Physical Activity Interventions for People With Mental Illness: A Systematic Review and Meta-Analysis

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ABSTRACT

Objective: To determine effects of physical activity on depressive symptoms (primary objective), symptoms of schizophrenia, anthropometric measures, aerobic capacity, and quality of life (secondary objectives) in people with mental illness and explore between-study heterogeneity.

Data Sources: MEDLINE, Cochrane Controlled Trials Register, PsycINFO, CINAHL, Embase, and the Physiotherapy Evidence Database (PEDro) were searched from earliest record to 2013.

Study Selection: Randomized controlled trials of adults with a *DSM-IV-TR, ICD-10*, or clinician-confirmed diagnosis of a mental illness other than dysthymia or eating disorders were selected. Interventions included exercise programs, exercise counseling, lifestyle interventions, tai chi, or physical yoga. Study methodological quality and intervention compliance with American College of Sports Medicine (ACSM) guidelines were also assessed.

Data Extraction and Analysis: Two investigators extracted data. Data were pooled using random-effects meta-analysis. Meta-regression was used to examine sources of between-study heterogeneity.

Results: Thirty-nine eligible trials were identified. The primary meta-analysis found a large effect of physical activity on depressive symptoms (n = 20; standardized mean difference (SMD) = 0.80). The effect size in trial interventions that met ACSM guidelines for aerobic exercise did not differ significantly from those that did not meet these guidelines. The effect for trials with higher methodological quality was smaller than that observed for trials with lower methodological quality (SMD = 0.39 vs 1.35); however, the difference was not statistically significant. A large effect was found for schizophrenia symptoms (SMD = 1.0), a small effect was found for anthropometry (SMD = 0.24), and moderate effects were found for aerobic capacity (SMD = 0.63) and quality of life (SMD = 0.64).

Conclusions: Physical activity reduced depressive symptoms in people with mental illness. Larger effects were seen in studies of poorer methodological quality. Physical activity reduced symptoms of schizophrenia and improved anthropometric measures, aerobic capacity, and quality of life among people with mental illness.

Trial Registration: PROSPERO registration #CRD42012002012

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Physical activity has been recognized as a key component of a holistic approach to recovery within mental health services,[1] with the potential benefits ranging from a reduction in symptoms to an improvement in service engagement and utilization.[1] In recent years, formal exercise, defined as a subset of physical activity,[2] has received considerable attention as both an alternative to and augmentation strategy to usual care for depressive disorders.[3,4] This increased scientific focus reflects the significance of mental illness as a public health priority, with National Institute of Mental Health data showing that 5% of all adults in the United States meet criteria for a serious mental illness as specified by the *DSM-IV*, with 9.5% of the US population meeting criteria for a mood disorder.[5]

The antidepressive benefits of structured exercise for both the general population and those affected by depressive illness have been established in previous systematic reviews[3] (summarized in Table 1).

These reviews have been limited largely to a focus on structured exercise. Physical activity is a broader concept than exercise and encompasses exercise as well as non-exercise interventions.[2] Previous reviews have focused on exercise[3,4,7,8,10–12,15] and so have excluded other physical activity interventions such as yoga, tai chi, exercise counseling, and other pragmatic lifestyle interventions that reflect real-world clinical practice in this area. In addition, key questions remain unanswered: Do physical activity interventions improve depressive symptoms in the large number of patients who experience depression comorbid with other psychiatric diagnoses?[16] What role do physical activity interventions have on physical health parameters in psychiatric patients?

Assessment of the impact of physical activity in the large number of patients who experience comorbid depression is a critical issue as depression is a common comorbid diagnosis in other psychiatric conditions; for example, an estimated 25% of people diagnosed with schizophrenia also suffer depression.[17] Despite this tendency for patients to suffer from comorbid psychiatric conditions, previous reviews have investigated a single diagnosis of depression,[8,11,15] anxiety,[7] or schizophrenia.[13,14] Previous reviews have included both studies of help-seeking participants and studies in which participants were drawn from community samples in which depression and/or anxiety symptoms were assessed by questionnaire alone,[11,12,15] leading to uncertainty about whether all participants met criteria for a formal psychiatric diagnosis and potentially limiting the applicability of the findings made to clinical populations.

Clinical Points

- Physical activity interventions reduce symptoms of depression regardless of psychiatric diagnoses.
- Physical activity reduces positive and negative symptoms of schizophrenia.
- Based on the available evidence, clinicians should refer patients to physical activity interventions to improve both mental and physical health outcomes.

Furthermore, there are known physical health inequalities in people with mental illness, with a reduced life expectancy of 12–15 years[18] and an increased prevalence of metabolic syndrome and type 2 diabetes in patients experiencing schizophrenia and bipolar disorder, compared with the general population.[19] The causes of compromised cardiometabolic health within this population are multifactorial and include low levels of physical activity[20] and higher prevalence of smoking[21] as well as weight gain, dyslipidemia, and insulin resistance, particularly associated with the use of second-generation antipsychotic medication.[22] Despite the established health benefits of physical activity,[23] the impact that physical activity may have on physical health outcomes in people diagnosed with mental illness is unclear and a neglected component of previous literature reviews and interventional studies. The potential impact of physical activity on self-reported quality of life (QOL) is another key outcome that requires more investigation.

Meta-analysis and meta-regression are key tools for synthesizing and interpreting the results of systematic reviews, with 4 previous reviews of exercise for mental health utilizing meta-analysis.[3,8,12,15] The PRISMA statement is designed to guide the quality of reporting of systematic reviews, yet only 2 previous reviews in this field cited the PRISMA statement[3,14] and only 4 searched for non–English language trials,[3,9,13,15] which raises the possibility of selection bias.

In order to obtain a comprehensive assessment of the impact of physical activity on mental illness, we conducted a review with meta-analysis and meta-regression of all studies assessing the impact of physical activity interventions in people with mental illness. To address the limitations of previous reviews, we included only studies that clearly identified specific psychiatric diagnoses as inclusion criteria. All *DSM-IV-TR* and *International Classification of Disease* (*ICD-10*) adult diagnoses were considered for inclusion with the exception of dysthymia and mild depression (n = 22) and eating disorders (n = 2). This sampling strategy provides a clearer picture of the current state of knowledge of the impact of physical activity and exercise interventions in help-seeking individuals with psychiatric diagnoses by excluding studies focused on questionnaire-based symptom assessment in opportunistic samples (eg, college students). This review extended the scope of previous reviews by including trials not reported in English.

Specific questions to be answered by the review included the following:

1. What is the effect of physical activity on depressive symptoms in people with a mental illness?
2. What is the effect of physical activity on symptoms of schizophrenia?
3. Does physical activity improve anthropometric measurements, aerobic capacity, and self-reported quality of life in people with a mental illness?

METHOD

Design

The aims and methods of this systematic review with meta-analysis were registered with the PROSPERO database prior to conducting the review (#CRD42012002012). Reporting has been conducted as per the PRISMA statement.[24]

Identification and Selection of Trials

An electronic database search was conducted from earliest record to January 2013 using MEDLINE, Embase, Cochrane Central Register of Clinical Trials, PsycINFO, CINAHL, and the PEDro Database. The search strategy is outlined in eAppendix 1. The reference lists of relevant systematic reviews were also hand searched. Study eligibility was assessed according to criteria shown in Supplementary eFigure 1 by 2 reviewers (S.R. and A.T.) with disagreements resolved by a third reviewer (C.S.). The same reviewers extracted the outcome data and trial quality information. Bilingual researchers translated studies not published in

Table 1. Summary of Previous Literature Reviews of Antidepressant Benefits of Structured Exercise Published From 2011 Through August 2013

Author	Year	Systematic Review	Meta-Analysis	Population	Interventions Assessed	Assessment of Risk of Bias	*DSM/ICD* Diagnostic Criteria	Reference to PRISMA Statement	Search Extended Beyond English
Cooney et al[3]	2013	Yes	Yes	Depression	Exercise	Yes	No	Yes	Yes
Berk[6]	2013	No	No	Unipolar depression	Lifestyle	No	No	No	No
Jayakody et al[7]	2013	Yes	No	Anxiety disorders	Exercise	No	Yes	No	No
Josefsson et al[8]	2013	Yes	Yes	Depression or depressive symptoms	Exercise	Yes	Yes	No	No
Malchow[9]	2013	No	No	Schizophrenia and affective disorders	Physical exercise	No	No	No	No
Morgan[10]	2013	No	No	Varied	Exercise	No	No	No	No
Stanton and Reaburn[11]	2013	Yes	No	Depression	Exercise	Yes	Yes	No	No
Rethorst and Trivedi[4]	2013	No	No	Major depressive disorder	Exercise	No	No	No	No
Rimer et al[12]	2012	Yes	Yes	Depression	Exercise	Yes	No	No	No
Vancampfort et al[13]	2012	Yes	No	Schizophrenia	Physical therapy	Yes	Yes	No	Yes
Vancampfort et al[14]	2012	Yes	Insufficient studies identified	Schizophrenia	Yoga	Yes	Yes	Yes	No
Krogh et al[15]	2011	Yes	Yes	Depression	Exercise	Yes	No	No	Yes

Table 2. Outcome Measures Pooled for Meta-Analysis

Outcome	Pooled Measures
Depressive symptoms	Hamilton Depression Rating Scale (HDRS) Beck Depression Inventory (BDI) Edinburgh Postnatal Depression Scale (EPDS) Global Depression Index (GDI) Center for Epidemiologic Studies-Depression scale (CES-D) Depression Anxiety and Stress Scale (DASS) Bech-Rafaelsen Melancholy Scale (BRMS) Inventory of Depressive Symptomatology (IDS)
Schizophrenia symptoms	Positive and Negative Syndrome Scale (PANSS) Scale for Assessment of Positive Symptoms (SAPS) Scale for Assessment of Negative Symptoms (SANS)
Anthropometry	Waist circumference Hip circumference Body weight Body fat percentage Body mass index (BMI; weight [kg]/height [m^2])
Exercise capacity	Maximal exercise testing (VO_2 max) Submaximal exercise testing (heart rate)
Quality of life (QOL)	Health Survey Short Form-36 (SF-36) World-Health Organization Quality of Life Scale (WHO-QOL) Manchester Short Assessment of Quality of Life (MANSA)

English. Individual measures pooled for meta-analysis are listed in Table 2, and Table 3 summarizes the characteristics of selected trials, including diagnosis and intervention.

Assessment of Trial Characteristics and Risk of Bias

Quality. The quality of included trials was rated according to the Physiotherapy Evidence Database[25] Scale (1–10), which assesses the internal validity of a randomized controlled trial (RCT).[26,27] PEDro scale scores and key features of the study design including the concealed allocation of participants to groups and the blinding of assessors are reported in Supplementary eTable 1 for all studies included in the primary analysis.

Participants. Eligible studies were those that included participants 18 years of age or older, in whom a *DSM* or *ICD* diagnosis of mental illness was made. Dysthymia, "mild-depression," and eating disorders were excluded. No restriction was placed on the source of the participants, ie, patients from primary care as well as community settings were eligible, and the source of recruitment was recorded. Gender, age, and number of participants were extracted from eligible trials.

Interventions. The terms *physical activity* and *exercise* were defined according to the American College of Sports Medicine (ACSM) definitions; *physical activity* is "any body movement that is produced by the contraction of skeletal muscles that increases energy expenditure,"[2] whereas *exercise* is "a subset of physical activity that is planned, structured and deliberate."[28] We included all forms of physical activity that met these definitions. Aerobic, resistance-based, or mixed-type interventions were eligible, as well as interventions designed to increase incidental physical activity. Yoga and tai chi programs were included if the intervention was movement based. Exercise counseling and lifestyle change programs in which increasing physical activity participation was a significant aim of the intervention were included.

Prescribed interventions were assessed according to the ACSM guidelines for both aerobic and resistance exercise.[2] The ACSM guidelines state that adults should engage in aerobic exercise for at least 20 to 30 minutes per day, 3 to 5 days per week depending on intensity. The guidelines also recommend that adults should perform resistance exercises for each of the major muscle groups (8 to 10 exercises, 8 to 15 repetitions per exercise) on 2 to 3 days per week.[2]

Three reviewers (S.R., A.T., and C.S.) assessed whether prescribed interventions met these ACSM guidelines based on the total amount of contact with the research team as well as the prescribed volume and intensity of physical activity for the individual trial (where available). The question of whether participants adhered to the prescribed intervention and subsequently met the guidelines is an important consideration but is considered beyond the scope of this review.

Interventions of any duration were included within the meta-analysis. Short-term interventions (eg, 10 days to 4 weeks) were included to assess their potential impact on psychiatric symptoms, although such interventions were unlikely to elicit significant improvements in physical health.

Outcome measures. Trials were included in the meta-analyses if they provided outcome data for at least 1 of the previously validated outcome measures listed in Supplementary eFigure 1.

Outcome data were extracted for preintervention and postintervention time points only, as the potential longevity of the benefits of physical activity were beyond the scope of this review. For 2 trials that utilized multiple interventions,[29,30] the physical activity groups were pooled for analysis as suggested by the Cochrane Handbook.[31]

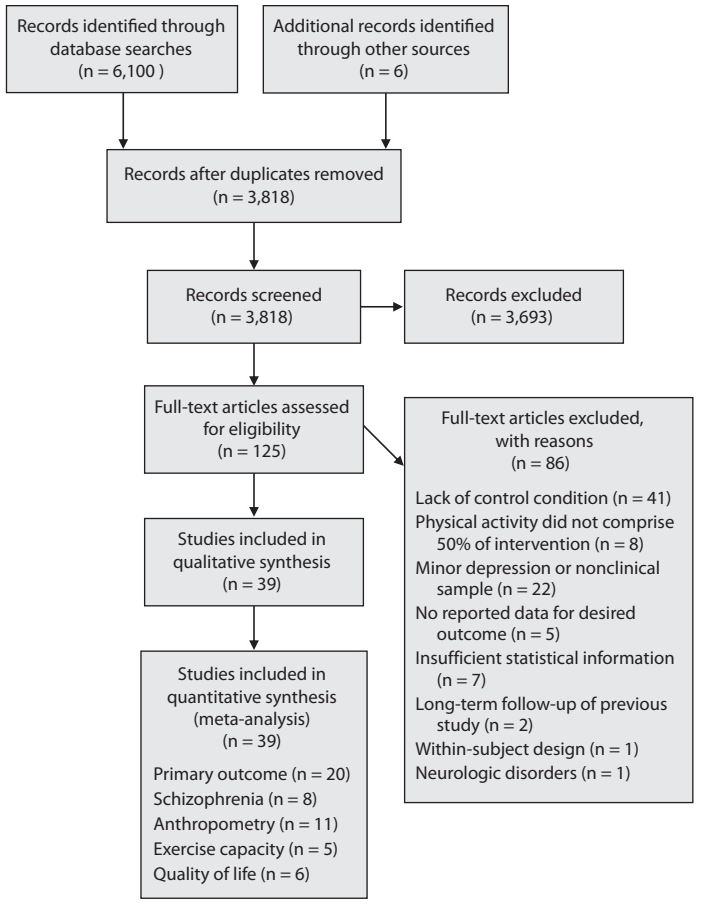
Data Analysis

Random-effects meta-analyses were conducted using Comprehensive Meta-Analysis software (Version 2.2, Biostat, Englewood, New Jersey) and Stata software packages (StataCorp LP, College Station, Texas). Intervention effect sizes (differences between intervention and control groups) for the primary and secondary outcome measures, standardized mean differences (SMDs) using Hedges' g statistic, and 95% confidence intervals (CIs) were calculated. When a posttest standard deviation was not available, an estimate was obtained using the standard deviation of the change between initial and final assessment scores,[31] assuming a correlation of 0.73 for the primary outcome (depressive symptoms), 0.73 (symptoms of schizophrenia), 0.9 (anthropometry), 0.65 (exercise capacity), and 0.84 (quality of life) between pretest and posttest scores, derived from the authors' previous research. Effect sizes were categorized as small (0.2), medium (0.5), or large (0.8 or greater).[32]

Statistical heterogeneity was quantified using the I^2 statistic: I^2 of more than 75% was considered to indicate considerable heterogeneity, I^2 of 50%–75% was considered to indicate substantial heterogeneity, and an I^2 of less than 40% was considered to indicate limited heterogeneity.[31]

Meta-regression was conducted for the primary outcome (depressive symptoms in participants with a mental illness), to determine if there were significant differences in the effect sizes between trials in which the prescribed intervention met the ACSM aerobic guidelines and trials in which the intervention did not meet these guidelines. Meta-regression to investigate the impact on intervention effects of resistance training protocols that met the relevant ACSM guidelines was not conducted due to the relatively small number of trials that included resistance training. Further meta-regression was carried out to determine the effect of study methodological quality, as measured with the PEDro scale, on pooled effect sizes. PEDro scores were dichotomized into categories of greater than or equal to 6 (indicating greater methodological quality) and less than 6 (indicating lower methodological quality). The meta-regression testing the impact on the pooled effect of an intervention that met the ACSM aerobic training guidelines was then repeated in the subset of trials in which the PEDro score was 6 or greater. Meta-regression was carried out in Stata 12 using the "metareg" command.

Figure 1. Identification and Selection of Studies for the Review



RESULTS

Flow of Trials Through the Review

A total of 3,818 records (excluding duplicates) were identified. After screening, 39 eligible randomized trials were identified. Twenty trials were included in the primary meta-analysis (depressive symptoms in participants with a mental illness).[29,30,33–50] For secondary analyses, 8 trials were pooled reporting schizophrenia symptoms,[51–58] 5 trials were pooled reporting measures of exercise capacity,[34,35,59–61] 11 trials were pooled reporting anthropometric outcomes,[40,51,61–69] and 6 were pooled with QOL measures.[47,50,52,57,61,70] Figure 1 presents the flow of studies through the review.

Characteristics of Included Trials

Table 3 summarizes the characteristics of included trials, including participant primary diagnosis, diagnostic criteria, summary of the physical activity intervention, and control group protocol. Twenty trials were included in the primary meta-analysis, involving a total of 1,298 participants. Trials included in the schizophrenia symptom analysis involved 389 participants, and trials included in the anthropometry analysis involved 55 participants. For exercise capacity, included trials involved 97 participants, and for QOL measures, the included trials involved 169 participants.

Quality. Nine trials used both blinded assessment of outcomes and concealed allocation.[29,30,38,39,46,47,51,62,71] Ten trials performed concealed allocation without blinded assessments,[34,35,42,48,52,59,60,63,72,73] and 3 trials used blinded assessment of outcomes without concealed allocation.[43,49,57] For the primary outcome, 10 trials[29,30,34,38,39,43,46–49] were of high methodological quality on the PEDro scale and 10 were of low quality.[33,35–37,40–42,44,45,50] For symptoms of schizophrenia, 1 trial[51] was of high methodological quality while 7 were low.[52–58] For anthropometry, 1 trial[51] was of high methodological quality while 10 were low[40,60–66,68,69]; for exercise capacity, 1 trial[34] was of high methodological quality and 4 were low[35,59–61]; and for QOL, 1[47] of the 6 trials was of high methodological quality and 5 were low.[50,52,57,61,70] The trial characteristics are shown in Table 3, and the methodological quality of trials included in the primary meta-analysis can be seen in Supplementary eTable 1.

Participants. The mean age of participants in the included trials ranged from 25 to 66 years. Twelve trials recruited participants with a *DSM* diagnosis of major depressive disorder.[29,30,38,40,43,45–48,50,74,75] A further 12 trials recruited participants with schizophrenia or schizoaffective disorder,[52–58,60,66,68,69,76] and of these, 6 used *DSM* criteria,[52,53,60,66,69,76] 3 used physician confirmation or hospital charts to confirm the diagnosis,[57,58,68] 2 used the Chinese Classification of Mental Disorders,[54,55] and 1 trial recruited patients from a long-stay psychiatric facility.[56]

Two trials recruited participants with a diagnosis of first episode psychosis, both of which referenced the *DSM*.[51,62] Five trials recruited participants with postnatal depression and all of these utilized the Edinburgh Postnatal Depression Scale (EPDS) to confirm the diagnosis (EPDS score ≥ 12[34,35,37,77]; EPDS score ≥ 10[71]). Another 12 trials recruited

Table 3. Description of the 39 Included Trials

Trial	Age Mean (SD, when reported), y: Experiment	Age Mean (SD, when reported), y: Control	Physical Activity Intervention and Intensity (when reported)	Exercise Guidelines: ACSM Aerobic	Exercise Guidelines: ACSM Resistance	Diagnosis; Diagnostic Criteria	Control	Setting (Recruitment)	Outcome(s)/Statistic
Abt, 2006[33] N = 31	46.5 (8.2)	45.6 (12.4)	6 wk of 2× weekly 60-min group classes of mixed-resistance and aerobic exercise	Yes	Yes	Depression/bipolar disorder; *DSM*	Social	Community	IDS-SR; mean, SD
Acil et al, 2008[52] N = 30	32.06	32.66	10 wk of 3 × weekly 40-min supervised aerobic exercise	Yes	No	Schizophrenia; *DSM*	Usual care	Previously hospitalized outpatients	SAPS, SANS, WHO-QOL-BREF-TR; mean, SD
Alvarez-Jimanez et al, 2006[62] N = 61	26 (15.5)	27.5 (8.5)	12-wk multifactorial intervention. 1–4 exercise sessions of varying intensities and duration	No	No	First-episode psychosis; *DSM*	Usual care	Referrals to community service	BMI, WT; mean change, SD
Armstrong and Edwards, 2003[34] N = 20	…	…	12 wk of 3 × weekly 30–40 min group aerobic exercise sessions at 60%–75% of age-predicted heart rate	Yes	No	Postnatal depression; EPDS score ≥ 12	Usual care	Referrals to program from general practice and community advertising	EPDS, DASS, VO_2; mean, SD
Armstrong and Edwards, 2004[35] N = 19	…	…	12 wk of 3 × weekly 40-min group aerobic exercise sessions at 60%–75% age-predicted heart rate	Yes	No	Postnatal depression; EPDS score ≥ 12	Social support	Referrals to program from general practice and community advertising	EPDS, VO_2; mean, SD
Behere et al, 2011[53] N = 39 (experiment vs control; yoga condition excluded)	30.2 (8)	33.6 (9.9)	12-wk combination of supervised and unsupervised exercises	No	No	Schizophrenia; *DSM*	Wait-list	Hospital outpatients	PANSS; mean, SD
Berlin et al, 2003[36] N = 39 (experiment vs control)	…	…	4 sessions of 45-min aquatic exercise within a single week	Yes	No	Depression; psychiatric inpatients	Wait-list	Psychiatric inpatients	BDI; mean change, SD
Blumenthal et al, 2007[30] N = 202 (HBE experiment vs control; SE vs control)	HBE: 53 (8) SE: 52 (7)	52 (8)	16 wk of 3 × weekly 45-min walking exercise sessions at 70%–85% maximum heart rate	Yes	No	Major depressive disorder; *DSM*	Placebo	Hospital	HDRS; change in each group
Brown et al, 2011[63] N = 136	…	…	12-mo varying intensity dietary modification and exercise counseling program	No	No	Varied serious mental illnesses; concurrent treatment with psychiatric medication	Usual care	Clients of community mental health programs	WT; mean, SD
Chalder et al, 2012[48] N = 361	40.9 (12.5)	38.8 (12.7)	Up to 3 face-to-face sessions and 10 telephone calls with a trained physical activity facilitator over 8 mo	No	No	Depressive episode; *ICD*	Usual care	General practitioner referral	BDI
Cole, 1998[59] N = 28	…	…	8 wk of 2× weekly 35-min low-impact aerobic sessions	No	No	Various psychiatric diagnoses; as per hospital diagnosis	Wait-list	Outpatients	Exercise HR; mean, SD
Daley et al, 2008[37] N = 38	…	…	2 × 60-min exercise counseling consultations over 12-wk period	No	No	Postnatal depression; EPDS score > 12	Usual care	Community	EPDS; mean, SD
Dunn et al, 2005[29] N = 80 (pooled groups)	36.15 (6.05)	34.5 (7.3)	12 wk of either 3 or 5 × weekly aerobic exercise sessions at either a "low" or "public-health" intensity	Yes	No	Major depressive disorder; *DSM*	Placebo	Community	HDRS; mean, SD
Forsberg et al, 2008[64] N = 41	39.8	42.8	56 wk of 2 × weekly 120-min group fitness and sport sessions	No	No	Various diagnoses; *DSM*	Aesthetic control	Supported housing facility	WC, WT; mean, SD
Forsberg et al, 2010[70] N = 41	39.8	42.8	56 wk of 2 × weekly 120-min group fitness and sport sessions	No	No	Various diagnoses; *DSM*	Usual care	Supported housing facility	SF-36, MANSA; mean, SD
Gholipou et al, 2012[58] (N = 30)	38 (8)	41 (7)	Not specified	No	No	Schizophrenia	Usual care	Hospital inpatients	SANS
Gilhoff et al, 2010[65] N = 50	48.1 (11.5)	48.9 (12)	20 wk of 1 × weekly 20-min lifestyle training including dietary modification and exercise	No	No	Bipolar disorder; *DSM*	Wait-list	Outpatients	BMI, WC, WT; mean, SD
Herring et al, 2011[49] N = 30 (pooled groups)	18–37	18–37	6 wk of 2× 16-min weekly sessions of either (a) lower-limb resistance training or (b) cycling	No	No	Generalized anxiety disorder; *DSM*	Wait-list	Community	BDI-II
Knubben et al, 2007[38] N = 38	49 (13)	50 (13)	10 × 30-min treadmill walking at 80% maximal heart rate over 10-d period	Yes	No	Major depressive disorder; *DSM*	Placebo	Hospital inpatients	BRMS, CES-D; mean, SD

(continued)

Table 3 (continued). Description of the 39 Included Trials

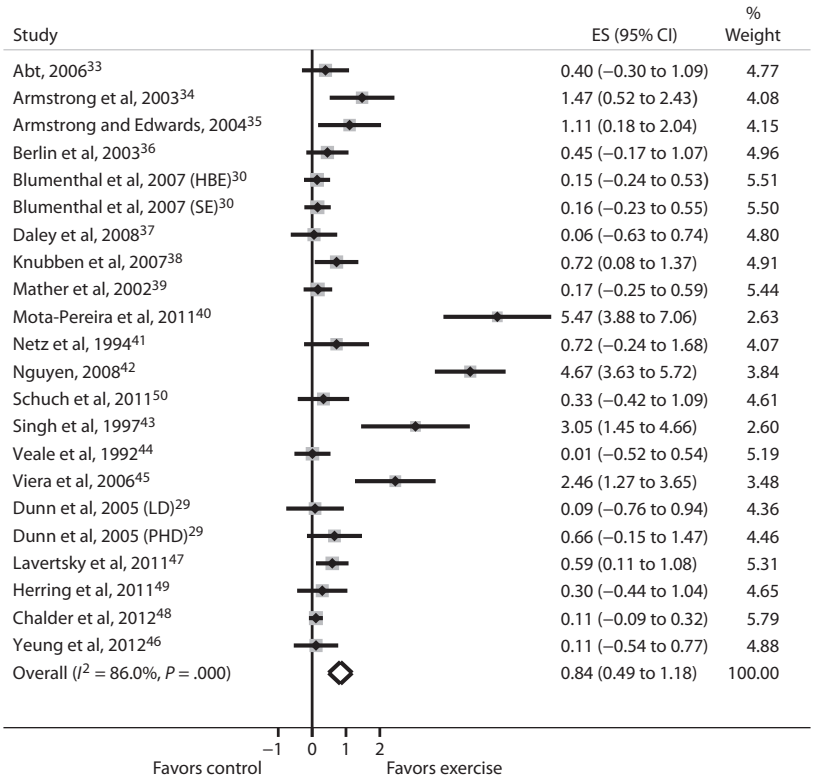
Trial	Age Mean (SD, when reported), y: Experiment	Age Mean (SD, when reported), y: Control	Physical Activity Intervention and Intensity (when reported)	Exercise Guidelines: ACSM Aerobic	Exercise Guidelines: ACSM Resistance	Diagnosis; Diagnostic Criteria	Control	Setting (Recruitment)	Outcome(s)/Statistic
Kwon et al, 2006[66] N = 48	32 (9.22)	29.8 (6.07)	8 × supervised lifestyle education and exercise counseling sessions over a 12-wk period	No	No	Schizophrenia/schizoaffective disorder; *DSM*	Usual care	Hospital outpatients	BMI, WT; mean change, SD
Lavertsky et al, 2011[47] N = 73	69.1 (7.0)	72.0 (7.4)	10 wk of 1 × weekly 120-min tai chi chih	No	No	Major depression; *DSM*	Health education	Community nonresponders to escitalopram	HDRS, QOL
Li et al, 2005[54] N = 68	35 (14)	37 (14)	3 mo of 5 × weekly 40-min physical activities including gym training, table-tennis, and gardening	Yes	Yes	Schizophrenia	Usual care	Hospital inpatients	SANS; mean, SD
Marzolini et al, 2008[60] N = 10	43 (6)	46.7 (12.25)	12 wk of 2 × weekly 90-min group aerobic and resistance exercise sessions	No	Yes	Schizophrenia/schizoaffective disorder; *DSM*	Usual care	Community treatment	BMI, HC, WC, WT, 6MWT; mean, SD
Mather et al, 2002[39] N = 86	63.7	66.2	10 wk of 2 × weekly 45-min group exercise sessions	Yes	Yes	Affective disorder; *ICD-10*	Social	Primary care psychiatric services/community	HDRS, GDS; raw difference, 95% CI
McKibbon et al, 2006[68] N = 64	53.1 (10.4)	54.8 (8.2)	24 wk of 1 × weekly 90-min diabetes, nutrition and exercise education sessions	No	No	Schizophrenia/schizoaffective disorder; physician confirmed diagnosis	Usual care	Community treatment facilities	BMI, WC, WT; mean, SD
Mota-Pereira et al, 2011[40] N = 29	46.68 (2.3)	45.33 (3.11)	12 wk of 5 × 30- to 45-min weekly walking sessions at moderate intensity (1 × supervised, 3 × unsupervised sessions per wk)	Yes	No	Major depressive disorder; *DSM*	Usual care	Outpatient psychiatric clinic	BDI, HDRS-17, BMI; change in each group
Netz et al, 1994[41] N = 17	64.3 (6.3)	69.5 (9.6)	8 wk of 3 × weekly 45 min of light intensity callisthenic exercises	No	No	Depression/ psychosis; *DSM*	Social	Hospital inpatients	GDS; mean, SD
Nguyen, 2008[42] N = 88	59.6 (9.3)	61.3 (9.9)	Daily 30 min of walking and psychotherapy for a period of 2 wk	Yes	No	Various psychiatric diagnoses; *DSM*	Usual care	Hospital inpatients	GDS; raw difference, SE
Ning et al, 2003[55] N = 80	34.8 (7.8)		12 wk of 12 × weekly 60-min group aerobic exercise with music	Yes	No	Schizophrenia	Usual care	Hospital inpatients	PANSS, SANS; mean, SD
Schuch et al, 2011[50] N = 26	42.8 (12.4)	42.5 (13.5)	16 kcal/kg per wk of exercise equivalent energy expenditure for period of hospitalization	No	No	Major depressive disorder; *DSM*	Usual care	University hospital	HDRS-17, WHO-QOL; mean, SD
Singh et al, 1997[43] N = 13 (major depression only)	…	…	10 wk of 3 × 45-min weekly high intensity resistance training (80% of 1 repetition maximum, 3 sets of 8 repetitions of all major muscle groups)	No	Yes	Major depressive disorder; *DSM*	Health education	Community	HDRS, BDI; mean, SD
Skrinar et al, 2005[61] N = 20	39.7 (8.17)	36.3 (11.3)	12 wk of 4 × 30- to 45-min weekly supervised aerobic and resistance based exercise at 70%–85% of age predicted maximal heart rate	Yes	Yes	Mood or psychotic disorders; *DSM*	Wait-list	Hospital (inpatients and outpatients)	%BF, BMI, watts, SF-36; mean, SD
Su, 1999[56] N = 60	35 (14)	37 (14)	5 wk of 6 × weekly 60-min dance therapy	Yes	No	Schizophrenia	Usual care	Hospital inpatients	SANS; mean change, SD
Veale et al, 1992[44] N = 65	…	…	12 wk of 3 × weekly supervised aerobic exercise sessions	Yes	No	Depression; psychiatric inpatients	Usual care	Practitioner referral	BDI; mean, SD
Viera et al, 2007[45] N = 18 (Brazil)	…	…	12 wk of 2 × weekly aquatic exercise	No	No	Major depressive disorder; *DSM*	Usual care	Hospital outpatients	HDRS; mean, SD
Visceglia and Lewis, 2011[57] N = 18	37.4 (13.7)	48.1 (11.2)	8 wk of 2 × 45-min weekly supervised yoga classes	No	No	Schizophrenia; hospital charts	Wait-list	Psychiatric facility	PANSS, WHO-QOL-BREF; mean change, SD
Wu et al, 2007[69] N = 53	…	…	24 wk of 3 × 60-min group walking + dietary intervention	Yes	No	Schizophrenia; *DSM*	Usual care	Hospital	BMI, %BF, HC, WC, WT; mean change, SD
Wu et al, 2008[51] N = 128	26.1	25.8	12 wk combination of supervised and home-based aerobic exercise at 70% of heart rate reserve	Yes	No	First-episode schizophrenia; *DSM*	Placebo	Hospital outpatients	PANSS, BMI, WC, WT; mean, SD
Yeung et al, 2012[46] N = 39	54 (12)	58 (7)	12 wk of 1 × weekly 60-min tai chi	No	No	Major depressive disorder; *DSM*	Wait-list	Community and clinician-referred Chinese Americans	HDRS-17

Abbreviations: 6MWT = 6-minute walk test; ACSM = American College of Sports Medicine; BF = body fat; BMI = body mass index; BREF-TR = Brief Report, Turkish Version; GDS = Geriatric Depression Scale; HC = hip circumference; VO_2 = volume of oxygen; watts = maximal wattage obtained during exercise assessment; WC = waist circumference; WT = body weight; abbreviations for all other rating scales are spelled out in Table 2.
Symbol: … = not reported.

participants with various psychiatric conditions; 8 of these referenced a *DSM* or *ICD* diagnosis,[33,41,42,61,64,70,73,78] 2 recruited psychiatric inpatients,[36,44] 1 recruited psychiatric outpatients,[59] and 1 required a diagnosis of a serious mental illness and concurrent treatment with an antipsychotic medication.[63] Single trials included participants with a *DSM* diagnosis of bipolar disorder,[65] participants with *DSM* diagnosis of panic disorder,[72] participants with an *ICD* diagnosis of affective disorder,[39] and participants with generalized anxiety disorder (GAD).[49]

Interventions. Thirteen of the 20 trials included within the primary meta-analysis incorporated an aerobic-based intervention, 11 of which met the ACSM aerobic guidelines. The length of the interventions ranged from short (ie, 10 days) to as long as 8 months, with 8 of the 20 trials utilizing a 12-week intervention,[29,34,35,37,40,44–46] 3 trials utilizing a 10-week intervention,[39,43,47] 2 utilizing 6-week interventions,[33,49] and single trials utilizing a 32-week,[48] a 16-week,[30] an 8-week,[41] a 2-week,[42] a 1-week,[36] and a 10-day[38] intervention. Interventions included aerobic exercise, resistance exercise, multimodal group-based exercise, walking, aquatic exercise, exercise counseling, tai chi, dance therapy, and yoga (see Table 2).

Figure 2. Forest Plot From Meta-Analysis of Physical Activity on Measures of Depression Showing Estimates of Effect Size With 95% CIs and Relative Weight (% weight) for Each Trial



Abbreviations: ES = effect size, HBE = home-based exercise, LD = low dose, PHD = public-health dose, SE = supervised exercise.

Outcome measures. For the primary outcome of depressive symptoms, the most commonly utilized measure was the Hamilton Depression Rating Scale (HDRS) followed by the Geriatric Depression Index (GDI), the Beck Depression Inventory (BDI, BDI-II) the Edinburgh Postnatal Depression Scale (EPDS), the Centre for Epidemiologic Studies Depression Scale (CES-D), the Depression Anxiety and Stress Scale (DASS), the Bech-Rafaelsen Melancholia Scale (BRMS), and the Inventory of Depressive Symptomatology (IDS).[79] For trials that reported more than one measure of depressive symptoms, the first outcome based on the above sequence was used in the meta-analysis. Scores from the Scale for Assessment of Positive Symptoms (SAPS), Scale for Assessment of Negative Symptoms (SANS),[78] and the Positive And Negative Syndrome Scale (PANSS) were pooled for the schizophrenia symptom analysis. Measures of anthropometry included waist circumference, body mass index (BMI), body weight, body fat percentage, and hip circumference, and when multiple measures were provided, the first outcome based on the above sequence was used. Measures of exercise capacity included volume of oxygen consumption (VO_2), heart rate response to a step test, 6-minute walk distance, and the maximum watts achieved during an exercise assessment. The World-Health Organization Quality of Life Scale (WHO-QOL-BREF), The Health Survey Short Form-36 (SF-36), and the Manchester Short Assessment of Quality of Life (MANSA) were pooled to investigate the impact of physical activity on quality of life.

The Effect of Physical Activity on Depressive Symptoms in People With a Mental Illness

The pooled effect of physical activity on depressive symptoms in participants with a mental illness was large (SMD = 0.80; 95% CI, 0.47–1.13; $P < .001$, $I^2 = 84\%$; Figure 2).

No significant difference in the effect of physical activity on depressive symptoms was found between trials in which the prescribed intervention met ACSM aerobic-training recommendations and those that did not ($P = .71$). In the 11 trials in which the prescribed intervention met the ACSM aerobic training recommendations there was a large pooled effect on depressive symptoms (SMD = 0.94; 95% CI, 0.42–1.45; $P < .001$), while in the 9 trials that did not meet ACSM aerobic training guidelines, a lower pooled effect on symptoms was found (SMD = 0.61; 95% CI, 0.18– 1.04; $P < .01$).

In the 10 trials with a PEDro score of 6 or more (indicating reduced risk of bias), the impact on depressive symptoms was moderate (SMD = 0.39; 95% CI, 0.15–0.63; $P < .005$). For the 10 trials with PEDro scores less than 6, a large

effect was found (SMD = 1.35; 95% CI, 0.52–2.17; $P < .005$). The difference between the subgroups was not statistically significant (P for comparison = .19).

In the subset of trials with a PEDro score of 6 or more, the impact of the intervention in the 5 trials in which the intervention met the guidelines for aerobic training was 0.36 (95% CI, 0.08–0.64; $P < .05$), which was comparable ($P = .97$) to the effect in the 5 trials in which the intervention did not meet the guideline (0.49; 95% CI, −0.03 to 1.0; $P = .06$).

The Effect of Physical Activity on Secondary Outcome Measures

The meta-analysis of schizophrenia symptoms found a large effect of physical activity (SMD = 1.0; 95% CI, 0.37–1.64; $P < .01$; $I^2 = 88\%$) (Supplementary eFigure 2). Meta-analysis of trials investigating the impact of physical activity on anthropometric measures found a small effect (SMD = 0.24; 95% CI, 0.06–0.41; $P < .05$; $I^2 = 0\%$) (Supplementary eFigure 3). Meta-analysis revealed a moderate effect of physical activity on exercise capacity (SMD = 0.63; 95% CI, 0.05–1.21; $P < .05$; $I^2 = 50\%$) (Supplementary eFigure 4). Meta-analysis to determine the impact of physical activity on quality of life found a moderate effect (SMD = 0.64; 95% CI, 0.35 to 0.92; $P < .001$; $I^2 = 0\%$).

DISCUSSION

This systematic review and meta-analysis found that physical activity reduced depressive symptoms among people with a psychiatric illness. This current meta-analysis differs from previous studies, as it included participants with depressive symptoms with a variety of psychiatric diagnoses (except dysthymia and eating disorders). This allowed for a more comprehensive assessment of the impact of physical activity on depressive symptoms across a range of mental health diagnoses, which is important given the high rates of comorbid depressive symptoms found in many psychiatric conditions.[5] The magnitude of the effect of physical activity on depressive symptoms (SMD = 0.80) is in line with previous meta-analyses of exercise and depression in both clinical and nonclinical populations[80] and demonstrates the significant potential of physical activity for reducing depressive symptoms in people with a mental illness.

This review provides strong evidence for the antidepressant effect of physical activity; however, the optimal exercise modality, volume, and intensity remain to be determined. Most of the trials included within this review utilized an aerobic-based intervention; however, there was significant heterogeneity between the trials relating to intensity, frequency, and total volume of prescribed exercise. No significant difference in the effect of physical activity on the primary outcome of depressive symptoms was found between trials in which prescribed interventions met the ACSM aerobic-training guidelines and trials in which the interventions did not. There was some evidence of greater impact in the studies that met the ACSM aerobic guidelines (SMD = 0.94 versus 0.61); however, this must be interpreted with caution as the difference was no longer present in the subset of trials that were methodologically stronger as indicated by higher PEDro scores.

There was a dearth of research regarding the impact of resistance training for people with a mental illness, despite evidence of a beneficial effect for reducing symptoms of depression in other clinical samples such as those with breast cancer[81] or at high risk for type 2 diabetes[82] and multiple sclerosis,[83] and this gap in the current evidence base requires more well-designed clinical trials.

Analysis of the effects of physical activity on schizophrenia symptoms revealed a significant effect of physical activity in reducing symptom severity. This result was largely driven by studies published in Chinese, not previously identified in other reviews.[54,55] Both positive and negative symptoms of schizophrenia were pooled within this secondary analysis. Interventions included dance, yoga, home-based exercise, and other group activity.

A small effect of physical activity on the anthropometric profile of people with a mental illness was found (SMD = 0.24). Greater impacts may be achieved with physical activity interventions that reflect current knowledge regarding the impact of such interventions in weight management. A moderate effect was found of physical activity for improving quality of life in people with a mental illness; however, this must be interpreted with caution as only 6 trials reported outcome data for quality-of-life measures. A similar caveat should be applied to the moderate effect of physical activity on exercise capacity that was found (SMD = 0.66), as only 5 studies reported sufficient data to be pooled.

The current systematic review revealed that substantial methodological limitations are present within the physical activity and mental health literature. This was demonstrated by the difference in effect sizes for the main outcome between the trials of high and low methodological quality (SMD = 0.39 versus 1.35). This difference was not statistically significant, which reflects the variability of individual study results and the relative statistical power of the analysis, but requires further investigation. Methodological limitations included small sample size, lack of concealed allocation and blinding of assessors, and inadequate reporting of outcome measures.

Exercise protocols were poorly described in many of the included trials, and this limited our investigation of the relative effects of different approaches to physical activity. Only 11 of the 42 studies identified for this review described the intensity of the intervention, while many simply stated that the intervention was "aerobic" or "'group-based," rendering the studies unreproducible. Use of the exercise reporting grid proposed by Slade and Keating[84] in physical activity and mental health trials would streamline and simplify reporting of interventions (see Supplementary eTable 2). A clearly defined exercise protocol including a specific "dose"[85] and modality of physical activity would facilitate the translation of research results into practice. Just as pharmacologic trials would not be acceptable if dose was not reported as per the CONSORT statement,[86] trials of physical activity and exercise interventions that

insufficiently report intervention details impede the goal of establishing the utility of such interventions for improving the lives of people experiencing a mental illness. Adherence to intervention is also an important aspect of pharmacologic research that is usually reported. Similarly, measurement and reporting of physical activity participation in physical activity trials, through the use of objective activity monitors or self-report questionnaires, will assist interpretation of results as well as identification of strategies that could increase the effectiveness of such interventions.

Adherence to physical activity interventions is a critical aspect of exercise-based research that requires further investigation to maximize the potential beneficial effects for people with mental illness. We elected to assess the theoretical strength of the physical activity interventions for this review against the ACSM guidelines based on the prescribed volume and intensity (dose) of the intervention as opposed to the reported adherence rates for two reasons: firstly, few trials adequately reported adherence to interventions, and secondly, in order to highlight the lack of integration of exercise guidelines and expertise in the design of interventions.

The role of psychotropic medication is beyond the scope of this review. Given the variety of medications and doses prescribed for patients with different psychiatric diagnoses, and the relatively few studies adequately reporting such detail, meta-regression to determine the effect of physical activity interventions based on medication consumption was not possible. This question does, however, require further investigation to assist clinicians in the prescription of physical activity recommendations.

This review included a range of interventions targeted at increasing physical activity, including structured exercise. Due to the relatively small number of trials identified, and the often poorly defined interventions, it was not possible to conduct separate analyses based on the type and intensity of the interventions. However, it is reasonable to assume that structured, supervised, and progressive exercise may yield superior results compared to nonstructured, unsupervised physical activity based on data from other clinical conditions such as stroke[87] and type 2 diabetes.[88] This review investigated preintervention and postintervention scores rather than pooling outcome data for multiple time points. The question of longevity of effects of physical activity on outcome measures requires further investigation. Furthermore, the effects of physical activity may be moderated by participant-specific factors such as age, comorbidities, and time since diagnosis. Investigation of these factors warrants attention, but was beyond the scope of the current review.

This systematic review has certain limitations that mainly relate to the trials selected for inclusion. These include lack of reporting of intervention adherence, poor methodological quality, and nonstandardized reporting of intervention protocols. These factors limited the ability of the review to measure the impact of greater intervention adherence and specific intervention protocols on the primary and secondary outcomes. Additionally many of the participants in the studies reviewed were receiving concomitant psychotropic medications, which could impact the outcomes reported. If participants experience a change in physical activity at the same time as a change in medication, it is not possible to ascribe the source of any outcomes to either or both of these potential interventions.

CONCLUSION

Few interventions exist whereby patients can hope to achieve improvements in both psychiatric symptoms and physical health simultaneously without significant risks of adverse effects. Physical activity offers substantial promise for improving outcomes for people living with mental illness, and inclusion of physical activity and exercise programs within treatment facilities is warranted given the results of this review. The future of physical activity and exercise as viable and accepted components of usual care within mental health settings will be enhanced by more methodologically rigorous clinical research, using well-designed intervention protocols that adhere to established principles of physical activity and exercise prescription.

Drug names: escitalopram (Lexapro and others).

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See supplementary material for this article at PSYCHIATRIST.COM.

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Supplementary Material

Article Title: Physical Activity Interventions for People With Mental Illness: A Systematic Review and Meta-Analysis

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List of Supplementary Material for the article

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Supplementary eFigure 1. Inclusion criteria

Design

- Randomized controlled trial

Participants

- Adults, aged 18 years or greater
- DSM, ICD or other diagnosis of a mental illness (excluding dysthymia, mild depression and eating disorders)

Interventions

- Physical activity or structured exercise program
- Exercise counselling
- Lifestyle interventions in which physical exercise was at least 50% of total intervention
- Tai Chi, physical yoga

Outcome measures

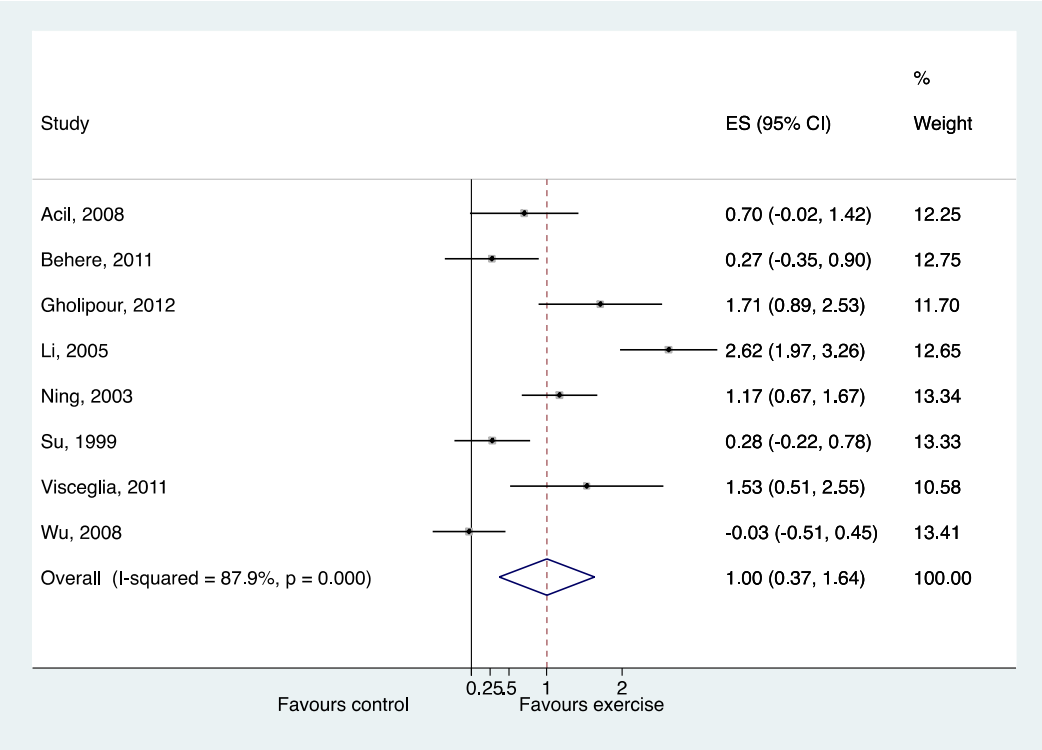
- Depressive symptoms
- Positive and negative symptoms of schizophrenia
- Anthropometry
- Exercise capacity
- Quality of life

Comparisons

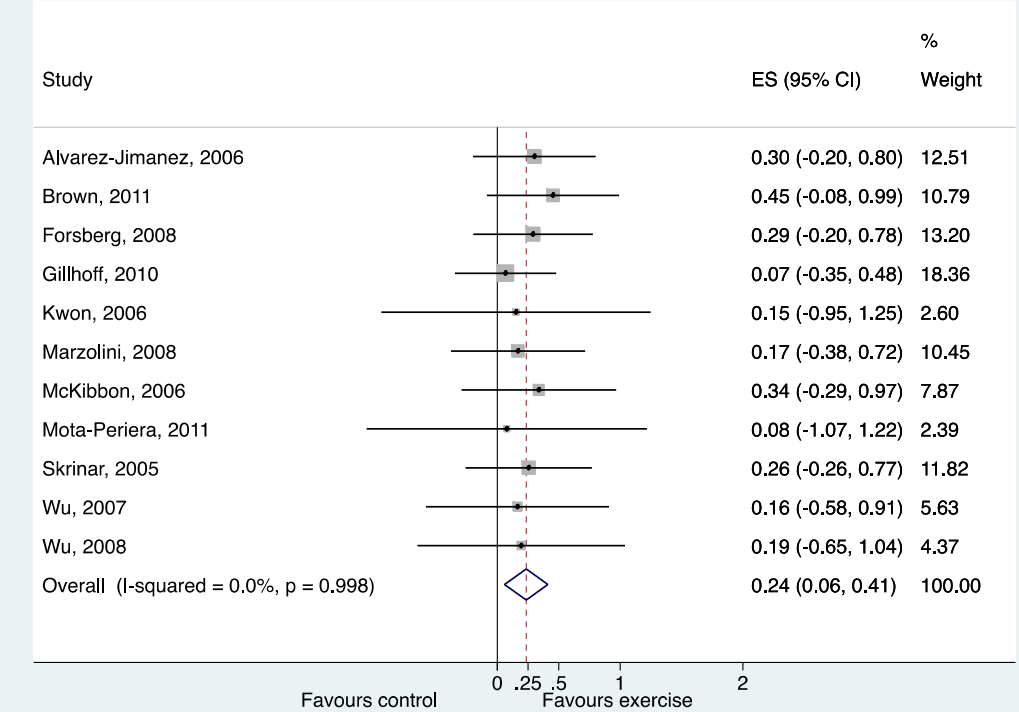
- Physical activity/ exercise program versus usual care
- Physical activity/ exercise program versus wait-list
- Physical activity/ exercise program versus health education (not physical activity based)
- Physical activity program versus no treatment

Supplementary eFigure 2.

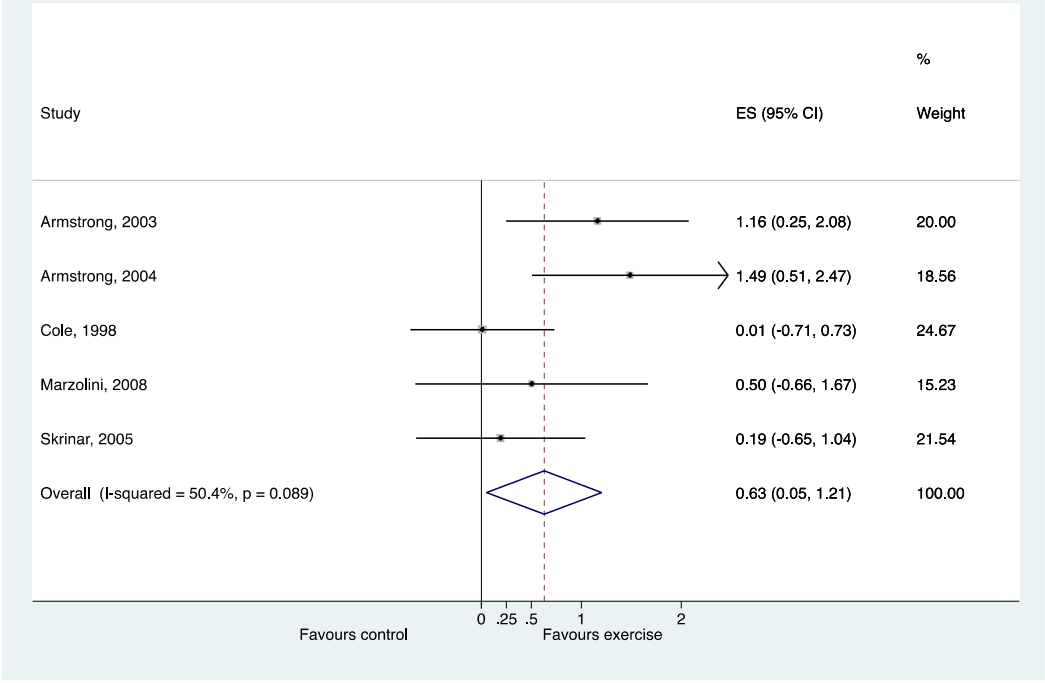
Forest plot from meta-analysis of physical activity on symptoms of schizophrenia showing estimates of effect size with 95% confidence intervals and relative weight (% weight) for each trial.



Supplementary eFigure 3. Forest plot from meta-analysis of physical activity on anthropometric measurements showing estimates of effect size with 95% confidence intervals and relative weight (% weight) for each trial.



Supplementary eFigure 4. Forest plot from meta-analysis of physical activity on exercise capacity showing estimates of effect size with 95% confidence intervals and relative weight (% weight) for each trial.



Supplementary eTable 1

Methodological quality of included trials for primary meta-analysis (n=20)

Trial	PEDro Score	Eligibility criteria specified	Random allocation	Concealed allocation to groups	Groups similar at baseline	Blinding of all subjects	Blinding of therapists who administered therapy	Blinding assessment of outcome measures	Measures obtained from more than 85% of subjects	Intention to treat analysis	Between-group statistical comparisons reported	Both point measures and measures of variability reported
Abt, 2006[33] N=31	5	Yes	Yes	No	Yes	No	No	No	No	Yes	Yes	Yes
Armstrong, 2003[34] N=20	6	Yes	Yes	Yes	Yes	No	No	No	Yes	No	Yes	Yes

Armstrong, 2004[35] N=19	5	Yes	Yes	Yes	Yes	No	No	No	No	No	Yes	Yes
[$]Berlin, 2003[36] N=39 (ex vs control)	3	Yes	Yes	No	No	No	No	No	No	No	Yes	Yes
Blumenthal, 2007[30] N= 202 (HE ex vs control; SE vs control)	8	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes

Chalder, 2012[48] N= 361	6	Yes	Yes	Yes	Yes	No	No	No	No	Yes	Yes	Yes
Daley, 2008[37] N=38	5	Yes	Yes	No	Yes	No	No	No	No	Yes	Yes	Yes
Dunn, 2005[29] N=80 (pooled groups)	8	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes
Herring, 2011[49] N=30 (pooled groups)	6	No	Yes	No	Yes	No	No	Yes	Yes	No	Yes	Yes

Knubben, 2007[38] N=38	7	Yes	Yes	Yes	Yes	No	No	Yes	No	Yes	Yes	Yes
Lavretsky, 2011[47] N=73	8	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes
Mather, 2002[39] N=86	8	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes
Mota-Pereira, 2011[40] N=29	5	Yes	Yes	No	Yes	No	No	No	Yes	No	Yes	Yes
Netz, 1994[41] N=17	3	Yes	Yes	No	No	No	No	No	Yes	No	Yes	No

Nguyen, 2008[42] N=88	4	Yes	Yes	No	No	No	No	No	Yes	No	Yes	Yes
Schuch, 2011[50] N=26	5	No	Yes	No	Yes	No	No	No	Yes	No	Yes	Yes
Singh, 1997[43] N=13 (major depression only)	6	Yes	Yes	No	Yes	No	No	Yes	Yes	No	Yes	Yes
Veale, 1992[44] N=65	3	No	Yes	No	No	No	No	No	No	No	Yes	Yes

Viera, 2007[45] N=18 (Brazil)	3	Yes	Yes	No	No	No	No	No	No	No	Yes	Yes
Yeung, 2012[46] N=39	8	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes

[a]*PEDro score* ≥6 high methodological quality; PEDro score <6 low methodological quality

Supplementary eTable 2. Proposed exercise reporting grid

(Adapted with permission from: Slade SC, Keating JL. Exercise prescription: a case for standardised reporting. Br J Sports Med. 2012;46:1110–3.)

	Intervention	Control
Total sample size		
Gender %		
Name of exercises		
Setting (clinic, gym etc)		
One-on-one		
Group		
Instructor qualification		
Supervision		
Adherence measures		
Motivation strategies		
Machinery/equipment		
Individually tailored		
One size fits all exercise program		
Muscle group(s)		
Resistance exercise		
Stretching		
Aerobic exercise		
Home program		
Exercise into pain		
Exercise without pain		
Warm-up (type & time)		
Cool-down (type & time)		
Starting position		
Initial exercise reps & sets		
Decision rule for starting ex dosage		
Final exercise reps and sets		
Session duration (mins)		
Number of sessions (per wk)		
Program duration (wks)		
Exercise speed		
Exercise sequence		
Rest between reps & sets		
Ex progression decision rules		
Outcome measures		
Compliance (%) and how measured		
Drop outs & reasons		
Adverse events		
Short-term follow-up		
Long-term follow-up		

eAppendix 1

MEDLINE search strategy

1	exp exercise	57203
2	exp exercise therapy	23899
3	exp physical exertion	50886
4	exp walking	14562
5	exp running	11311
6	exp swimming	16230
7	exp jogging	655
8	exp bicyling	6157
9	exp physical education/ and train.mp [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier]	11138
10	exp resistance training	1470
11	exp aerobic exercise	57203
12	exp physical activity	98445
13	exercise$.tw.	161807
14	(physical adj1 activ$).mp.	39824
15	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15	327242
16	exp mental disorders	832439
17	exp depression	61934
18	exp anxiety disorder	57409

19	exp bipolar disorder	27615
20	exp post traumatic stress disorder	17017
21	exp schizophrenia	76406
22	exp eating disorder	19351
23	exp mood disorder	100468
24	exp obsessive compulsive disorder	10042
25	exp panic disorder	5415
26	mental health.tw.	56966
27	mental illness.tw.	12319
28	16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27	897437
29	randomized controlled trial.pt.	314563
30	random.tw.	126398
31	randomly.ab.	159149
32	random$.tw.	531657
33	29 or 30 or 31 or 32	618930
34	15 and 28 and 33	1724