivalents (METs) (Norton *et al.* 2010;
 311 Ainsworth *et al.* 2011). Most trials involved moderate

Table 1. Included trial characteristics

Trial ID	Country	N	Age, mean (range)	Gender, % female	Recruitment setting	Depression inclusion criteria	Baseline depression severity	Baseline activity threshold for inclusion	Depression outcome measures
Balchin <i>et al.</i> (2016)	South Africa	33	25.4 (18–42)	0	University	Elevated symptoms, HAM-D ≥ 14 , ≤ 18	Moderate, HAM-D = 16.5	No prior high-intensity exercise (<70% HRR 3/wk)	Observer-rated: HAM-D, MADRS
Carter <i>et al.</i> (2015)	UK	87	15.4 (14–17)	78	Community clinic referral	Elevated symptoms, CDI-2 > 14	Severe*, CDI-2 = 28.7	60% insufficiently active	Self-report: CDI-2
Cecchini-Estrada <i>et al.</i> (2015)	Spain	106	19.6 (18–30)	64	University	Elevated symptoms, 6-item depression scale ≥ 29	Moderate*, score = 30.73	Sedentary (<20 min vigorous activity 3/wk)	Self-report: 6-item depression scale
Chu <i>et al.</i> (2009)	USA	54	25.8 (18–43)	100	University	Elevated symptoms, BDI ≥ 14	Moderate, BDI = 22.5	Sedentary (<20 min exercise 3/wk)	Self-report: BDI
Hemat-Far <i>et al.</i> (2012)	Iran	20	– (18–25)	100	University	Diagnosis, psychiatry review/BDI	Moderate, BDI = 24.4	No sports history	Self-report: BDI
Hughes <i>et al.</i> (2013)	USA	30	17 (12–18)	58	Outpatient clinic referral	Diagnosis, DSM. CDRS-R ≥ 35 , ≤ 70	Moderate*, CDRS-R = 52.1	No current exercise (<30 min vigorous activity 5/wk)	Self-report: QIDS-A-SR Observer-rated: CDRS-R, QIDS-A-C17
Jeong <i>et al.</i> (2005)	Korea	40	16 (–)	100	High-school	Elevated symptoms, BDI = mild depression	Mild*, –	No regular exercise in past 6 months	Self-report: SCL-90-R, depression subscale
Legrand (2014)	France	44	– (19–30)	100	Low SES housing project	Elevated symptoms, BDI ≥ 14	Moderate, BDI = 19.5	Not physically active (<30 min moderate activity 2/wk)	Self-report: BDI
McCann & Holmes (1984)	USA	47	Student, university	100	University	Elevated symptoms, BDI > 11	Mild, BDI = 15.35	–	Self-report: BDI
Moghaddam <i>et al.</i> (2012)	Iran	60	Student, high-school	0	High-school	Elevated symptoms, BDI = ‘moderate to deep depression’	–	–	Self-report: BDI
Mohammadi (2011)	Iran	100	Student, high-school	–	High-school	Elevated symptoms, BDI = ‘borderline to severe depression’	Moderate, BDI = 20.46	No regular exercise or sport activities	Self-report: BDI
Nabkasorn <i>et al.</i> (2006)	Thailand	59	– (18–20)	100	University	Elevated symptoms, CES-D ≥ 16	Mild, CES-D = 19.4	No regular vigorous sports activity in past 6 months	Self-report: CES-D
Noorbakhsh & Alijani (2013)	Iran	75	18.8 (18–20)	100	University	Elevated symptoms, BDI = ‘mild-to-moderate depression’	Moderate, BDI = 19.8	–	Self-report: BDI

Table 1 (cont.)

Trial ID	Country	N	Age, mean (range)	Gender, % female	Recruitment setting	Depression inclusion criteria	Baseline depression severity	Baseline activity threshold for inclusion	Depression outcome measures
Roshan <i>et al.</i> (2011)	Iran	24	16.9 (15–18)	100	High-school	Diagnosis, DSM. HAM-D ≥ 18	Severe, HAM-D=29.9	-	Observer-rated: HAM-D
Sadeghi <i>et al.</i> (2016)	Iran	46	21 (18–25)	22	University counselling centre	Diagnosis, DSM. BDI ≥ 13 , ≤ 28	Moderate, BDI=22.8	-	Self-report: BDI
Woolery <i>et al.</i> (2004)	USA	28	21.5 (18–29)	79	University	Elevated symptoms, BDI ≥ 10 , ≤ 15	Mild, BDI=12.4	Not practicing yoga	Self-report: BDI
Yavari (2008)	Iran	74	-(19–22)	0	University	Elevated symptoms, BDI > 19	Moderate, BDI=24.2	-	Self-report: BDI

BDI, Beck Depression Inventory; CDI-2, Children's Depression Inventory-2; CES-D, Centre for Epidemiological Studies Depression scale; CDRS-R, Childs Depression Rating Scale - Revised; DSM, Diagnostic & Statistical Manual of Mental Disorders; HAM-D, Hamilton Depression Rating Scale; N, total participants randomised; QIDS-A-C17, Quick Inventory of Depression Symptomatology - Adolescent - Clinician Rated; QIDS-A-SR, Quick Inventory of Depression Symptomatology - Adolescent - Self-report; *, author reported severity category; -, not-reported or unclear.

(3–6METs, $n=6$) to vigorous activity (>6 METs, $n=4$). All trials prescribed either the type or intensity of activity, although four incorporated participant preference. Intervention periods ranged from 5 to 12 weeks (median = 8, IQR = 4) with one to five activity sessions per week (median = 3, IQR = 1). Session duration ranged from 30 to 90 min (median = 60, IQR = 15). Most trials used supervised activity sessions ($n=11$), with seven using trained and qualified professionals. Eight trials implemented interventions in group settings, one of which combined group and individual components. Three additional trials were done with individuals. Control groups were no-treatment (NT, $n=5$), wait-list (WL, $n=5$), and attention/activity placebo (AP, $n=7$). Placebo conditions consisted of stretching/flexibility ($n=3$), relaxation ($n=1$), a physical education class ($n=1$), very light activity ($n=1$) and an unguided group meeting ($n=1$). Eight trials had multiple intervention arms. Six contained two or more physical activity arms *v.* control. These multiple activity arms were collapsed within trials for the primary meta-analysis (Chu *et al.* 2009; Mohammadi, 2011; Noorbakhsh & Alijani, 2013; Cecchini-Estrada *et al.* 2015; Balchin *et al.* 2016). One trial was physical activity *v.* AP *v.* WL and the comparison against AP was selected for meta-analysis (McCann & Holmes, 1984). One trial was physical activity *v.* CBT *v.* control and another trial added physical activity to TAU compared with TAU alone. No trials were identified comparing physical activity to medication.

Outcomes

Fifteen trials used self-report measures, most commonly the Beck Depression Inventory (BDI) ($n=9$), and three reported observer-rated depression symptom measures.

Risk of bias

Risk of bias assessments within and across trials is displayed in Fig. 2a and b. Generation of the randomisation sequence was adequate in only five trials. Four trials adequately concealed allocation. Blinding of intervention personnel and participants to group allocation cannot be adequately achieved in physical activity trials. Blinding of outcome assessor cannot be achieved for self-report outcome measures. Two of three trials using an observer-rated outcome measure masked assessors to group allocation. Six trials were rated as low risk of bias for handling of incomplete post-treatment data. Baseline imbalance on the primary outcome was not detected in 15 trials. Protocols were identified for only three trials resulting in a low risk of bias rating for selective reporting. Overall, selection bias could not be ruled out in 88% of trials, performance bias was likely present in 100% of trials,

Table 2. Characteristics of physical activity interventions from included trials

Trial ID	Physical activity arms and content	Setting	Aerobic/ resistance	Duration (weeks)	Session (min)	Sessions per week	Intensity (MET)*	Activity protocol adherence	Control arm
Balchin <i>et al.</i> (2016)	1. High Intensity: stationary cycling @ 70–75% HR reserve 2. Moderate intensity: stationary cycling @ 45–50% HR reserve	S – I	Aerobic	6	60	3	1. Vig (6–9) 2. Mod (3–6)	64% completed all sessions	1. AP = walking/very light cycling control
Carter <i>et al.</i> (2015)	1. TAU + preferred intensity circuit training: strength + aerobic exercise	S Q G	Mixed	6	60	2	–	Ave. sessions attended = 66%	1. TAU = psychological therapy/medication
Cecchini-Estrada <i>et al.</i> (2015)	1. Physical activity program with motivation enhancement 2. Physical activity program without motivation enhancement 3. Physical activity done individually	S Q G – U – I	–	8	60	3	–	100% completed ≥ 22 of 24 sessions	1. AP = stretching, flexibility control
Chu <i>et al.</i> (2009)	1a. High intensity: treadmill exercise @ 65–75% MaxVO ₂ reserve 1b. +exercise in own time @ 65–75% MaxVO ₂ reserve (EEG = 1000 kcal/wk) 2a. Low intensity: treadmill exercise @ 40–55% MaxVO ₂ reserve 2b. +exercise in own time @ 40–55% MaxVO ₂ reserve (EEG = 1000 kcal/wk)	S – I U S U	Aerobic	10	30–40	1 – 1 – 3–4	1. Vig (6–9) 2. Mod (3–6)	Ave. sessions attended: 1. 87% 2. 77%	1. AP = stretching control
Hemat-Far <i>et al.</i> (2012)	1. Running, 3 × 6–13 min sets @ 60–65% HR max, 3 min rest between sets	S – –	Aerobic	8	40–60	3	Mod (3–6)	–	1. NT = no physical activity control
Hughes <i>et al.</i> (2013)	1a. Treadmill/stationary bike exercises @ 1/4 to 1/3 of EEG 1b. +exercise in own time @ 1/4 to 1/3 of EEG (=12 kcal/kg/week)	S Q I U	Aerobic –	12	30–40	1 – 2–3	Mod (3–6)	Ave. adherence to EEG = 77%	1. AP = stretching control

Table 2 (cont.)

Trial ID	Physical activity arms and content	Setting	Aerobic/ resistance	Duration (weeks)	Session (min)	Sessions per week	Intensity (MET)*	Activity protocol adherence	Control arm
Jeong <i>et al.</i> (2005)	1. Dance movement therapy	- - - -		12	45	3	-	-	1. WL
Legrand (2014)	1. Jogging @ 65–80% HR max + zumba dance class + calisthenics	S Q G	Mixed	7	60	2	Vig (6–9)	68% attended all sessions	1. WL
McCann & Holmes (1984)	1a. Aerobics class = dance, jogging, running 1b. +exercise in own time	S - G U I	Aerobic	10	60	2	-	-	1. AP = relaxation control; 2. WL
Moghaddam <i>et al.</i> (2012)	1. Swimming 2. Football 3. Athletics	- - -	Aerobic	12	90	2	-	-	1. NT
Mohammadi (2011)	1. Team sport (soccer or volleyball) 2. Individual sport (table tennis or badminton)	- - G I	Aerobic	8	75	3	-	-	1. NT = prevented from doing sports
Nabkasorn <i>et al.</i> (2006)	1. Self-paced jogging @ <50% maximal HR reserve	S Q G	Aerobic	8	50	5	Mod (3–6)	Ave. sessions attended = 78%	1. WL = daily activity monitoring
Noorbakhsh & Alijani (2013)	1. Aerobics 2. Swimming	- - -	Aerobic	6	60	3	-	-	1. AP = phys. ed. class control
Roshan <i>et al.</i> (2011)	1. Pool walking exercise @ 60– 70% HR max	S - G	Aerobic	6	-	3	Mod (3–6)	-	1. NT = no exercise control
Sadeghi <i>et al.</i> (2016)	1. Aerobic exercise @ 60–80% HR reserve	S Q -	Aerobic	8	45–60	3	Vig (6–9)	-	1. AP = unguided group meeting control; 2. CBT
Woolery <i>et al.</i> (2004)	1. Iyengar yoga classes (Hatha yoga)	S Q G	Resistance	5	60	2	Light (2.5)	-	1. WL = no yoga control, maintain routine activity
Yavari (2008)	1. Swimming	- - -	Aerobic	12–15	-	1	-	-	1. NT = no swimming control

Supervised (S) or unsupervised (U), qualified instructor (Q), group (G) or individual (I); EEG, energy expenditure goal; AP, attention/activity placebo; NT, no-treatment control; WL, wait-list control; TAU, treatment as usual; HR, heart rate; MaxVO₂, maximal oxygen uptake; *MET, metabolic equivalent estimate (based on Ainsworth *et al.* 2011 and Norton *et al.* 2010); (Ainsworth). -, not reported or unclear.

(a)

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants (performance bias)	Blinding of personnel (performance bias, interventionist)	Blinding of outcome assessment (detection bias, primary outcome)	Incomplete outcome data (attrition bias, primary outcome)	Selective reporting (reporting bias)	Baseline imbalance (primary outcome)
Balchin 2016	+	?	-	-	+	-	?	+
Carter 2015	+	+	-	-	-	?	+	+
Cecchini-Estrada 2015	?	+	-	-	-	+	?	+
Chu 2009	+	?	-	-	-	-	?	+
Hemat-Far 2012	?	?	-	-	-	?	?	+
Hughes 2013	+	+	-	-	+	+	+	+
Jeong 2005	?	+	-	-	-	+	-	-
Legrand 2014	+	?	-	-	-	-	?	+
McCann 1984	?	?	-	-	-	+	?	+
Moghaddam 2012	?	?	-	-	-	?	-	?
Mohammadi 2011	?	?	-	-	-	+	?	+
Nabkasorn 2006	?	?	-	-	-	-	?	+
Noorbakhsh 2013	?	?	-	-	-	+	?	+
Roshan 2011	?	?	-	-	?	?	?	+
Sadeghi 2016	?	?	-	-	-	?	+	+
Woolery 2004	?	?	-	-	-	-	?	+
Yavari 2008	?	?	-	-	-	?	?	+

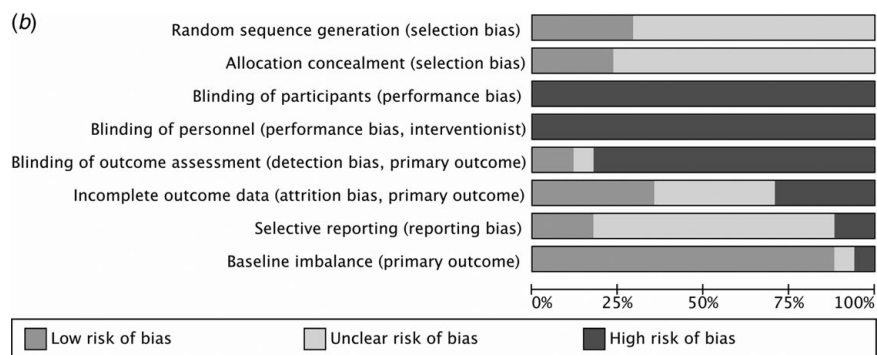


Fig. 2 - B/W online, B/W in print

Fig. 2. (a) Risk of bias ratings. (b) Risk of bias graph: percentage of trials receiving low, unclear or high risk of bias rating for each domain.

364 detection bias was present or could not be ruled out in
 365 88% of trials and attrition bias was present or could not
 366 ruled out in 59% of trials.

367 *Intervention adherence*

368 Seven trials reported intervention adherence or attend-
 369 ance data. Three reported that on average 66% to 87%
 370 of intervention sessions were attended, one reported
 371 an average energy expenditure target adherence of
 372 77%, two reported that 64% and 68% of participants
 373 completed all activity sessions and one trial reported
 374 that all participants attended at least 22 of 24 sessions.

375 *Imputation of trial outcome data*

376 Two trials reported graphical outcome data which we
 377 converted to numerical format as described above
 378 (McCann & Holmes, 1984; Nabkasorn et al. 2006). One
 379 trial did not report an estimate of variability (McCann
 380 & Holmes, 1984), therefore we imputed the missing
 381 standard deviation with an estimate pooled[†] from
 382 the eight included trials that had used the same out-
 383 come measure (BDI) at post-intervention, based on the
 384 recommendations by Furukawa et al. (2006) and in the
 385 Cochrane Handbook (Higgins et al. 2011a). One trial
 386 did not report extractable outcome data and is therefore
 387 not included in meta-analysis (Moghaddam et al. 2012).

388 *Meta-analysis results*

389 The primary meta-analysis pooled 16 trials ($n=771$)
 390 testing the effect of physical activity on depression
 391 symptoms at post-intervention compared with a con-
 392 trol condition (Fig. 3), finding a large effect in favour
 393 of physical activity (SMD = -0.82, 95% CI = -1.02, to
 394 -0.61, $p < 0.05$, $I^2 = 38\%$).

395 *Publication bias*

396 Estimation of the fail-safe N suggests that 430 trials
 397 with no effect would be needed before the pooled
 398 effect was no longer statistically significant. The
 399 fill-and-trim analysis suggests four trials may be miss-
 400 ing from the right side of the funnel plot (see
 401 Supplementary Material Fig. S2). Imputing these miss-
 402 ing trials produced an adjusted pooled effect in favour
 403 of physical activity of -0.69 (95% CI = -0.90 to -0.48).

404 *Sensitivity analysis (Table 3)*

405 We were unable to conduct a sensitivity analysis
 406 restricted to better quality trials as there were not
 407 enough available trials at low risk of bias across all
 408 or most domains of bias. Therefore we conducted

four separate sensitivity analyses excluding trials that
 were rated as either unclear or high risk of bias for
 sequence generation, allocation concealment, outcome
 assessor blinding and incomplete outcome data. The
 pooled effect remained in favour of physical activity
 for trials at low risk of bias for sequence generation
 ($k=5$, SMD = -0.63, 95% CI = -0.97 to -0.29), for
 blinding of outcome assessor ($k=2$, SMD = -0.90,
 95% CI = -1.47 to -0.32) and for incomplete outcome
 data ($k=6$, SMD = -0.72, 95% CI = -1.03 to -0.40),
 but not for allocation concealment ($k=4$, SMD =
 -0.48, 95% CI = -1.02 to 0.05). When multiple activity
 and control arms were available within a trial, the com-
 parison identified as producing the largest effect size
 was selected for sensitivity analysis. This was in con-
 trast to the primary analysis where a more conserva-
 tive approach was taken by pooling activity arms
 within trials and selecting the more rigorous control
 group for comparison. This sensitivity analysis pro-
 duced a larger effect (SMD = -1.00) when compared
 with the primary analysis (SMD = -0.82), however het-
 erogeneity was substantially increased ($I^2 = 38\%$ to
 61%). Four trials appeared to categorically differ from
 the others and therefore may have introduced heterogen-
 eity to the primary analysis; two employed alternative
 intervention modalities (yoga in Woolery et al. (2004);
 dance movement therapy in Jeong et al. (2005)), and
 two used control conditions, which may not be equiva-
 lent to NT, WL or AP (physical activity + TAU v. TAU
 in Carter et al. (2015); the AP control group engaged in
 significant levels of activity in Balchin et al. (2016)).
 Removal of these trials reduced heterogeneity ($I^2 = 0\%$),
 but did not substantially alter the pattern of results
 (SMD = -0.92). Similar magnitudes of effect were found
 when the analysis was restricted to either observer-rated
 or self-report depression symptom measure outcomes
 and when trials with imputed data from graphical
 representations were removed from the analysis.

Analysis of dropout

Dropout rate from randomisation to post-intervention
 was 11% (95% CI = 4.8–17.6) in physical activity arms
 and 18% (95% CI = 9.5–27.8) in control arms, however
 there was no significant difference between arms
 when trial dropout was pooled ($k=12$, RD = -0.01,
 95% CI = -0.04 to 0.03, $p = 0.70$) (Fig. 4).

Subgroup analyses

The observational results in Table 4 show that in these
 included trials, the effect sizes did not significantly dif-
 fer by type of control group (WL/NT v. AP), age group
 (<18 v. ≥ 18), diagnostic status (diagnosis v. threshold
 symptoms), sample recruitment (clinical v. non-clinical),
 depression severity category (mild, moderate, severe),

[†] The notes appear after the main text.

Fig. 3 - B/W online, B/W in print

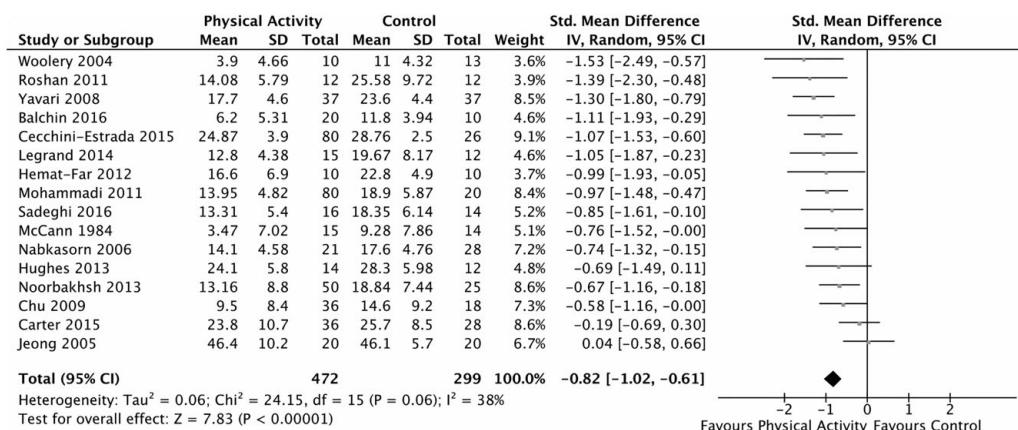


Fig. 3 Primary meta-analysis forest plot: physical activity v. control at post-intervention, depression symptom measure.

Table 3. Sensitivity analyses

Sensitivity analyses	k	n	SMD	95% CI	p value	Heterogeneity
Primary meta-analysis	16	771	-0.82	-1.02 to -0.61	p < 0.00001	$\chi^2 = 24.15$, df = 15 (p = 0.06); I ² = 38%
Selection of largest effect size when multiple arms available	16	624	-1.00	-1.28 to -0.72	p < 0.00001	$\chi^2 = 38.55$, df = 15 (p = 0.0007); I ² = 61%
Randomisation sequence generation: low risk of bias	5	201	-0.63	-0.97 to -0.29	p < 0.001	$\chi^2 = 5.18$, df = 4 (p = 0.27); I ² = 23%
Allocation concealment: low risk of bias	4	236	-0.48	-1.02 to 0.05	p = 0.08	$\chi^2 = 10.28$, df = 3 (p = 0.02); I ² = 71%
Outcome assessor blinding: low risk of bias	2	56	-0.90	-1.47 to -0.32	p < 0.001	$\chi^2 = 0.52$, df = 1 (p = 0.47); I ² = 0%
Incomplete outcome data: low risk of bias	6	376	-0.72	-1.03 to -0.40	p < 0.00001	$\chi^2 = 8.83$, df = 5 (p = 0.12); I ² = 43%
Self-report depression symptom measure	14	717	-0.77	-0.99 to -0.55	p < 0.00001	$\chi^2 = 22.19$, df = 13 (p = 0.05); I ² = 41%
Observer-rated depression symptom measure	3	80	-1.03	-1.52 to -0.55	p < 0.00001	$\chi^2 = 1.33$, df = 2 (p = 0.52); I ² = 0%
Excluding trials with heterogeneous control groups ^a	14	677	-0.86	-1.06 to -0.67	p < 0.00001	$\chi^2 = 17.23$, df = 13 (p = 0.19); I ² = 25%
Excluding trials with heterogeneous physical activity groups ^b	14	708	-0.85	-1.02 to -0.67	p < 0.00001	$\chi^2 = 14.66$, df = 13 (p = 0.33); I ² = 11%
Excluding trials with heterogeneous physical activity & control groups	12	614	-0.92	-1.09 to -0.74	p < 0.00001	$\chi^2 = 6.95$, df = 11 (p = 0.80); I ² = 0%
Excluding trials with graphical/imputed data	14	693	-0.83	-1.07 to -0.60	p < 0.00001	$\chi^2 = 24.07$, df = 13 (p = 0.03); I ² = 46%

k, number of trials; n, number of participants; SMD, standardised mean difference; CI, confidence interval.

^a Excluded from analysis are Carter *et al.* (2015) and Balchin *et al.* (2016).

^b Excluded from analysis are Jeong *et al.* (2005) and Woolery *et al.* (2004).

461 type of physical activity (aerobic v. resistance) and
 462 intensity (light, moderate, vigorous). Meta-regression
 463 analyses found no relationship between physical activ-
 464 ity's observed effect and either of the two continuous
 465 variables (mean age and standardised mean depression
 466 symptoms at baseline, both p > 0.1).

Grade

Overall quality of the evidence contributing to the primary meta-analysis was rated as LOW to VERY LOW. Serious or very serious limitations in study design and suspected publication bias led to a downgrading of the

Table 4. Subgroup analyses based on the primary meta-analysis

Subgroup analysis	<i>k</i>	<i>N</i>	SMD	95% CI	<i>p</i> value	Heterogeneity	Test for subgroup difference
Primary meta-analysis	16	771	-0.82	-1.02 to -0.61	$p < 0.00001$	$\chi^2 = 24.15$, $df = 15$ ($p = 0.06$); $I^2 = 38\%$	
Sample recruitment							
Clinical	5	164	-0.72	-1.16 to -0.29	$p < 0.01$	$\chi^2 = 6.62$, $df = 4$ ($p = 0.16$); $I^2 = 40\%$	$\chi^2 = 0.29$, $df = 1$, ($p = 0.59$); $I^2 = 0\%$
Non-Clinical	11	607	-0.86	-1.09 to -0.63	$p < 0.00001$	$\chi^2 = 16.05$, $df = 10$ ($p = 0.10$); $I^2 = 38\%$	
Diagnostic status							
Diagnosis	4	100	-0.95	-1.37 to -0.53	$p < 0.00001$	$\chi^2 = 1.37$, $df = 3$ ($p = 0.71$); $I^2 = 0\%$	$\chi^2 = 0.40$, $df = 1$, ($p = 0.53$); $I^2 = 0\%$
Threshold symptoms	12	671	-0.79	-1.04 to -0.55	$p < 0.00001$	$\chi^2 = 22.25$, $df = 11$ ($p = 0.02$); $I^2 = 51\%$	
Depression symptom severity (baseline)							
Mild	4	141	-0.68	-1.26 to -0.10	$p < 0.05$	$\chi^2 = 8.05$, $df = 3$ ($p = 0.04$); $I^2 = 63\%$	$\chi^2 = 0.75$, $df = 2$, ($p = 0.69$); $I^2 = 0\%$
Moderate	10	542	-0.94	-1.13 to -0.74	$p < 0.05$	$\chi^2 = 5.56$, $df = 9$ ($p = 0.78$); $I^2 = 0\%$	
Severe	2	88	-0.73	-1.89 to 0.42	$p = 0.21$	$\chi^2 = 5.03$, $df = 1$ ($p = 0.02$); $I^2 = 80\%$	
Age group							
Mean age < 18	5	254	-0.59	-1.08 to -0.11	$p < 0.05$	$\chi^2 = 11.50$, $df = 4$ ($p = 0.02$); $I^2 = 65\%$	$\chi^2 = 1.67$, $df = 1$, ($p = 0.20$); $I^2 = 40.2\%$
Mean age \geq 18	11	517	-0.94	-1.13 to -0.74	$p < 0.00001$	$\chi^2 = 7.32$, $df = 10$ ($p = 0.70$); $I^2 = 0\%$	
Type of control							
PA v. NT/WL	8	357	-0.95	-1.30 to -0.60	$p < 0.00001$	$\chi^2 = 14.41$, $df = 7$ ($p = 0.04$); $I^2 = 51\%$	$\chi^2 = 0.35$, $df = 1$, ($p = 0.55$); $I^2 = 0\%$
PA v. attention/activity placebo	7	350	-0.82	-1.05 to -0.59	$p < 0.00001$	$\chi^2 = 2.73$, $df = 6$ ($p = 0.84$); $I^2 = 0\%$	
Type of activity							
Aerobic	13	657	-0.84	-1.04 to -0.64	$p < 0.00001$	$\chi^2 = 15.47$, $df = 12$ ($p = 0.22$); $I^2 = 22\%$	$\chi^2 = 2.42$, $df = 2$, ($p = 0.30$); $I^2 = 17.5\%$
Resistance	1	23	-1.53	-2.49 to -0.57	$p < 0.01$	NA	
Mixed	2	91	-0.56	-1.39 to 0.28	$p = 0.19$	$\chi^2 = 3.11$, $df = 1$ ($p = 0.08$); $I^2 = 68\%$	
Intensity							
Light	1	23	-1.53	-2.49 to -0.57	$p < 0.05$	NA	$\chi^2 = 2.87$, $df = 2$ ($p = 0.24$); $I^2 = 30.2\%$
Moderate ^a	6	176	-0.76	-1.09 to -0.43	$p < 0.00001$	$\chi^2 = 5.48$, $df = 5$ ($p = 0.36$); $I^2 = 9\%$	
Vigorous ^a	4	112	-1.04	-1.44 to -0.64	$p < 0.00001$	$\chi^2 = 0.39$, $df = 3$ ($p = 0.94$); $I^2 = 0\%$	

k, number of trials; *n*, number of participants; SMD, standardised mean difference; CI, confidence interval; PA, physical activity; NT, no-treatment; WL, wait-list.

^a Two trials (Chu *et al.* 2009; Balchin *et al.* 2016) have multiple physical activity arms of differing intensity and thus contribute non-independent effects to the intensity sub-group analysis.

Fig. 4 - B/W online, B/W in print

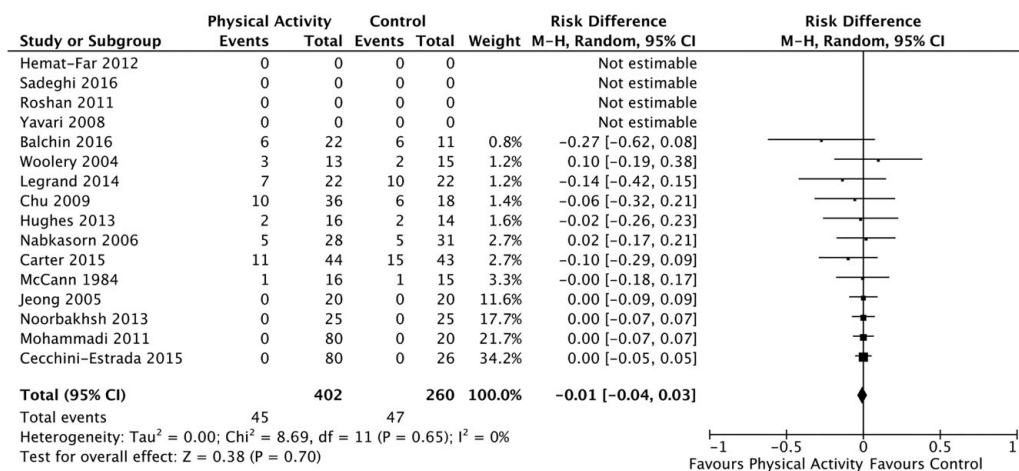


Fig. 4. Acceptability forest plot: physical activity v. control, number of participants dropping out of intervention and control arms (Events) from number randomised (Total).

472 evidence by two to three levels (See Supplementary
 473 Material for GRADE ratings). The level of evidence
 474 was not downgraded for either imprecision, inconsis-
 475 tency, or indirectness.

476 **Discussion**

477 *Main findings*

478 Physical activity appears to show efficacy for improv-
 479 ing depression symptoms in adolescents and young
 480 adults experiencing a diagnosis or threshold symp-
 481 toms of depression. However the risk of bias within
 482 included trials and the low quality of the overall evi-
 483 dence base limit our confidence in this finding.
 484 None-the-less, physical activity does appear to be an
 485 acceptable and feasible intervention modality for
 486 young people experiencing depression given the low
 487 dropout rate. Subgroup and meta-regression analyses
 488 suggest that the treatment effect may not be modified
 489 by characteristics such as age, depression severity,
 490 diagnostic status, physical activity type or intensity,
 491 however these analyses are observational, likely under-
 492 powered to detect effects and should be interpreted
 493 with caution. While we do not yet know the specific
 494 intervention characteristics required to bring about
 495 symptom improvement, we identify a number of char-
 496 acteristics common across trials that may inform future
 497 research agendas and the implementation of physical
 498 activity interventions.

499 *Context of main findings*

500 To provide a clinical interpretation of the large pooled
 501 effect, the SMD (-0.82) was back-transformed into
 502 units of the BDI (Higgins *et al.* 2011a), showing that
 503 those receiving a physical activity intervention would

score, on average, 5.38 (95% CI = 4.00–6.69) points
 504 lower on the BDI than those in a control condition².
 505 The minimal clinically important difference on the
 506 BDI has been estimated at between three and five
 507 points (Hiroe *et al.* 2005) and elsewhere as a 17.5%
 508 reduction from baseline (Button *et al.* 2015). This sug-
 509 gests that physical activity may produce a clinically
 510 significant reduction in depression symptoms.
 511 Furthermore, the effect was robust when restricting
 512 the analysis to the seven trials comparing physical
 513 activity to attention/activity placebo controls (-0.82,
 514 I² = 0%). Importantly this provides some indication
 515 that the effect estimate may be due to the physical
 516 activity intervention rather than the non-specific factors
 517 that cannot be controlled in comparison with
 518 no-treatment/wait-list controls (Lindheimer *et al.* 2015;
 519 Stubbs *et al.* 2016a). However further research is
 520 needed to establish this finding given the observational
 521 nature of the analysis, the small number and the low
 522 quality of included trials.
 523

The large effect generated from this meta-analysis is
 524 consistent in size with meta-analytic findings of phys-
 525 ical activity for depression in adults (Cooney *et al.* 2013;
 526 Kvam *et al.* 2016; Schuch *et al.* 2016b). In terms of pre-
 527 vious child and adolescent meta-analyses, these have
 528 included trials of healthy young people, those with
 529 other medical or mental health conditions or children
 530 under 12 years, potentially complicating the generalis-
 531 ability of their findings to the treatment of depression
 532 (Larun *et al.* 2006; Brown *et al.* 2013; Carter *et al.*
 533 2016). The current meta-analysis synthesised only trials
 534 of adolescents and young adults with either a diagno-
 535 sis or threshold symptoms of depression highlighting
 536 its relevance to young people needing treatment, par-
 537 ticularly as our subgroup analysis suggests a robust
 538 effect size in trials that recruited clinical samples. We
 539

540 also identified and included seven RCTs that had not
541 appeared in any previous adult or child-adolescent
542 review.

543 In the context of established treatments for youth
544 depression, psychological interventions demonstrate
545 small-to-moderate treatment effects (Weisz *et al.* 2006,
546 2017; Watanabe *et al.* 2007). While our meta-analysis
547 generated a large preliminary effect size, physical
548 activity is considerably less researched than estab-
549 lished psychotherapies and we have limited informa-
550 tion regarding head-to-head comparisons. Only one
551 trial to date has compared physical activity with CBT
552 for depression in young people, finding equivalent
553 treatment effects in comparison with control (Sadeghi
554 *et al.* 2016). Physical activity interventions may exert
555 some influence on depression via a general behav-
556 ioural activation effect, an often-utilised treatment
557 component of CBT. This is potentially relevant to
558 youth depression given that behavioural-based inter-
559 ventions may be better suited to younger age groups
560 (Hetrick *et al.* 2015). Preliminary work is exploring
561 the use of physical activity-based interventions deliv-
562 ered via behavioural activation frameworks for depres-
563 sion in both young people and adults (Parker *et al.*
564 2016; Euteneuer *et al.* 2017).

565 Our investigation of attrition rates as a proxy for
566 intervention acceptability showed that dropout across
567 physical activity arms was 11%, which did not differ
568 from controls. This rate is comparable with that estab-
569 lished in a recent meta-analysis of dropout from phys-
570 ical activity trials in adults with depression (15.2%,
571 (Stubbs *et al.* 2016b)). It is also equivalent to pooled
572 attrition rates observed from psychotherapy trials for
573 depression in young people (12%, (Weisz *et al.* 2006))
574 and substantially better than rates identified for anti-
575 depressant medication (19% to 38%, (Hetrick *et al.*
576 2012)), suggesting that physical activity is at least as
577 acceptable as psychotherapy and may be more accept-
578 able than medication. Additionally, young people
579 appear more likely to endorse physical activity as a
580 helpful intervention for depression, than either medi-
581 cation or psychotherapy (Jorm & Wright, 2007;
582 Reavley & Jorm, 2011), further highlighting the poten-
583 tial acceptability and feasibility of employing this inter-
584 vention modality with young people.

585 *Quality of evidence*

586 The overall quality of evidence contributing to the
587 meta-analysis is low, suggesting the current findings
588 should be interpreted caution. We were unable to
589 undertake an analysis restricted to high quality trials,
590 because there are currently not enough available trials
591 at low risk of bias across all or most domains, to do so.
592 While the effect sizes from three of our four sensitivity

analyses by individual risk of bias domain remained 593
largely unchanged compared with the overall effect, 594
each analysis was restricted to a very small number 595
of trials meaning we cannot rule out bias from the 596
overall effect size. This uncertainty is likely a result 597
of inadequate reporting of trial methods, particularly 598
as many domains (e.g., selection and attrition bias) 599
received unclear ratings across trials. Both trial-level 600
selection and attrition bias have been shown to impact 601
the size of effect estimate (Schulz *et al.* 1995; Bell *et al.* 602
2013). Of particular concern to the internal validity of 603
the current finding is that physical activity is an 604
unblinded intervention (risk of performance bias), 605
and in the context of a self-report outcome measure 606
(risk of detection bias), there is the potential to inflate 607
the effect in favour of the intervention. Large, robust, 608
adequately reported trials that attempt to reduce the 609
risk of bias in their methodologies are therefore needed 610
to increase confidence in the current finding. 611
Publication bias cannot be ruled out given the small 612
attenuation of effect size using the trim and fill 613
method, however its potential effect appears small 614
given the adjusted effect size (after imputing poten- 615
tially suppressed trials) was moderate and remained 616
significant, coupled with the large observed fail-safe 617
N. Ratings for two of the five GRADE domains (limita- 618
tions of study design, publication bias) resulted in a 619
downgrading of the current RCT-generated evidence 620
from HIGH to LOW or VERY LOW, suggesting that 621
confidence in the effect is limited and the effect size 622
may be substantially different from the estimate 623
presented (Balshem *et al.* 2011; Schünemann *et al.* 624
2013). 625

626 *Implementation and further research*

We do not yet know the specific characteristics or type 627
of young people who might be suited to, or benefit 628
most from a physical activity intervention. Our ana- 629
lysis suggests that in these trials, physical activity 630
may produce a similar, large magnitude of effect for 631
young people irrespective of whether they were 632
recruited with a diagnosis or threshold symptoms of 633
depression, and appears unchanged when restricted to 634
trials conducted with clinical samples. Similarly, 635
the treatment effect does not appear to be associated 636
with baseline depression symptom severity, however 637
given the small number of clinical-based trials, further 638
work is needed to confirm these findings. While 639
appearing consistent with a recent adult level moder- 640
ator analysis of physical activity trials (Schuch *et al.* 641
2016c), caution should still be taken when interpreting 642
these subgroup analyses as they are likely underpow- 643
ered and only observational in nature. All but two 644
included trials in this analysis were in the mild and 645

646 moderate severity range suggesting that physical activ-
 647 ity may be clinically relevant for young people experi-
 648 encing this symptom severity, and that further research
 649 is needed to explore the benefits for severe depression.
 650 Current treatment guidelines recommend providing
 651 general advice on the benefit of physical activity,
 652 alongside first-line interventions (e.g., CBT), to all
 653 young people presenting with depression, regardless
 654 of severity (NICE, 2015). While the current finding
 655 highlights the potential of physical activity as
 656 stand-alone intervention, larger scale replication trials,
 657 particularly with clinical samples, are needed before
 658 this work can be used to inform treatment guidelines.

659 Common intervention characteristics were observed
 660 across trials that may guide further research and the
 661 clinical implementation of physical activity protocols,
 662 including the use of supervised group sessions of mod-
 663 erate or vigorous intensity aerobic activity over 60 min
 664 sessions, multiple times per week, over at least an
 665 8-week period. Adult-level syntheses have identified
 666 a similar pattern of common characteristics that may
 667 lead to symptom improvement (Perraton *et al.* 2010;
 668 Silveira *et al.* 2013; Stanton & Reaburn, 2014;
 669 Nyström *et al.* 2015). Our observational subgroup ana-
 670 lyses suggest that the intervention characteristics we
 671 investigated may not have modified the treatment
 672 effect in the included trials. However, caution should
 673 be taken when interpreting this finding given the
 674 small number of trials in subgroups leaving analyses
 675 underpowered to detect differences if they exist. The
 676 current evidence base is therefore limited to the
 677 characteristics common in the small number of trials
 678 published to date, with further work needed to deter-
 679 mine the component ingredients required to bring
 680 about improvement in depression and if identified,
 681 how best to implement them in clinical settings.

682 To date, an optimum dose of activity for depression
 683 cannot be recommended due to a lack of available trial
 684 data. Only two trials with young people have directly
 685 tested the effect of differing intensities of aerobic activ-
 686 ity (Chu *et al.* 2009; Balchin *et al.* 2016), with equivocal
 687 findings. Pooling of included trials according to inten-
 688 sity appeared to suggest that those implementing mod-
 689 erate and vigorous intensity activities produced large
 690 effects, however there were too few trials of low inten-
 691 sity activity to allow meaningful comparison, requiring
 692 further investigation. Two highly cited trials in adults
 693 suggest that more physical activity, whether in the
 694 form of higher intensity or overall energy expenditure
 695 may produce better results for the treatment of depres-
 696 sion (Dunn *et al.* 2005; Trivedi *et al.* 2011). While the
 697 dose-response relationship looks promising, further
 698 trials are required, particularly in young people.
 699 Investment in dose-response trials needs to be consid-
 700 ered alongside an alternative treatment option that

701 focuses less on minimum thresholds and more on pro-
 702 moting incidental physical activity and reducing sed-
 703 entary behaviour (Vancampfort *et al.* 2015; Parker
 704 *et al.* 2016).

705 Our pooled effect was based on variable types of
 706 physical activity, yet it remained unchanged when
 707 trials that differed substantially were removed (e.g.,
 708 yoga, dance movement therapy), suggesting that the
 709 type of activity may not be important. Although the
 710 type was variable, most interventions consisted of an
 711 aerobic-based activity, with only one trial using
 712 resistance-based activity (Woolery *et al.* 2004) and
 713 two others using a combination (Legrand, 2014;
 714 Carter *et al.* 2015). In adults, resistance-based activity
 715 has produced reductions in depression symptoms
 716 and direct comparison suggests both modalities per-
 717 form equally well (Doynie *et al.* 1987; Martinsen *et al.*
 718 1989; Krogh *et al.* 2009; Cooney *et al.* 2013). Further
 719 investigation of resistance-based activity in young peo-
 720 ple is warranted, particularly as some may show pre-
 721 ference for this modality (Firth *et al.* 2016).

722 Supervision is a common feature of physical activity
 723 protocols (Perraton *et al.* 2010), and may lead to lower
 724 dropout, particularly when delivered by a qualified
 725 professional (e.g., exercise physiologist or physiother-
 726 apist) (Stubbs *et al.* 2016b). Conversely, a lack of super-
 727 vision may contribute to poor engagement and
 728 compliance (Knapen *et al.* 2015), and is a likely factor
 729 in null findings in some adult level trials (Chalder
 730 *et al.* 2012; Pfaff *et al.* 2014). Most trials in this review
 731 utilised supervision, with seven employing a qualified
 732 professional, potentially contributing to the positive
 733 pooled effect.

734 *Strengths and limitations*

735 The rigour of this review is enhanced by the inclusion
 736 of RCTs, the use a comprehensive and exhaustive
 737 search, systematic methodology to identify trials and
 738 extract data, and the use of systematic tools to assess
 739 bias and overall evidence quality. Additionally the
 740 requirement of a diagnosis or threshold depression
 741 symptoms for trial inclusion highlights the potential
 742 clinical applicability of the findings. This is the first
 743 meta-analysis to examine the effects of physical activ-
 744 ity interventions for depression spanning the
 745 adolescent-young adult period, providing valuable
 746 knowledge about a period that overlaps with the
 747 peak onset of depression.

748 A number of factors may limit the generalisability of
 749 the findings, including the overall low quality of the
 750 evidence base contributing to the main analysis, over-
 751 representation of female-only samples, use of poten-
 752 tially heterogeneous activity protocols, small sample
 753 sizes and the limited number of available trials,

754 particularly those recruiting from clinical settings.
 755 Our subgroup findings are limited by being observa-
 756 tional in nature and underpowered due to the small
 757 number of trials in many subgroupings. We were
 758 unable to investigate a number of important factors
 759 due to the paucity of available trials, including the
 760 effect of physical activity over longer-term follow-up
 761 (as maintenance of post-intervention benefit is often
 762 an important clinical goal) and the relative benefits of
 763 physical activity compared with established depres-
 764 sion treatments such as medication and psychother-
 765 apy. Determining whether these interventions are
 766 equivalent may provide young people who do not
 767 want, are not suited for or do not benefit from estab-
 768 lished therapies, a viable and effective treatment
 769 option. Exploring the mechanisms by which physical
 770 activity improves depression is also needed to better
 771 understand the necessary ingredients for symptom
 772 change and to inform the design of more targeted
 773 intervention strategies. Also missing from the current
 774 evidence base is an investigation of the effect that
 775 physical activity interventions have on physical health
 776 outcomes in depression, particularly given the risk that
 777 both depression and low activity levels confer to nega-
 778 tive health consequences (Lee *et al.* 2012; Goldstein
 779 *et al.* 2015).

780 Conclusion

781 This review indicates that physical activity is a promis-
 782 ing primary intervention for adolescents and young
 783 adults experiencing a diagnosis or threshold symp-
 784 toms of depression, however concerns surrounding
 785 methodological quality of included trials limit our abil-
 786 ity to conclude on its effectiveness. While the effect of
 787 physical activity appears large and robust in compar-
 788 ison with attention/activity placebo control conditions,
 789 and when restricted to trials in clinical samples, the
 790 findings should be interpreted with caution given the
 791 quality of the underlying evidence base is currently
 792 low. This suggests uncertainty surrounding the size
 793 of the effect and indicates that large, well-reported
 794 and robust trials conducted with help-seeking clinical
 795 samples in real-world treatment settings are required
 796 to increase confidence in the current finding. Physical
 797 activity appears to be acceptable to young people,
 798 suggesting the potential feasibility of incorporating
 799 it into the routine clinical treatment of depression,
 800 however research is still required to establish the inter-
 801 vention characteristics that are necessary to improve
 802 depression.

803 Notes

804 ¹ Pooled standard deviation = $\sqrt{\sum(n_i - 1)SD_i^2 / (n_i - 1)}$.

² SMD multiplied by the pooled baseline standard deviation 805
 of the eight included trials ($n = 424$) reporting the BDI in 806
 numerical format. 807

Supplementary material 808

The supplementary material for this article can be 809
 found at <https://doi.org/10.1017/S0033291717002653> 810

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Declaration of Interest 820

None. 821

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