Psychological Medicine (2015), **45**, 1343–1361. © Cambridge University Press 2015
doi:10.1017/S0033291714003110

REVIEW ARTICLE

A systematic review and meta-analysis of exercise interventions in schizophrenia patients

J. Firth[1]*, J. Cotter[1], R. Elliott[1,2], P. French[3,4] and A. R. Yung[1,5]

[1] *Institute of Brain, Behaviour and Mental Health, University of Manchester, UK*
[2] *Manchester Academic Health Sciences Centre, University of Manchester, UK*
[3] *Psychosis Research Unit, Greater Manchester West NHS Mental Health Trust, UK*
[4] *Institute of Psychology, Health and Society, The University of Liverpool, UK*
[5] *Orygen Youth Health Research Centre, University of Melbourne, Australia*

Background. The typically poor outcomes of schizophrenia could be improved through interventions that reduce cardiometabolic risk, negative symptoms and cognitive deficits; aspects of the illness which often go untreated. The present review and meta-analysis aimed to establish the effectiveness of exercise for improving both physical and mental health outcomes in schizophrenia patients.

Method. We conducted a systematic literature search to identify all studies that examined the physical or mental effects of exercise interventions in non-affective psychotic disorders. Of 1581 references, 20 eligible studies were identified. Data on study design, sample characteristics, outcomes and feasibility were extracted from all studies and systematically reviewed. Meta-analyses were also conducted on the physical and mental health outcomes of randomized controlled trials.

Results. Exercise interventions had no significant effect on body mass index, but can improve physical fitness and other cardiometabolic risk factors. Psychiatric symptoms were significantly reduced by interventions using around 90 min of moderate-to-vigorous exercise per week (standardized mean difference: 0.72, 95% confidence interval −1.14 to −0.29). This amount of exercise was also reported to significantly improve functioning, co-morbid disorders and neurocognition.

Conclusions. Interventions that implement a sufficient dose of exercise, in supervised or group settings, can be feasible and effective interventions for schizophrenia.

Received 15 August 2014; Revised 1 December 2014; Accepted 9 December 2014; First published online 4 February 2015

Key words: Exercise, functional recovery, physical activity, psychotic disorders, schizophrenia.

Introduction

Schizophrenia is a common disorder with high personal, social and economic impact. Most people with schizophrenia are unemployed, supported by benefits and require high levels of health and social care (Knapp *et al.* 2004; Schizophrenia Commission, 2012). In the UK, the direct and indirect costs of the illness reach an estimated £55 000 per person per year (Mangalore & Knapp, 2007), higher than cancer.

Although anti-psychotic medication is effective for positive psychotic symptoms, usually within the first few months of treatment (Crespo-Facorro *et al.* 2006; Malla *et al.* 2006), it is of less benefit for negative symptoms and cognitive deficits (Erhart *et al.* 2006; Kirkpatrick *et al.* 2006; Goldberg *et al.* 2007). Unfortunately, it is these features that cause most disability (Green, 1996; Albert *et al.* 2011; Rabinowitz *et al.* 2012). This has been recognized by researchers and clinicians, and the National Institute for Health and Care Excellence (NICE; previously National Institute for Health and Clinical Excellence) guidelines for schizophrenia now recommended the use of adjunctive psychosocial interventions to facilitate complete and sustained recovery (National Institute for Health and Clinical Excellence, 2010). Cognitive–behavioural therapy, family therapy and skills training may reduce negative and cognitive symptoms, improve functioning and reduce long-term disability (Bustillo *et al.* 2001; Kern *et al.* 2009). However, these interventions tend to be costly and access is poor (Schizophrenia Commission, 2012). Thus, new low-cost and accessible treatments that decrease negative symptoms, reduce cognitive deficits and promote functional recovery are needed.

In addition to its lack of efficacy for negative and cognitive symptoms, anti-psychotic treatment is also

* Address for correspondence: J. Firth, University of Manchester, Room 3.306, Jean McFarlane Building, Oxford Road, Manchester M13 9PL, UK.

(Email: joseph.firth@postgrad.manchester.ac.uk)

https://doi.org/10.1017/S0033291714003110 Published online by Cambridge University Press

associated with the 'metabolic syndrome' (Hert *et al.* 2009), a cluster of co-occurring risk factors for diabetes and cardiovascular disease such as obesity, high blood pressure and hyperglycaemia (Alberti *et al.* 2005). At the onset of psychotic illnesses, the prevalence of these risk factors is no different from that in the general population (Foley & Morley, 2011). However, over the first few years of taking antipsychotics, the incidence of the metabolic syndrome increases fivefold (De Hert *et al.* 2008) and body weight increases by up to 15 kg (Alvarez-Jiménez *et al*. 2008*a*). This decline in physical health continues over time, and reduces the life expectancy of people with schizophrenia by 15–20 years (Hennekens *et al.* 2005; Laursen, 2011).

There are therefore two pressing issues in the management of schizophrenia: the need to develop feasible interventions for negative symptoms and cognitive dysfunction, and the need to reduce physical health inequalities. Exercise is one possible candidate that could meet both of these needs. For instance, exercise can reduce symptoms in clinical depression (Cooney *et al.* 2013) and improve cognitive functioning in neurological disorders (Angevaren *et al.* 2008; Smith *et al.* 2010). The National Institute for Health and Care Excellence (2014) now recommends using physical activity and dietary advice to improve the physical health of people with schizophrenia, based on their recent systematic review. However, the National Institute for Health and Care Excellence (2014) review focused on behavioural interventions to promote healthy lifestyles, but did not evaluate the impact of directly administered exercise in schizophrenia. Furthermore, effects of physical activity on psychiatric symptoms were not considered.

Therefore, the effectiveness of exercise as a treatment for schizophrenia still needs to be established. A Cochrane review was conducted in 2010, but could not reach any strong conclusions due to the small number of trials ($n = 3$) (Gorczynski & Faulkner, 2010). Since then, many more trials have taken place. However, the currently available evidence has yet to be reviewed in full.

We conducted a systematic review and meta-analysis to provide a comprehensive summary of all exercise trials in schizophrenia, and to quantify effects on both physical and mental health. Physical outcomes include metabolic risk and physical fitness. Mental health outcomes include positive and negative symptoms, psychosocial functioning, co-morbid disorders and neurocognitive dysfunction. The feasibility of different exercise treatments will also be assessed by comparing adherence and attrition across trials. This has been overlooked in previous reviews but is a crucial factor for determining the clinical applicability of exercise in schizophrenia and informing future trial design.

Method

Eligibility criteria

Only original English-language, peer-reviewed research articles were included in the present review. Studies comprised entirely of participants with any non-affective psychotic disorder were considered, with no restrictions placed on the severity or duration of illness. However, studies published prior to 1994 were excluded to increase diagnostic homogeneity, since this is when the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) and International Classification of Diseases (ICD)-10 came into use. First-episode psychosis (FEP) studies were also eligible regardless of formal diagnostic status of participants since, in these early stages, diagnoses are often changed or postponed until temporal criteria are fulfilled (Schwartz *et al.* 2000).

Eligible studies must have reported the effect of exercise on at least one quantitative measure of physical or mental health. Within health research, 'exercise' is defined as any structured and repetitive physical activity that has an objective of improving or maintaining physical fitness (Caspersen *et al.* 1985). Any intervention using physical activity matching this description was considered, regardless of trial design. Interventions that only used yoga, muscular relaxation or adventure activities were excluded, since their effects are theoretically derived from factors distinct from exercise. Multi-modal programmes that incorporated exercise within a broader lifestyle or psychosocial intervention were also excluded, as the effects of exercise alone cannot be determined.

Search strategy

An electronic database search of Ovid MEDLINE, Embase, PsycINFO and the Cochrane Central Register of Controlled Trials (CENTRAL) was conducted on 1 November 2013 (with an updated search on 6 April 2014) using the following keyword search terms: 'exercise' or 'physical activity' or 'sport*' or 'aerobic training' or 'anaerobic training' or 'endurance training' or 'resistance training' or 'walking' or 'muscle strengthening' and 'psychotic' or 'psychosis' or 'psychoses' or 'schizo*' and 'intervention' or 'treatment' or 'trial' or 'program*'. The reference lists of retrieved articles were searched to identify any additional papers.

Study selection and data extraction

Two reviewers (J.F. and J.C.) independently screened articles for eligibility; disagreements were resolved through discussion. A systematic tool was developed, and quantitative data from each study were extracted and categorized into the following domains:

https://doi.org/10.1017/S0033291714003110 Published online by Cambridge University Press

- P1: metabolic health – body composition and cardio-metabolic risk factors;
- P2: physical fitness – cardiorespiratory fitness and physical capacities;
- M1: psychiatric symptoms – positive, negative and general symptoms;
- M2: functioning and disability – quality of life (QoL), socio-occupational functioning and overall illness severity;
- M3: co-morbid disorders – specific or subscale measures of depression/anxiety;
- M4: neurocognitive effects – brain structure and neurocognitive functioning.

Secondary data on sample characteristics, study design, exercise details, adherence and attrition were also extracted to examine factors that may alter the effectiveness or feasibility of exercise.

Meta-analysis

Meta-analyses were conducted to examine effects on body mass index (BMI) and psychiatric symptoms, as these were the most commonly reported physical and mental health outcomes. Although single-arm studies, non-randomized trials and randomized controlled trials (RCTs) were all included within the review, only RCTs were used in the meta-analyses (to increase the validity of findings).

All analyses were performed in Review Manager 5, the recommended meta-analytic software of the Cochrane Collaboration (Higgins & Green, 2008). The risk of bias for each RCT was also assessed using the Cochrane's Collaboration respective tool (Higgins *et al.* 2011). This examines six different aspects of trial methodology that could potentially introduce bias; summaries are presented in the Appendix (Figs A1 and A2). To quantify the amount of variation in studies' effect estimates due to heterogeneity, the I^2 test was used. These values can be described as small (0–25%), medium (25–50%) or large (>50%). Due to the considerable variation across exercise studies, a random-effects model (based on the method of DerSimonian & Laird, 1986) was applied throughout. This accounts for variation through providing conservative estimates adjusted in relation to the extent of heterogeneity.

When pooling outcomes data across studies, effects on BMI were calculated by pooling mean differences. Standardized mean difference (SMDs) was used for psychiatric symptoms, to allow for integration of various assessment measures. In both cases, effects were calculated by comparing change in the exercise condition with change in the control condition(s). In studies with more than two conditions, all data from non-exercise conditions were pooled into a single comparator group (Higgins & Green, 2008).

Results

The database search returned 2275 results, providing 1581 unique citations after duplicates were removed. A further 1521 articles were excluded at the title–abstract stage. For the remaining 60, the full paper was sought. Of these, 20, reporting data from 17 different trials, met full eligibility criteria and were included in the review. Searching the reference lists of eligible studies did not identify any additional eligible studies. The full study selection process is shown in Fig. 1.

We could not evaluate publication bias using the Cochrane test for funnel plot asymmetry, since fewer than 10 studies were included in each analysis (Higgins *et al.* 2011). To address publication bias, we applied our initial search terms to four 'grey literature' databases (MetaRegistry of Controlled Trials, Index to Thesis, Health Management Information Consortium and OpenGrey). The search returned 227 results, although 203 articles were removed by screening titles and deleting duplicates (including those from the main search). For the remaining 14 studies, all available details were examined and trial protocols were sought. This information revealed that all of these would be excluded from our review due to an ineligible sample ($n = 1$), ineligible intervention ($n = 8$) or both ($n = 5$). Therefore, there is no evidence of existing unpublished trials that would influence our results.

Study characteristics

Across all 17 trials, the total number of participants with non-affective psychotic disorders was 659. The median age was 33 years (range = 25–52 years). The median illness duration was 10 years. Only one study used a FEP sample (less than 5 years illness duration).

Of the trials, four implemented exercise as a physical activity control for assessing the effects of yoga (Duraiswamy *et al.* 2007; Behere *et al.* 2011; Varambally *et al.* 2012; Manjunath *et al.* 2013). The 13 other trials investigated the benefits of exercise, with primary outcomes of physical health ($n = 5$), mental health ($n = 5$) or both ($n = 3$). Of the trials, 10 described themselves as pilots, with five stating their primary objective as assessing the feasibility of exercise (Archie *et al.* 2003; Marzolini *et al.* 2009; Dodd *et al.* 2011; Abdel-Baki *et al.* 2013; Bredin *et al.* 2013).

International physical activity guidelines structure their recommendations around time spent exercising at a moderate or vigorous intensity per week (World Health Organization, 2010; Garber *et al.* 2011). Therefore, we recorded the amount of moderate or vigorous exercise applied by each exercise intervention per week, in order to provide an approximate measure of exercise quantity across studies. Moderate-to-vigorous exercise constitutes activities such as jogging,

https://doi.org/10.1017/S0033291714003110 Published online by Cambridge University Press

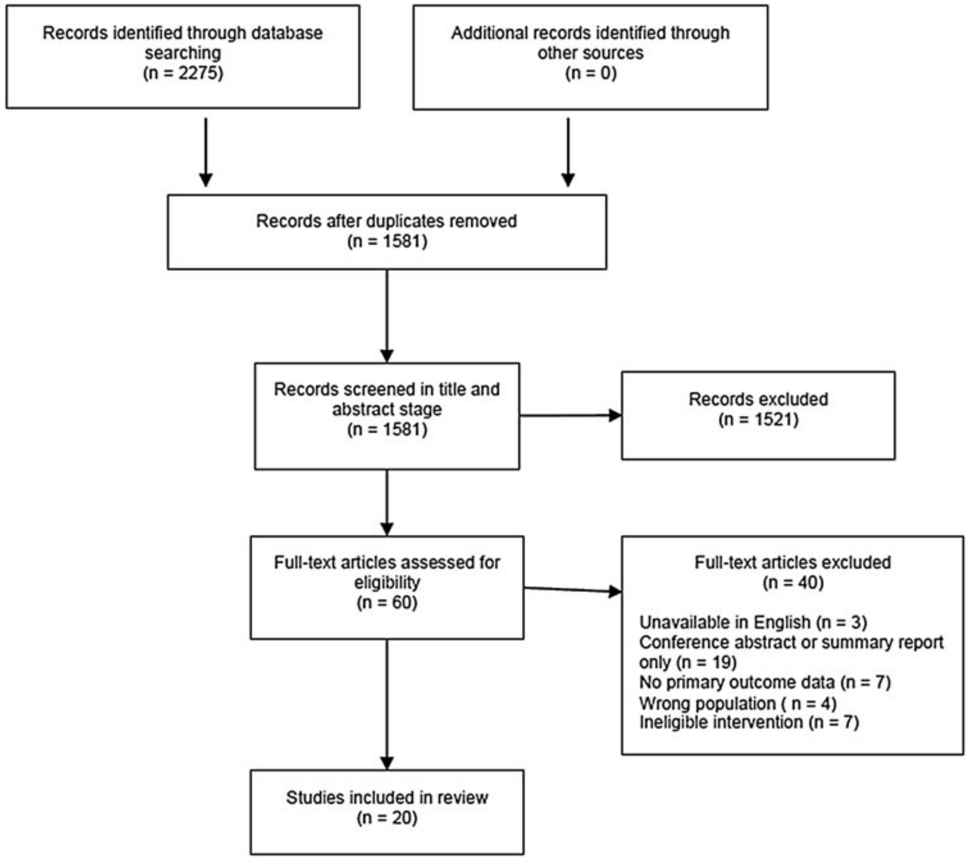

Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram.

cycling, sports or resistance training, while stretching, warm-ups or self-paced walking are classified as low intensity (World Health Organization, 2010; Garber *et al.* 2011). In all, 15 trials specified some moderate-to-vigorous intensity exercise. The median amount was 75 min per week (mean 72 min, range 25–160 min).

Of the trials, 11 were RCTs. Risk of bias assessments are presented in the Appendix (Figs A1 and A2). To summarize, nine used adequate random sequence generation, six had allocation concealment procedures, six stated that assessors were blinded to intervention status and eight may have been affected by attrition or reporting bias. As only one study used an intention-to-treat analysis, our analyses were based on per-protocol outcome data. Due to the very limited number of randomized trials, all RCTs were included in our analyses, regardless of their bias assessment.

Physical health outcomes (Table 1)

P1: markers of metabolic health

Of the 11 trials assessing physical health, 10 observed significant improvement from exercise in at least one measure. Body weight (or BMI) was the most common measure of physical health. This was examined in nine studies, four of which were RCTs. The pooled mean difference from the RCTs (Beebe *et al.* 2005; Marzolini *et al.* 2009; Battaglia *et al.* 2013; Scheewe *et al.* 2013*a*) was calculated using the random-effects model, and it was found that exercise did not significantly reduce BMI across 80 participants [mean difference = $-0.98\ \mathrm{kg/m^2}$; 95% confidence interval (CI) -3.17 to $1.22\ \mathrm{kg/m^2}$] (Fig. 2).

Six non-randomized trials also reported body weight/BMI. Two studies observed a significant reduction in body weight from group training programmes (Dodd *et al.* 2011; Bredin *et al.* 2013). Two other studies, using solitary exercise, observed clinically significant improvements among the few participants who attended exercise sessions, but experienced very high attrition (Archie *et al.* 2003; Abdel-Baki *et al.* 2013). Two further studies, using high-intensity interval training (Heggelund *et al.* 2011) and maximal strength training (Heggelund *et al.* 2012), observed no change in body weight.

Findings were inconsistent for several other measures of metabolic health. This was the case both within and between studies. For example, Bredin *et al.* (2013) and Abdel-Baki *et al.* (2013) reported substantial decreases in waist circumference, while others observed no change (Marzolini *et al.* 2009; Scheewe

https://doi.org/10.1017/S0033291714003110 Published online by Cambridge University Press

https://doi.org/10.1017/S0033291714003110 Published online by Cambridge University Press

Table 1. *Outcomes of exercise trials in psychotic disorders*

Study	Primary outcomes	Patient group	Mean age, years	Duration of illness, years	Study arms	RCT, yes/no)	Key findings
Abdel-Baki *et al.* (2013)	Feasibility of exercise, and effects on metabolic health/fitness	FEP	25	About 3.6	Aerobic interval training (*n* = 25) No control	No	Participants completing the programme had: P1: reduced body weight (↓ 1 kg), WC (↓ 4.3 cm*) and resting heart rate (↓ 8.6 bpm*) P2: improved CV fitness (↑ 38%* in V_{O2max}) M2: no change in psychosocial functioning (GAF, SOFAS) or illness severity (CGI-S)
Acil *et al.* (2008)	Effects on QoL and psychotic symptoms	SZ	30	About 10	Aerobic exercise (*n* = 15) TAU control (*n* = 15)	Yes	Only changes from baseline were reported. TAU group showed no significant change M1: exercise decreased positive and negative symptoms (↓ 38%* SAPS, ↓ 41% SANS*) M2: exercise improved mental and physical QoL (↑ 14%* in WHO-QOL-BREF mental and physical subscales) and overall mental health (↓ 40% BSI*) M3: exercise improved in BSI subscale anxiety, but had no effect on depression
Archie *et al.* (2003)	Adherence to unsupervised exercise	SZ SZ-AF	27	N/R	Gym access (*n* = 10) TAU (*n* = 10)	No	P1: participants gained a mean of 2 kg over the intervention period. However, the one who adhered to recommended exercise significantly reduced body weight (−15 kg)
Battaglia *et al.* (2013)	Effects on fitness and QoL	SZ SZ-AF	36	N/R	Soccer training (*n* = 10) TAU control (*n* = 8)	Yes	P1: soccer training decreased body weight/BMI more than TAU control (Δ5.4%*) P2: soccer training improved functional exercise capability (30 m* sprint) M2: soccer training improved QoL more than TAU control (↑ 10.6%* SF-12)
Beebe *et al.* (2005)	Effects on fitness, body weight and psychotic symptoms	SZ SZ-AF	52	N/R	Treadmill walking (*n* = 6) Waitlist control (*n* = 6)	Yes	P1: treadmill walking reduced body fat (3.7%* *v.* 0.02% control) P2: treadmill walking improved CV fitness (↑ 11%** walking distance, *v.* 4% control) M1: treadmill walking reduced psychotic symptom severity compared with TAU (Δ19%** PANSS total)
Behere *et al.* (2011)	Effects of yoga on facial emotion recognition	SZ	32	About 10	Yoga (*n* = 34) NFP (*n* = 31) Waitlist (*n* = 26)	Yes	Note: yoga showed significantly greater effects than exercise (NFP) in all measures M1: no change in psychotic symptoms in NFP or waitlist control (PANSS)

https://doi.org/10.1017/S0033291714003110 Published online by Cambridge University Press

Table 1 (*cont.*)

Study	Primary outcomes	Patient group	Mean age, years	Duration of illness, years	Study arms	RCT, yes/no)	Key findings
							M2: no significant change in social functioning in NFP or waitlist control (SOFS)
Bredin *et al.* (2013)	The risk of CV disease in SZ, and feasibility of exercise for reducing this	SZ	31	N/R	Aerobic–resistance training ($n = 13$) No control	No	Before-and-after comparisons showed: P1: reduction in weight (↓ 3 kg**), WC (↓ 6.6 cm**) and blood pressure P2: improvement in CV fitness (↑ 12%** V_{O2max}, ↑ time to exhaustion, ↑ power) M1: reduction in psychotic symptom severity (↓ 15.8%** PANSS total)
Dodd *et al.* (2011)	Feasibility of exercise, and effects on body weight	SZ SZ-AF	46	>10	Group aerobic programme ($n = 8$) No control	No	Before-and-after comparisons showed: P1: reduction in body weight (↓ 2.4%*) and BMI (↓ 2.2%*) P2: improvement in CV fitness (↑ 11% V_{O2max}) M1: no significant change in psychotic symptom severity (↑ 6.2% PANSS-P, ↓ 6.7% PANSS-N, ↓ 6.4% PANSS-G)
Duraiswamy *et al.* (2007)	Efficacy of yoga as an adjunctive treatment for reducing psychiatric symptoms	SZ	32	About 7	Yoga ($n = 31$) NFP ($n = 30$)	Yes	Note: yoga resulted in significantly more improvement than NFP across all measures M1: NFP reduced positive and negative psychotic symptoms from baseline (↓ 24% PANSS-P, ↓ 18%* PANSS-N, ↓ 21%* PANSS total) M2: NFP improved socio-occupational functioning from baseline (↓ 23%* SOFS) M3: NFP reduced depression from baseline (↓ 21%* PANSS subscale)
Pajonk *et al.* (2010), Falkai *et al.* (2013)	Effects of exercise on fitness, symptoms, cognition and hippocampal volume	SZ	35	About 10.4	Aerobic exercise ($n = 13$) Table football ($n = 11$)	Yes	P2: exercise improved fitness more than table football (Δ10% power, Δ8%V_{O2max}) M1: exercise reduced psychotic symptoms more than table football (Δ22%* PANSS) M4: exercise increased verbal STM (↑ 34%*) and hippocampal volume (↑ 12%*) more than table football. Increases in brain volume correlated with fitness ($r = 0.83$*)
Gholipour *et al.* (2012)	Effect of exercise and behavioural	SZ	41	N/R	Exercise ($n = 15$) Behavioural	Yes	M1: exercise reduced negative symptoms more than TAU (↓ 30% SANS*). However, there was a greater effect from behavioural therapy (↓ 47% SANS*)

https://doi.org/10.1017/S0033291714003110 Published online by Cambridge University Press

	therapy on negative symptoms				therapy ($n = 15$) TAU ($n = 15$)		
Heggelund *et al.* (2011)	Effects of HIT on walking ability and CV risk factors	SZ SZ-AF DD	34	About 8.7	HIT ($n = 16$) Computer games control ($n = 9$)	No	P1: HIT improved HDL-cholesterol. No significant changes in weight/BMI P2: HIT improved CV fitness (↑ 12% V_{O2}*) and walking efficiency (↑ 12% E-net*) M1: no significant change in psychotic symptom severity (PANSS) M2: no significant change in QoL (SF-36) M3: no significant change in depression (CGSS)
Heggelund *et al.* (2012)	Effect of strength training on gait deficits	SZ SZ-AF DD	38	About 14	Strength training ($n = 7$) Computer games control ($n = 9$)	No	P1: no significant change in body weight/BMI P2: strength training increased strength (↓ 38%*), walking efficiency (↑ 3.4% E-net*) M1: no significant change in psychotic symptoms (PANSS) M2: no significant change in QoL (SF-36)
Manjunath *et al.* (2013)	Efficacy of yoga as an adjunctive treatment for reducing psychiatric symptoms	SZ	32	About 9	Yoga ($n = 44$) Exercise ($n = 44$)	Yes	Note: yoga resulted in significantly more improvement than exercise in all measures M1: exercise reduced positive and negative symptoms from baseline (↓ 51% PANSS*) M2: exercise reduced overall mental illness from baseline (↓ 35%* CGI-S) M3: exercise reduced depression from baseline (↓ 56%* HAMD)
Marzolini *et al.* (2009)	Feasibility of using aerobic–resistance training for fitness and overall mental health	SZ SZ-AF	45	N/R	Aerobic-resistance training ($n = 7$) TAU control ($n = 6$)	Yes	P1: aerobic–resistance had no significant effect on BMI or WC P2: aerobic–resistance increased fitness (Δ13%* walk test) and strength (↑ 21%*) M2: aerobic–resistance improved overall mental health from baseline (15%* MHI) M3: aerobic-resistance improved depression (25% MHI subscale). This change was non-significant, but increased fitness did correlate with reduced depression ($r = 0.9$*)
Scheewe *et al.* (2013*a*), Scheewe *et al.* (2013*b*), Scheewe *et al.* (2012)	Efficacy of exercise for improving fitness, symptoms and brain volume	SZ SZ-AF SZ-P	30	About 7	Aerobic–resistance training ($n = 31$) Occupational therapy ($n = 32$)	Yes	In comparison with occupational therapy: P1: exercise decreased triglycerides (↓ 13.5%) but had no effect on BMI, HDL or WC P2: exercise increased CV fitness (Δ13%* peak work rate, Δ9% V_{O2max})

Table 1 (*cont.*)

Study	Primary outcomes	Patient group	Mean age, years	Duration of illness, years	Study arms	RCT, yes/no)	Key findings
							M1: exercise reduced psychotic symptoms (↓ 20.7% *v.* ↑3.3% PANSS*) M2: exercise reduced 'need of care' (↓ 22% *v.* ↓ 4% CAN*) M3: exercise reduced depression (↓ 36.6% *v.* ↓ 4.4% MADRS*) M4: there were no significant changes in brain volume. However, changes in brain volume correlated significantly with increased CV fitness
Varambally *et al.* (2012)	Efficacy of yoga as an adjunctive treatment for reducing psychiatric symptoms	SZ	33	About 10	Yoga ($n = 47$) NFP ($n = 37$) Waitlist ($n = 36$)	Yes	Note: yoga produced greater improvement than exercise across all measures M1: NFP had no effect on psychotic symptoms in comparison with waitlist control (↓ 13% *v.* ↓ 9% PANSS total) M2: NFP improved socio-occupational functioning (17%* SOFS *v.* 9% control)

RCT, Randomized controlled trial; FEP, first-episode psychosis; P1, metabolic health; ↓, decrease; WC, waist circumference; bpm, beats per min; P2, physical fitness; CV, cardiovascular; ↑, increase; V_{O2max}, maximal oxygen consumption; M2, functioning and disability; GAF, Global Assessment of Functioning; SOFAS, Social Occupational Functioning Assessment Scale; CGI-S, Clinical Global Impressions Severity; QoL, quality of life; SZ, schizophrenia; TAU, treatment as usual; M1, psychiatric symptoms; SAPS, Scale for Assessment of Positive Symptoms; SANS, Scale for Assessment of Negative Symptoms; WHO-QOL-BREF, World Health Organization Quality of Life Abbreviated; BSI, Brief Symptom Inventory; M3, co-morbid disorders; SZ-AF, schizo-affective disorder; N/R, not reported; BMI, body mass index; SF-12, Short Form Health Survey – 12 items; PANSS, Positive and Negative Syndrome Scale; NFP, National Fitness Corps Programme; SOFS, Socio-Occupational Functioning Scale; PANSS-P, Positive and Negative Syndrome Scale, positive symptoms scale; PANSS-N, Positive and Negative Syndrome Scale, negative symptoms scale; PANSS-G, Positive and Negative Syndrome Scale; general scale; M4, neurocognitive effects; STM, short-term memory; HIT, high-intensity training; DD, delusional disorder; HDL, high-density lipoprotein; E-Net, net efficiency of walking; SF-36, Short Form Health Survey – 36 items; CGSS, Calgary Depression Scale for Schizophrenia; HAMD, Hamilton Depression Rating Scale; MHI, Mental Health Inventory; SZ-P, schizophreniform disorder; CAN, Camberwell Assessment of Need; MADRS, Montgomery–Åsberg Depression Rating Scale.

* $p < 0.05$; ** reported as 'clinically significant' improvement.

https://doi.org/10.1017/S0033291714003110 Published online by Cambridge University Press

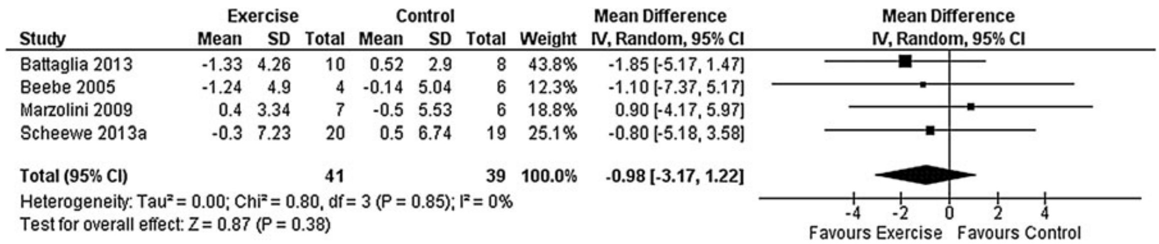

Fig. 2. Forest plot showing change in body mass index in exercise and control conditions. SD, Standard deviation; IV, inverse variance; CI, confidence interval; df, degrees of freedom.

et al. 2013*a*). Heggelund *et al.* (2011) reported improvement in high-density lipoprotein (HDL) levels with no change in triglycerides, while Scheewe *et al.* (2013*a*) reported the opposite of this (i.e. improved triglycerides with no change in HDL).

P2: physical fitness

Seven studies used V_{O2max} as an assessment of fitness (Pajonk *et al.* 2010; Dodd *et al.* 2011; Heggelund *et al.* 2011, 2012; Abdel-Baki *et al.* 2013; Bredin *et al.* 2013; Scheewe *et al.* 2013*a*), which measures maximal oxygen consumption and reflects overall aerobic capacity. Three studies reported clinically significant increases in V_{O2max} (Dodd *et al.* 2011; Heggelund *et al.* 2011; Abdel-Baki *et al.* 2013), defined as sufficient to reduce cardiovascular disease risk by 15%, and mortality by 20% (Myers *et al.* 2004; Kodama *et al.* 2009). These improvements occurred in as little as 8 weeks. Eight studies reported other fitness outcomes: seven of these observed significant increases in running/walking capacities (Beebe *et al.* 2005; Heggelund *et al.* 2011, 2012; Battaglia *et al.* 2013) and power output/strength (Marzolini *et al.* 2009; Heggelund *et al.* 2012; Bredin *et al.* 2013; Scheewe *et al.* 2013*a*).

Mental health outcomes (*Table 1*)

M1: psychiatric symptoms

Of the trials, 16 provided data for effects on mental health. The most commonly assessed mental health outcome was total change in positive and negative symptoms. For the eight RCTs examining total symptoms scores (357 participants), the pooled SMD was calculated, and showed no significant effect of exercise (SMD = −0.16, 95% CI −0.51 to 0.18) (Fig. 3). There was also substantial heterogeneity between studies ($I^2 = 54\%$). However, four of these eight trials implemented exercise only as a 'physical activity control' for yoga (Duraiswamy *et al.* 2007; Behere *et al.* 2011; Varambally *et al.* 2012; Manjunath *et al.* 2013) and their exercise interventions consisted almost entirely of low-intensity exercise such as walking, stretches and postures.

Therefore, a sensitivity analysis was performed to exclude these interventions, and thus investigate the effects of moderate-to-vigorous exercise on psychiatric symptoms (by only including interventions that used >30 min of moderate-to-vigorous exercise per week). Four trials remained, which implemented an average of 90 min per week (range = 75–120 min) (Beebe *et al.* 2005; Acil *et al.* 2008; Pajonk *et al.* 2010; Scheewe *et al.* 2013*a*). These showed a strong effect of exercise on total psychiatric symptoms (SMD = −0.72, 95% CI −1.14 to −0.29) (Fig. 3). Furthermore, no heterogeneity was found amongst these trials ($I^2 = 0\%$). Further analyses were carried out to determine the effect of moderate-to-vigorous exercise on separate scales of positive and negative symptoms. Both positive and negative symptoms were significantly reduced by moderate-to-vigorous exercise, with pooled SMDs of −0.54 (95% CI −0.95 to −0.13) and −0.44 (95% CI −0.78 to −0.09), respectively (Fig. 3).

Meta-analytic techniques were not applied to the other mental health outcomes (i.e. functioning, co-morbid disorders and neurocognition), as no common measures were used across the RCTs. Instead, effects in each domain were systematically reviewed (see Table 1) and summarized below.

M2: functioning and disability

Functioning and QoL were assessed in seven trials. Two RCTs, which both used 120 min of moderate-to-vigorous exercise per week, reported significant improvements in QoL (Battaglia *et al.* 2013) and functional disability (Scheewe *et al.* 2013*a*). Two RCTs which used low-intensity exercise as an active control for yoga observed increases in social functioning from baseline, although this improvement was significantly less than in the comparator condition (Duraiswamy *et al.* 2007; Varambally *et al.* 2012). Two non-randomized trials also assessed QoL, but observed no significant change (Heggelund *et al.* 2011, 2012).

Non-specific measures of overall illness severity were applied in three RCTs (Acil *et al.* 2008; Marzolini *et al.* 2009; Manjunath *et al.* 2013). All

https://doi.org/10.1017/S0033291714003110 Published online by Cambridge University Press

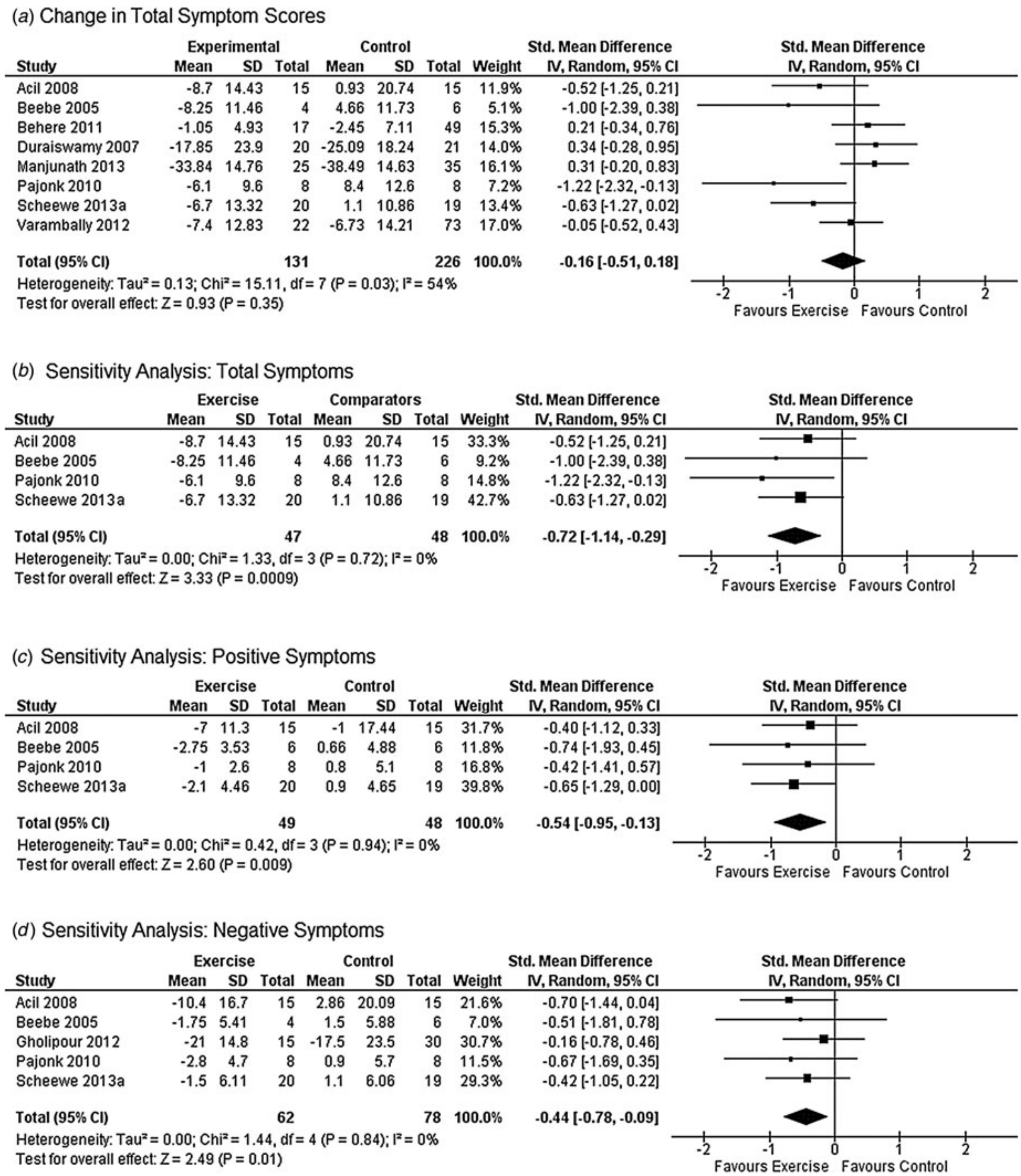

Fig. 3. Forest plots showing change in psychiatric symptoms in exercise and control conditions. 'Std. Mean Difference' indicates the effect size, with 95% confidence intervals (CIs). The *Z* value and associated *p* value indicate whether the effect size differs significantly from zero. The squares in the figure indicate the weight of the particular study in the meta-analysis. SD, Standard deviation; IV, inverse variance; df, degrees of freedom.

reported improvement following their exercise interventions, but did not find changes to significantly exceed control conditions.

M3: co-morbid disorders

Three trials used specific measures of depression (Heggelund *et al.* 2011; Manjunath *et al.* 2013; Scheewe *et al.* 2013*a*). Scheewe *et al.* (2013*a*) reported 120 min per week of aerobic–resistance exercise reduced depression significantly more than the occupational therapy control. The other two trials, both using ⩾75 min per week, observed no significant benefits of exercise (Heggelund *et al.* 2011; Manjunath *et al.* 2013). Three trials also observed exercise to reduce

https://doi.org/10.1017/S0033291714003110 Published online by Cambridge University Press

https://doi.org/10.1017/S0033291714003110 Published online by Cambridge University Press

Table 2. *Exercise intervention details and feasibility*

Study	Summary of exercise sessions	Sessions per week	Moderate-to-vigorous exercise per week	Duration, weeks	Exercise setting	Attrition in exercise condition, % (*n*/*n*)	Average attendance, % completers
Abdel-Baki *et al.* (2013)	Supervised aerobic interval training. 5 min warm-up. 10 × 30 s running intervals (with 90 s of walking between each). 5 min cool-down	2	40 min: 80–95% of HR max running, 50–65% of HR max walking	14	Solitary Supervised	36 (9/25)	48
Acil *et al.* (2008)	Home-based aerobic exercise plan. 10 min stretching. 25 min aerobic work-out with heart rate feedback. 5 min cool down/stretches	3	75 min: HR monitoring used, but target HR was not specified	10	Solitary Unsupervised	0 (0/15)	N/R
Archie *et al.* (2003)	Gym access. Provided access to an exercise facility (swimming, weights, aerobics, etc.) and recommended regular attendance	3	Not specified: recommended 3 × 30 min sessions per week	24	Solitary Unsupervised	90 (9/10)	30
Battaglia *et al.* (2013)	Soccer training. Sessions totalled 2 h including warm-up, social time, etc. 60 min of each session was active training, consisting of football matches and skills training	2	120 min: 50–85% of maximal HR during training period	12	Group Supervised	17 (2/12)	>80%
Beebe *et al.* (2005)	Treadmill walking programme. 10 min stretching. 30 min treadmill walking at a target HR	3	90 min: target HR set at baseline	16	Group Supervised	33 (2/6)	43–91
Behere *et al.* (2011)	National Fitness Corps Programme. 10 min walking. 5 min self-paced jogging. 45 min of postures. Supervised by a yoga instructor 5 days per week for 1 month, then continued alone	5	25 min: HR monitoring not used, but jogging is often 'moderate exercise'	16	Solitary Unsupervised	45 (14/31)	N/R
Bredin *et al.* (2013)	Supervised aerobics or resistance programme. 10 min warm-up. Then either (i) 30 min of bicycle, treadmill and elliptical training or (ii) 8–10 resistance exercises for major muscle groups. 10 min cool down	3	90 min: aerobic; target HR increased weekly. Resistance; 50–70% of 1 RM	12	Group Supervised	31 (4/13)	81
Dodd *et al.* (2011)	Group aerobic programme. 2–3 people, 30 min circuit of gym exercises conducted by an expert, suited to each person's abilities/preferences	2	60 min: 65–75% of HR max	24	Group Supervised	0 (0/8)	73
Duraiswamy *et al.* (2007)	National Fitness Corps Programme. See Behere *et al.* (2011). Supervised for 15 days, then continued alone	5	25 min: See Behere *et al.* (2011)	16	Solitary Unsupervised	33 (10/30)	N/R
Pajonk *et al.* (2010)	Group aerobic sessions. Groups of 2–4 participants cycling on stationary bikes	3	90 min: Target HR determined at baseline	12	Group Supervised	38 (5/13)	85

https://doi.org/10.1017/S0033291714003110 Published online by Cambridge University Press

Table 2 (*cont.*)

Study	Summary of exercise sessions	Sessions per week	Moderate-to-vigorous exercise per week	Duration, weeks	Exercise setting	Attrition in exercise condition, % (*n*/*n*)	Average attendance, % completers
Gholipour *et al.* (2012)	Therapeutic exercise sessions. 2 h sessions delivered to in-patients three times per week	3	Not specified: up to 360 min	16	N/R	(0/15)	N/R
Heggelund *et al.* (2011)	High intensity interval training. Four bouts of 4 min running with 3 min walking intervals	3	75 min: 85–95% of max HR for running, 70% for walking	8	Supervised	25 (4/16)	85
Heggelund *et al.* (2012)	Maximal strength training. 5 min treadmill walking. Four sets of four repetitions in a leg press machine with 3 min breaks between each set	3	<60 min: 70% of max HR walking. 16 repetitions at 85–90% 1 RM	8	Supervised	17 (1/7)	85
Manjunath *et al.* (2013)	National Fitness Corps Programme. See Behere *et al.* (2011). Supervised for 2 weeks, then continued alone	5	25 min: see Behere *et al.* (2011)	6	Solitary Unsupervised	43 (19/44)	N/R
Marzolini *et al.* (2009)	Group aerobics and weights training at a leisure centre. 10 min warm up, 20 min of resistance training, 60 min of aerobic training, 5 min cool-down	2	160 min: 60% of 1 RM for resistance. 60–80% of HR reserve for aerobic	12	Group Supervised	(0/7)	72
Scheewe *et al.* (2013*a*)	Combined aerobic and resistance training. 40 min aerobic training plus 20 min resistance exercise	2	120 min: 45–75% of HR reserve	24	Solitary Supervised	42 (13/31)	79
Varambally *et al.* (2012)	National Fitness Corps Programme. See Behere *et al.* (2011). Supervised for 1 month, then continued alone	5	25 min: see Behere *et al.* (2011)	16	Solitary Unsupervised	41 (22/37)	N/R

HR, Heart rate; max, maximum; N/R, not reported; 1 RM, one repetition maximum.

depression/anxiety subscales within broader mental health assessments (Duraiswamy *et al.* 2007; Acil *et al.* 2008; Marzolini *et al.* 2009), although only in relation to baseline scores (rather than control conditions).

M4: brain structure and neurocognitive functioning

Two studies examined effects of exercise on brain volume. Only Pajonk *et al.* (2010) observed a significant main effect, as exercise increased hippocampal volume by 12% (significantly more than the table-football control). Both Pajonk *et al.* (2010) and Scheewe *et al.* (2013*b*) found that increased physical fitness was significantly correlated with increases in brain volume. Pajonk *et al.* (2010) also examined cognition, and found that exercise improved verbal short-term memory by 34% ($p < 0.05$).

Different exercise types

Tables 1 and 2 reveal that significant improvements in mental health (in any domain) were only observed from interventions which used some form of aerobic exercise; with cycling (Pajonk *et al.* 2010), treadmill walking (Beebe *et al.* 2005) and sports training (Battaglia *et al.* 2013) all proving beneficial. However, some aerobic interventions had no effect on mental health, perhaps due to the relatively low dose applied (less than 90 min per week) (e.g. Dodd *et al.* 2011; Heggelund *et al.* 2011).

All three studies that incorporated aerobic with resistance training methods observed significant improvements in overall mental health (Marzolini *et al.* 2009; Bredin *et al.* 2013; Scheewe *et al.* 2013*a*). No studies used traditional resistance training alone, so the relative effectiveness of aerobic *versus* resistance components cannot be determined. It should also be noted that three 'high-intensity' training interventions, involving short bursts of strenuous physical activity, had no effect on symptoms or functioning, despite improving physical strength/fitness (Heggelund *et al.* 2011, 2012; Abdel-Baki *et al.* 2013).

Feasibility of exercise (Table 2)

All trials reported drop-out rates. Total attrition was 32.5% (118/362 participants). Attrition from group exercise was 22% (13/59 participants). However, attrition from solitary exercise, which mostly involved exercising alone after a briefly supervised introductory period, was almost double this, at 43% (96/223 participants). Adherence rate (i.e. attendance of exercise sessions) was reported in 10 studies. Group exercise adherence was substantially higher than solitary training interventions (78.8% *v.* 55%).

Another factor affecting exercise adherence was supervision. Across nine supervised trials, participant attendance averaged 77% (range = 48–85%). Only one unsupervised intervention monitored adherence effectively; by recording participants' gym attendance after providing them with a free membership, a gym induction session and an advised exercise programme to complete by themselves three times per week (Archie *et al.* 2003). Total adherence to the training routine was only 30%.

Discussion

This review aimed to capture all relevant studies of exercise in schizophrenia and related psychotic disorders by including single-arm trials, non-randomized trials and RCTs to provide a complete picture of the research. A total of 17 trials were reviewed in full and outcomes were categorized into six domains of physical and mental health. We found that exercise can improve cardiometabolic risk, functional disability, psychiatric symptoms, co-morbid disorders and neurocognition in schizophrenia (Table 1). Meta-analytic techniques were also applied to the most commonly reported outcomes for physical and mental health. Although there was no change in BMI, moderate-to-vigorous exercise was found to significantly improve positive and negative symptoms.

Exercise and physical health in schizophrenia

Reduction in body weight and BMI was not consistently found following exercise interventions. A more realistic goal may be the attenuation of expected weight gain, to which FEP patients are particularly susceptible (Alvarez-Jiménez *et al.* 2008*a*). Thus, the finding of no weight gain after 14 weeks of exercise in FEP (Abdel-Baki *et al.* 2013), along with a significant reduction in waist circumference (−4.3 cm), is noteworthy. Waist circumference may in fact be a more appropriate target than BMI for future exercise studies, especially if resistance training is included; reductions in body fat co-occurring with increases in muscle can improve overall body composition, while leaving BMI unchanged. Additionally, waist circumference is more useful than BMI for assessing cardiometabolic health (Janssen *et al.* 2004).

Physical fitness is also more important than body weight for protecting against cardiometabolic diseases (Fogelholm 2010; McNamee *et al.* 2013). Among the 11 studies measuring cardiovascular fitness and/or exercise capacity, 10 reported significant improvement from exercise. While the prevalence of cardiometabolic diseases is elevated in established schizophrenia (Hennekens *et al.* 2005; Vancampfort *et al.* 2013), this

https://doi.org/10.1017/S0033291714003110 Published online by Cambridge University Press

is not the case in early psychosis (Foley & Morley 2011; Phutane *et al.* 2011). Since preventing these issues from arising is more effective than reversing them (Scott 2003; Alvarez-Jiménez *et al*. 2008*b*), FEP could be the optimal phase for using exercise to increase fitness, minimize cardiometabolic risk, and thus reduce premature mortality in schizophrenia (Schizophrenia Commission, 2012; McNamee *et al.* 2013).

Exercise and psychiatric symptoms

Eight RCTs were included in our meta-analysis of total symptom scores (Fig. 3). This found no effect of exercise. However, after excluding trials that used only very low-intensity exercise, we found that moderate-to-vigorous exercise significantly improved total symptom scores, along with the scores of both the positive and negative symptom subscales. Meta-analytic techniques were not applied to other domains of mental health due to the paucity of common measures across studies. Instead, effects of exercise in each mental health domain (detailed in Table 1) were systematically reviewed, and considered alongside the intervention characteristics in Table 2, in order to elucidate which factors may determine effectiveness. Aerobic exercise was a component in all interventions that improved mental health. However, some effective interventions also included resistance training, while several low-dose aerobic interventions had no effect (e.g. Dodd *et al.* 2011; Heggelund *et al.* 2011). In all, there was no clearly superior modality of exercise for improving mental health in psychotic disorders.

Rather, it was dose of exercise that seemed to determine effectiveness. Interventions using at least 90 min per week of any moderate-to-vigorous exercise, such as aerobic/resistance gym sessions (Marzolini *et al.* 2009; Bredin *et al.* 2013; Scheewe *et al.* 2013*a*), football practice (Battaglia *et al.* 2013) or stationary bike training (Pajonk *et al.* 2010), proved beneficial across all domains of mental health assessed, including psychiatric symptoms, functional disability and cognition. On the other hand, all interventions that failed to improve mental health beyond control conditions had used lower amounts, through either quick burst, maximal-effort training (Heggelund *et al.* 2012; Abdel-Baki *et al.* 2013), low-intensity interventions (acting as a control for yoga), or simply shorter durations of endurance exercise (Dodd *et al.* 2011; Heggelund *et al.* 2011). This is consistent with research in depression, which shows that benefits are most reliably observed from interventions that implement 90 min per week of any aerobic exercise, provided it is at least moderately intense (Perraton *et al.* 2010). A recent review commissioned by 'Exercise and Sports Science Australia' also concluded that interventions which use at least 90 min per week of moderate-to-vigorous exercise, regardless of modality, can be effective for a range of mental health problems (Morgan *et al.* 2013).

Using exercise to improve outcomes of schizophrenia

Our review found that exercise can significantly improve both positive and negative symptoms (even when measured independently) and verbal short-term memory. Thus exercise could target aspects of schizophrenia that are resistant to conventional treatments. Indeed, exercise may be particularly effective in these areas, as correlational research shows that physical activity and fitness levels bear especially strong relationships with negative and cognitive symptoms (Vancampfort *et al.* 2012*a*, *b*, *c*).

The only study of exercise in FEP to date primarily examined physical health (Abdel-Baki *et al.* 2013). Although single-item scales of mental health were included, the study had no control condition. Therefore, the effects of exercise in early psychosis have yet to be explored. Using exercise to treat negative and cognitive symptoms during FEP could facilitate long-term recovery, as early improvements in these areas reduce the likelihood of enduring symptoms and functional disability (de Haan *et al.* 2003; Alvarez-Jiménez *et al.* 2012; Galderisi *et al.* 2013).

Exercise may also attenuate the neurological deterioration associated with psychotic disorders (Pajonk *et al.* 2010). Since the neurological deficits present in schizophrenia occur mostly in the first few years after onset (Andreasen *et al.* 2011; McIntosh *et al.* 2011), implementing exercise during this 'critical period' (McGowan *et al.* 2008) may limit neurological deterioration, or prevent it from occurring. Future trials should explore both the immediate and long-term benefits of implementing exercise in the early stages of psychosis, as along with these theoretical benefits, a recent longitudinal study has also observed that greater amounts of physical activity during FEP predict better functional outcomes (Lee *et al.* 2013).

Feasibility of exercise in psychotic disorders

The average attendance of exercise sessions in final-sample participants was 72%. Supervised interventions and group exercise resulted in substantially higher attendance and retention than unsupervised or solitary exercise. Therefore, offering supervised exercise in a group setting could maximise adherence.

The drop-out rate across all participants was only 32.5% (118/362). This compares favourably with exercise interventions in the general population and antipsychotic medication trials, both of which have drop-out rates of around 50% (Dishman 1991; Robison & Rogers, 1994; Martin *et al.* 2006). Furthermore, in the Schizophrenia Commission (2012) report, exercise ranked as the third

https://doi.org/10.1017/S0033291714003110 Published online by Cambridge University Press

most desirable intervention (ahead of family therapy, art, self-help and others). Thus, exercise is a feasible and highly valued intervention for schizophrenia.

Limitations and future research

One limitation of this review is that we focused entirely on studies that administered exercise as the sole component of the intervention. Therefore, broader 'healthy-living' programmes were excluded. This prevented us from evaluating how exercise can work in synergy with other health behaviours, such as diet. Although we found no effect on BMI, other reviews have found that exercise does stimulate weight loss in schizophrenia when used alongside dietary advice (National Institute for Health and Care Excellence, 2014), while interventions that focus solely on diet or physical activity alone are unsuccessful for reducing body weight (Bonfioli *et al.* 2012; Fernández-San-Martín *et al.* 2014).

Another limitation is that patients with schizophrenia who opt in to exercise interventions could be an atypical subgroup. If this is the case, the observed effects may not generalize across the whole population. Our findings were also based on outcome data from participants who completed the exercise interventions. This may also skew results, favouring individuals who fully engage with exercise. Indeed, the single study that did compare per-protocol and intention-to-treat analyses found that significant improvements in fitness, psychiatric symptoms and overall functioning only occurred in participants who attended $\geqslant$50% of exercise sessions (Scheewe *et al.* 2013*a*).

Since improvements in mental health appear to depend upon the dose of exercise applied, rather than the modality, interventions could be tailored around patient preferences, so that they can readily achieve 90 min of moderate-to-vigorous exercise per week. Participation could also be maximized through use of groups and supervision. Future research should aim to establish the efficacy of exercise for psychotic disorders using large-scale RCTs, especially in early psychosis. Furthermore, there is a need to explore how effective and engaging interventions can be implemented in clinical practice.

Acknowledgements

This research received no specific grant from any funding agency, commercial or not-for-profit sectors. J.F. is supported by a Medical Research Council Ph.D. Studentship Award.

Declaration of Interest

A.R.Y. has received unrestricted research grant support from Janssen Cilag and honoraria from Janssen Cilag and Autifony Therapeutics. All other authors declare that they have no competing interests.

References

Abdel-Baki A, Brazzini-Poisson V, Marois F, Letendre T, Karelis AD (2013). Effects of aerobic interval training on metabolic complications and cardiorespiratory fitness in young adults with psychotic disorders: a pilot study. *Schizophrenia Research* **149**, 112–115.

Acil AA, Dogan S, Dogan O (2008). The effects of physical exercises to mental state and quality of life in patients with schizophrenia. *Journal of Psychiatric and Mental Health Nursing* **15**, 808–815.

Albert N, Bertelsen M, Thorup A, Petersen L, Jeppesen P, Le Quack P, Krarup G, Jørgensen P, Nordentoft M (2011). Predictors of recovery from psychosis: analyses of clinical and social factors associated with recovery among patients with first-episode psychosis after 5 years. *Schizophrenia Research* **125**, 257–266.

Alberti KGM, Zimmet P, Shaw J (2005). The metabolic syndrome – a new worldwide definition. *Lancet* **366**, 1059–1062.

Alvarez-Jiménez M, Gleeson J, Henry L, Harrigan S, Harris M, Killackey E, Bendall S, Amminger G, Yung A, Herrman H (2012). Road to full recovery: longitudinal relationship between symptomatic remission and psychosocial recovery in first-episode psychosis over 7.5 years. *Psychological Medicine* **42**, 595.

Alvarez-Jiménez M, Gonzalez-Blanch C, Crespo-Facorro B, Hetrick S, Rodriguez-Sanchez JM, Perez-Iglesias R, Luis J (2008*a*). Antipsychotic-induced weight gain in chronic and first-episode psychotic disorders. *CNS Drugs* **22**, 547–562.

Alvarez-Jiménez M, Hetrick SE, González-Blanch C, Gleeson JF, Mcgorry PD (2008*b*). Non-pharmacological management of antipsychotic-induced weight gain: systematic review and meta-analysis of randomised controlled trials. *British Journal of Psychiatry* **193**, 101–107.

Andreasen NC, Nopoulos P, Magnotta V, Pierson R, Ziebell S, Ho B-C (2011). Progressive brain change in schizophrenia: a prospective longitudinal study of first-episode schizophrenia. *Biological Psychiatry* **70**, 672–679.

Angevaren M, Aufdemkampe G, Verhaar H, Aleman A, Vanhees L (2008). Physical activity and enhanced fitness to improve cognitive function in older people without known cognitive impairment. *Cochrane Database of Systematic Reviews*, Issue 2. Art. No.: CD005381. doi:10.1002/14651858.CD005381.pub2.

Archie S, Wilson JH, Osborne S, Hobbs H, Mcniven J (2003). Pilot study: access to fitness facility and exercise levels in olanzapine-treated patients. *Canadian Journal of Psychiatry* **48**, 628–632.

Battaglia G, Alesi M, Inguglia M, Roccella M, Caramazza G, Bellafiore M, Palma A (2013). Soccer practice as an add-on treatment in the management of individuals with a diagnosis of schizophrenia. *Neuropsychiatric Disease and Treatment* **9**, 595–603.

https://doi.org/10.1017/S0033291714003110 Published online by Cambridge University Press

Beebe LH, Tian L, Morris N, Goodwin A, Allen SS, Kuldau J (2005). Effects of exercise on mental and physical health parameters of persons with schizophrenia. *Issues in Mental Health Nursing* **26**, 661–676.

Behere RV, Arasappa R, Jagannathan A, Varambally S, Venkatasubramanian G, Thirthalli J, Subbakrishna DK, Nagendra HR, Gangadhar BN (2011). Effect of yoga therapy on facial emotion recognition deficits, symptoms and functioning in patients with schizophrenia. *Acta Psychiatrica Scandinavica* **123**, 147–153.

Bonfioli E, Berti L, Goss C, Muraro F, Burti L (2012). Health promotion lifestyle interventions for weight management in psychosis: a systematic review and meta-analysis of randomised controlled trials. *BMC Psychiatry* **12**, 78.

Bredin SSD, Warburton DER, Lang DJ (2013). The health benefits and challenges of exercise training in persons living with schizophrenia: a pilot study. *Brain Sciences* **3**, 821–848.

Bustillo JR, Lauriello J, Horan WP, Keith SJ (2001). The psychosocial treatment of schizophrenia: an update. *American Journal of Psychiatry* **158**, 163–175.

Caspersen CJ, Powell KE, Christenson GM (1985). Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. *Public Health Reports* **100**, 126.

Cooney GM, Dwan K, Greig CA, Lawlor DA, Rimer J, Waugh FR, Mcmurdo M, Mead GE (2013). Exercise for depression. *Cochrane Database of Systematic Reviews* Issue 9. Art. No.: CD004366. doi:10.1002/14651858.CD004366.pub6.

Crespo-Facorro B, Perez-Iglesias R, Ramirez-Bonilla M, Martínez-García O, Llorca J, Luis V-BJ (2006). A practical clinical trial comparing haloperidol, risperidone, and olanzapine for the acute treatment of first-episode nonaffective psychosis. *Journal of Clinical Psychiatry* **67**, 1511–1521.

De Haan L, Linszen DH, Lenior ME, De Win ED, Gorsira R (2003). Duration of untreated psychosis and outcome of schizophrenia: delay in intensive psychosocial treatment *versus* delay in treatment with antipsychotic medication. *Schizophrenia Bulletin* **29**, 341–348.

De Hert M, Schreurs V, Sweers K, Van Eyck D, Hanssens L, Šinko S, Wampers M, Scheen A, Peuskens J, Van Winkel R (2008). Typical and atypical antipsychotics differentially affect long-term incidence rates of the metabolic syndrome in first-episode patients with schizophrenia: a retrospective chart review. *Schizophrenia Research* **101**, 295–303.

Dersimonian R, Laird N (1986). Meta-analysis in clinical trials. *Controlled Clinical Trials* **7**, 177–188.

Dishman RK (1991). Increasing and maintaining exercise and physical activity. *Behavior Therapy* **22**, 345–378.

Dodd KJ, Duffy S, Stewart JA, Impey J, Taylor N (2011). A small group aerobic exercise programme that reduces body weight is feasible in adults with severe chronic schizophrenia: a pilot study. *Disability and Rehabilitation* **33**, 1222–1229.

Duraiswamy G, Thirthalli J, Nagendra HR, Gangadhar BN (2007). Yoga therapy as an add-on treatment in the management of patients with schizophrenia – a randomized controlled trial. *Acta Psychiatrica Scandinavica* **116**, 226–232.

Erhart SM, Marder SR, Carpenter WT (2006). Treatment of schizophrenia negative symptoms: future prospects. *Schizophrenia Bulletin* **32**, 234–237.

Falkai P, Malchow B, Wobrock T, Gruber O, Schmitt A, Honer WG, Pajonk FG, Sun F, Cannon TD (2013). The effect of aerobic exercise on cortical architecture in patients with chronic schizophrenia: a randomized controlled MRI study. *European Archives of Psychiatry and Clinical Neuroscience* **263**, 469–473.

Fernández-San-Martín MI, Martín-López LM, Masa-Font R, Olona-Tabueña N, Roman Y, Martin-Royo J, Oller-Canet S, González-Tejón S, San-Emeterio L, Barroso-Garcia A (2014). The effectiveness of lifestyle interventions to reduce cardiovascular risk in patients with severe mental disorders: meta-analysis of intervention studies. *Community Mental Health Journal* **50**, 81–95.

Fogelholm M (2010). Physical activity, fitness and fatness: relations to mortality, morbidity and disease risk factors. A systematic review. *Obesity Reviews* **11**, 202–221.

Foley DL, Morley KI (2011). Systematic review of early cardiometabolic outcomes of the first treated episode of psychosis. *Archives of General Psychiatry* **68**, 609.

Galderisi S, Mucci A, Bitter I, Libiger J, Bucci P, Wolfgang Fleischhacker W, Kahn RS (2013). Persistent negative symptoms in first episode patients with schizophrenia: results from the European First Episode Schizophrenia Trial. *European Neuropsychopharmacology* **23**, 196–204.

Garber CE, Blissmer B, Deschenes MR, Franklin BA, Lamonte MJ, Lee IM, Nieman DC, Swain DP; American College of Sports Medicine (2011). American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. *Medicine and Science in Sports and Exercise* **43**, 1334–1359.

Gholipour A, Abolghasemi SH, Gholinia K, Taheri S (2012). Token reinforcement therapeutic approach is more effective than exercise for controlling negative symptoms of schizophrenic patients: a randomized controlled trial. *International Journal of Preventive Medicine* **3**, 466–470.

Goldberg TE, Goldman RS, Burdick KE, Malhotra AK, Lencz T, Patel RC, Woerner MG, Schooler NR, Kane JM, Robinson DG (2007). Cognitive improvement after treatment with second-generation antipsychotic medications in first-episode schizophrenia: is it a practice effect? *Archives of General Psychiatry* **64**, 1115.

Gorczynski P, Faulkner G (2010). Exercise therapy for schizophrenia. *Cochrane Database of Systematic Reviews* Issue 5. Art. No.: CD004412. doi:10.1002/14651858.CD004412.pub2.

Green MF (1996). What are the functional consequences of neurocognitive deficits in schizophrenia? *American Journal of Psychiatry* **153**, 321–330.

Heggelund J, Morken G, Helgerud J, Nilsberg GE, Hoff J (2012). Therapeutic effects of maximal strength training on walking efficiency in patients with schizophrenia – a pilot study. *BMC Research Notes* **5**, 344.

Heggelund J, Nilsberg GE, Hoff J, Morken G, Helgerud J (2011). Effects of high aerobic intensity training in patients with schizophrenia – a controlled trial. *Nordic Journal of Psychiatry* **65**, 269–275.

https://doi.org/10.1017/S0033291714003110 Published online by Cambridge University Press

Hennekens CH, Hennekens AR, Hollar D, Casey DE (2005). Schizophrenia and increased risks of cardiovascular disease. *American Heart Journal* **150**, 1115–1121.

Hert M, Schreurs V, Vancampfort D, Winkel R (2009). Metabolic syndrome in people with schizophrenia: a review. *World Psychiatry* **8**, 15–22.

Higgins J, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, Savović J, Schulz KF, Weeks L, Sterne JA (2011). The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ* (*Clinical Research Ed.*) **343**, d5928.

Higgins JP, Green S (2008). *Cochrane Handbook for Systematic Reviews of Interventions*. John Wiley & Sons Ltd: Chichester.

Janssen I, Katzmarzyk PT, Ross R (2004). Waist circumference and not body mass index explains obesity-related health risk. *American Journal of Clinical Nutrition* **79**, 379–384.

Kern RS, Glynn SM, Horan WP, Marder SR (2009). Psychosocial treatments to promote functional recovery in schizophrenia. *Schizophrenia Bulletin* **35**, 347–361.

Kirkpatrick B, Fenton WS, Carpenter WT, Marder SR (2006). The NIMH-MATRICS consensus statement on negative symptoms. *Schizophrenia Bulletin* **32**, 214–219.

Knapp M, Mangalore R, Simon J (2004). The global costs of schizophrenia. *Schizophrenia Bulletin* **30**, 279–293.

Kodama S, Saito K, Tanaka S, Maki M, Yachi Y, Asumi M, Sugawara A, Totsuka K, Shimano H, Ohashi Y (2009). Cardiorespiratory fitness as a quantitative predictor of all-cause mortality and cardiovascular events in healthy men and women. *JAMA: The Journal of the American Medical Association* **301**, 2024–2035.

Laursen TM (2011). Life expectancy among persons with schizophrenia or bipolar affective disorder. *Schizophrenia Research* **131**, 101–104.

Lee EH, Hui CL, Chang W, Chan SK, Li Y, Lee J, Lin JJ, Chen EY (2013). Impact of physical activity on functioning of patients with first-episode psychosis – a 6 months prospective longitudinal study. *Schizophrenia Research* **150**, 538–541.

Malla A, Norman R, Schmitz N, Manchanda R, Bechard-Evans L, Takhar J, Haricharan R (2006). Predictors of rate and time to remission in first-episode psychosis: a two-year outcome study. *Psychological Medicine* **36**, 649–658.

Mangalore R, Knapp M (2007). Cost of schizophrenia in England. *Journal of Mental Health Policy and Economics* **10**, 23.

Manjunath RB, Varambally S, Thirthalli J, Basavaraddi IV, Gangadhar BN (2013). Efficacy of yoga as an add-on treatment for in-patients with functional psychotic disorder. *Indian Journal of Psychiatry* **55**, S374–S378.

Martin JLR, Pérez V, Sacristán M, Rodríguez-Artalejo F, Martínez C, Álvarez E (2006). Meta-analysis of drop-out rates in randomised clinical trials, comparing typical and atypical antipsychotics in the treatment of schizophrenia. *European Psychiatry* **21**, 11–20.

Marzolini S, Jensen B, Melville P (2009). Feasibility and effects of a group-based resistance and aerobic exercise program for individuals with severe schizophrenia: a multidisciplinary approach. *Mental Health and Physical Activity* **2**, 29–36.

McGowan S, Iqbal Z, Birchwood M (2008). Early interventions in psychosis. In *Mental Health: From Policy to Practice* (ed. C. Brooker, J. Repper and M. Brown), pp. 137–150. Elsevier: Oxford.

McIntosh AM, Owens DC, Moorhead WJ, Whalley HC, Stanfield AC, Hall J, Johnstone EC, Lawrie SM (2011). Longitudinal volume reductions in people at high genetic risk of schizophrenia as they develop psychosis. *Biological Psychiatry* **69**, 953–958.

McNamee L, Mead G, MacGillivray S, Lawrie SM (2013). Schizophrenia, poor physical health and physical activity: evidence-based interventions are required to reduce major health inequalities. *British Journal of Psychiatry* **203**, 239–241.

Morgan AJ, Parker AG, Alvarez-Jimenez M, Jorm AF (2013). Exercise and mental health: an Exercise and Sports Science Australia commissioned review. *Journal of Exercise Physiology Online* **16**, 64–73.

Myers J, Kaykha A, George S, Abella J, Zaheer N, Lear S, Yamazaki T, Froelicher V (2004). Fitness *versus* physical activity patterns in predicting mortality in men. *American Journal of Medicine* **117**, 912–918.

National Institute for Health and Care Excellence (2014). *Psychosis and Schizophrenia in Adults: Treatment and Management* (Clinical guideline 178). National Institute for Health and Care Excellence: London.

National Institute for Health and Clinical Excellence (2010). *Schizophrenia: The NICE Guideline on Core Interventions in the Treatment and Management of Schizophrenia in Adults in Primary and Secondary Care (Updated edition)*. The British Psychological Society and the Royal College of Psychiatrists: London.

Pajonk FG, Wobrock T, Gruber O, Scherk H, Berner D, Kaizl I, Kierer A, Muller S, Oest M, Meyer T, Backens M, Schneider-Axmann T, Thornton AE, Honer WG, Falkai P (2010). Hippocampal plasticity in response to exercise in schizophrenia. *Archives of General Psychiatry* **67**, 133–143.

Perraton LG, Kumar S, Machotka Z (2010). Exercise parameters in the treatment of clinical depression: a systematic review of randomized controlled trials. *Journal of Evaluation in Clinical Practice* **16**, 597–604.

Phutane VH, Tek C, Chwastiak L, Ratliff JC, Ozyuksel B, Woods SW, Srihari VH (2011). Cardiovascular risk in a first-episode psychosis sample: a 'critical period' for prevention? *Schizophrenia Research* **127**, 257–261.

Rabinowitz J, Levine SZ, Garibaldi G, Bugarski-Kirola D, Berardo CG, Kapur S (2012). Negative symptoms have greater impact on functioning than positive symptoms in schizophrenia: analysis of CATIE data. *Schizophrenia Research* **137**, 147–150.

Robison J, Rogers MA (1994). Adherence to exercise programmes. *Sports Medicine* **17**, 39–52.

Scheewe TW, Backx FJG, Takken T, Jorg F, Van Strater ACP, Kroes AG, Kahn RS, Cahn W (2013*a*). Exercise therapy improves mental and physical health in schizophrenia: a randomised controlled trial. *Acta Psychiatrica Scandinavica* **127**, 464–473.

https://doi.org/10.1017/S0033291714003110 Published online by Cambridge University Press

Scheewe TW, Takken T, Kahn RS, Cahn W, Backx FJG (2012). Effects of exercise therapy on cardiorespiratory fitness in patients with schizophrenia. *Medicine and Science in Sports and Exercise* **44**, 1834–1842.

Scheewe TW, Van Haren NEM, Sarkisyan G, Schnack HG, Brouwer RM, De Glint M, Hulshoff Pol HE, Backx FJG, Kahn RS, Cahn W (2013*b*). Exercise therapy, cardiorespiratory fitness and their effect on brain volumes: a randomised controlled trial in patients with schizophrenia and healthy controls. *European Neuropsychopharmacology* **23**, 675–685.

Schizophrenia Commission (2012). *The Abandoned Illness: A Report from the Schizophrenia Commission*. Rethink Mental Illness: London.

Schwartz JE, Fennig S, Tanenberg-Karant M, Carlson G, Craig T, Galambos N, Lavelle J, Bromet EJ (2000). Congruence of diagnoses 2 years after a first-admission diagnosis of psychosis. *Archives of General Psychiatry* **57**, 593–600.

Scott CL (2003). Diagnosis, prevention, and intervention for the metabolic syndrome. *American Journal of Cardiology* **92**, 35–42.

Smith PJ, Blumenthal JA, Hoffman BM, Cooper H, Strauman TA, Welsh-Bohmer K, Browndyke JN, Sherwood A (2010). Aerobic exercise and neurocognitive performance: a meta-analytic review of randomized controlled trials. *Psychosomatic Medicine* **72**, 239–252.

Vancampfort D, Knapen J, Probst M, Scheewe T, Remans S, De Hert M (2012*a*). A systematic review of correlates of physical activity in patients with schizophrenia. *Acta Psychiatrica Scandinavica* **125**, 352–362.

Vancampfort D, Probst M, Scheewe T, Knapen J, De Herdt A, De Hert M (2012*b*). The functional exercise capacity is correlated with global functioning in patients with schizophrenia. *Acta Psychiatrica Scandinavica* **125**, 382–387.

Vancampfort D, Probst M, Sweers K, Maurissen K, Knapen J, Willems J, Heip T, De Hert M (2012*c*). Eurofit test battery in patients with schizophrenia or schizoaffective disorder: reliability and clinical correlates. *European Psychiatry* **27**, 416–421.

Vancampfort D, Wampers M, Mitchell AJ, Correll CU, Herdt A, Probst M, Hert M (2013). A meta-analysis of cardio-metabolic abnormalities in drug naïve, first-episode and multi-episode patients with schizophrenia *versus* general population controls. *World Psychiatry* **12**, 240–250.

Varambally S, Gangadhar BN, Thirthalli J, Jagannathan A, Kumar S, Venkatasubramanian G, Muralidhar D, Subbakrishna DK, Nagendra HR (2012). Therapeutic efficacy of add-on yoga as an intervention in stabilized outpatient schizophrenia: randomized controlled comparison with exercise and waitlist. *Indian Journal of Psychiatry* **54**, 227–232.

World Health Organization (2010). *Global Recommendations on Physical Activity for Health*, pp. 8–10. World Health Organization: Geneva.

https://doi.org/10.1017/S0033291714003110 Published online by Cambridge University Press

Appendix

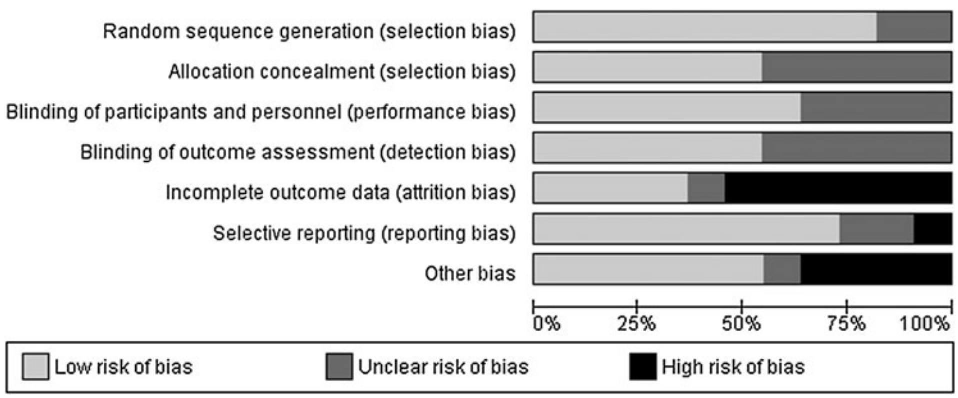

Fig. A1. Cochrane 'risk of bias' assessment: across trials.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Acil 2008	?	?	?	?	+	+	+
Battaglia 2013	+	?	+	?	–	+	+
Beebe 2005	+	?	+	+	+	–	+
Behere 2011	+	+	?	?	–	+	–
Duraiswamy 2007	+	+	+	+	–	+	–
Gholipour 2012	?	?	?	?	+	+	?
Manjunath 2013	+	?	+	+	?	+	–
Marzolini 2009	+	+	?	?	–	?	+
Pajonk 2010	+	+	+	+	–	?	+
Scheewe 2013a	+	+	+	+	+	+	+
Varambally 2012	+	+	+	+	–	+	–

Fig. A2. Cochrane 'risk of bias' assessment: within trials.

https://doi.org/10.1017/S0033291714003110 Published online by Cambridge University Press