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# Prevalence and predictors of treatment dropout from physical activity interventions in schizophrenia: a meta-analysis

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ABSTRACT

*Objective:* Physical activity interventions have been shown to improve the health of people with schizophrenia, yet treatment dropout poses an important challenge in this population, and rates vary substantially across studies. We conducted a meta-analysis to investigate the prevalence and predictors of treatment dropout in physical activity interventions in people with schizophrenia.
*Method:* We systematically searched major electronic databases from inception until August 2015. Randomized controlled trials of physical activity interventions in people with schizophrenia reporting dropout rates were included. Two independent authors conducted searches and extracted data. Random-effects meta-analysis and meta-regression analyses were conducted.
*Results:* In 19 studies, 594 patients with schizophrenia assigned to exercise interventions were investigated (age=37.2 years, 67.5% male, range=37.5%–100%). Trim and fill adjusted treatment dropout rate was 26.7% [95% confidence interval (CI)=19.7%–35.0%], which is more than double than in nonactive control interventions (odds ratio=2.15, 95% CI=1.29–3.58, $P$=.003). In the multivariate regression, qualification of the professional delivering the intervention ($\beta$=−1.06, 95% CI=−1.77 to −0.35, $P$=.003) moderated treatment dropout rates, while continuous supervision of physical activity approached statistical significance ($P$=.05).
*Conclusions:* Qualified professionals (e.g., physical therapists/exercise physiologists) should prescribe supervised physical activity for people with schizophrenia to enhance adherence, improve psychiatric symptoms and reduce the onset and burden of cardiovascular disease.



## 1. Introduction

Compared with the general population, life expectancy in people with schizophrenia is shortened by 10 to 20 years [1,2], with evidence indicating that the mortality gap still is growing [3]. The underlying causes for the increased risk for premature mortality in this population are complex and multifactorial. It is well established that people with schizophrenia are at an increased risk for cardiovascular diseases [4], metabolic syndrome [5], diabetes [6] and respiratory diseases [7]. Although genetic factors [8], psychotropic medication use [9] and shared pathophysiological mechanisms [10] contribute significantly to this high-risk profile, unhealthy lifestyle habits such as smoking [11,12], poor diet [13] and low levels of physical activity [14] play a prominent role.

Increasing premature mortality and increased prevalence of unhealthy lifestyle choices of people with schizophrenia suggest that this population has not yet fully benefited from the health care improvements implemented in the general population. Although in previous years there has been a greater focus on improving the health status of people with schizophrenia [15,16], there are still important health inequalities present even at the very early stages of the disease [17]. A primary reason for this is that, despite empirical evidence of moderate efficacy of pharmacotherapy [18–20], psychotherapeutic treatments [21,22] and exercise [23], a large proportion of people with schizophrenia fail to respond to these treatment modalities. In pharmacological treatments for schizophrenia, it is not uncommon that the treatment dropout rate exceeds 50% [24]. Dropout represents a major barrier to the achievement of a successful treatment outcome. Patients who drop out generally experience worse clinical outcomes [25]. At societal

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level, dropout and lack of adherence to treatment are of major concern for budget holders and policy makers as they are associated with greater risk of rehospitalization and thus greater resource utilization [26]. Patients who fail to complete study protocols can affect statistical analyses, research outcomes and interpretation of results [27]. For example, the current research evidence for physical activity interventions in patients with schizophrenia is mainly based on data from participants completing the interventions [28]. This may skew results, favoring individuals who fully engage with physical activity [28]. Only a single trial [29] to date compared per-protocol and intention-to-treat analyses and found that significant improvements in physical fitness, psychiatric symptoms and overall functioning only occurred in participants who attended greater than 50% of the exercise sessions.

Some features common to randomized controlled trials (RCTs) investigating physical activity interventions in people with schizophrenia, such as the use of predetermined manualized protocols e.g., in terms of frequency, intensity, time, type) and specific eligibility criteria [e.g., inclusion of only patients with a higher body mass index (BMI)] have the potential to affect dropout rates. This suggests the need to consider dropout from RCTs separately from pragmatic or real-world interventions [30]. To date, no meta-analysis has examined the prevalence and predictors of dropout data from physical activity RCTs in people with schizophrenia. The current evidence on adherence to physical activity is mainly based on cross-sectional, prospective and qualitative research. Correlates that have been consistently associated with lower physical activity participation are the presence of negative symptoms and cardiometabolic comorbidity. Side effects of antipsychotic medication, lack of knowledge regarding cardiovascular disease risk factors, no belief in health benefits, lower self-efficacy, other unhealthy lifestyle habits and social isolation have also been associated with lower physical activity participation [31]. Qualitative research has identified that the most frequently cited barriers towards participation in physical activity for people with schizophrenia are patients' lack of motivation and a lack of priority given to physical activity by health care professionals. The most frequently cited facilitators include the provision of esteem support by health care professionals and the promotion of enjoyment and autonomy for the patient [32]. Given the increasing burden of cardiovascular diseases among people with schizophrenia and the potential for exercise to ameliorate this leading cause of mortality, understanding the prevalence and predictors of dropouts in physical activity RCTs is an important research question. Moreover, an empirically derived estimate of typical frequency of dropout from RCTs and an exploration of its moderators would inform the design of new RCTs, in addition to informing clinical practice and policy.

Recognizing that dropout from treatment protocols is high among people with schizophrenia, the current meta-analysis had the following aims: (a) to establish the prevalence of dropout in physical activity RCTs among people with schizophrenia; (b) to compare the prevalence of dropout from physical activity with the dropout in nonactive control conditions; (c) to identify predictors that may influence dropout such as demographics (e.g., mean age, % male), illness-related factors (psychiatric symptoms, illness duration, psychotropic medication use) and physical activity intervention parameters (e.g., frequency, intensity, time and type of physical activity) and the professional qualifications of the person delivering the intervention.

## 2. Method

This systematic review was conducted in accordance with the Meta-analysis of Observational Studies in Epidemiology guidelines [33] and in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement [34].

### 2.1. Inclusion criteria

Included in this meta-analysis were RCTs that (a) included adult participants with schizophrenia-spectrum disorders (schizophrenia, schizoaffective disorder, schizophreniform disorder, brief psychotic disorder, or psychotic disorder not otherwise specified), diagnosed according to established criteria (e.g., *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV) [35] or *International Classification of Diseases, 10th Revision* [36]). (b) Investigated physical activity interventions. Physical activity was defined in accordance with Caspersen et al. [37] as any interventions that use bodily movement produced by skeletal muscles and which require energy expenditure. Exercise interventions were defined as physical activity that is planned, structured, repetitive and purposive in the sense that improvement or maintenance of physical fitness or health was an objective. (c) Provided information on dropout rates. (d) Were published in an international peer review journal in English language. Multiple physical activity conditions within a single RCT were included in the analyses as long as individuals only participated in one active arm of the trial. We considered any type of physical activity meeting the above criteria. For studies reporting follow-up assessments, the data collection focused on the active phase of the condition and as defined by the authors of each publication.

### 2.2. Information sources and searches

Two independent reviewers (D.V. and B.S.) searched Embase, PsycARTICLES and Medline without language restrictions from database inception until August 1, 2015, using the key words schizo* OR 'psychosis' AND 'exercise' OR 'physical activity'. In addition, reference lists of all eligible articles and recent systematic reviews [23,28] were screened to identify additional studies.

### 2.3. Study selection

After removal of duplicates, two independent reviewers screened the titles and abstracts of all potentially eligible articles. Two authors applied the eligibility criteria, and a list of full text articles was developed through consensus. Two authors (D.V. and B.S.) considered the full texts of included articles, and a final list of included articles was reached through consensus.

### 2.4. Outcomes

The primary outcome was the treatment dropout rate in physical activity interventions in people with schizophrenia. We adopted a definition of dropout consistent with its typical use in RCTs: unexpected patient attrition among individuals who were randomized to a treatment but failed to complete it [30]. This definition included any patient who would be included in intent-to-treat analyses, such as those who refused their randomization, never attended a session, stopped attending sessions or withdrew consent before completing the designated treatment. Patients who were lost prior to randomization were not considered dropouts. Additionally, administrative removals of study patients and instances of data loss were not treated as dropouts. For comparison purposes, we also collected overall dropout rates in all nonactive control conditions (e.g., wait list conditions, treatment as usual).

### 2.5. Data extraction

Two authors (D.V. and B.S.) extracted data using a data extraction form. In this extraction form, we divided moderators of the extracted dropout rates broadly into three domains: provider variables, exerciser/participant variables and design/implementation variables. For the provider variables, expertise was coded as experts on one side or no experts or no qualification provided on the other. Providers of physical activity/exercise interventions were considered experts when they had at a minimum a bachelor-level degree in physical therapy, exercise physiology or a similar that included education in exercise prescription

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and assessment. Providers of yoga interventions needed to be certified by an international accepted agency, for example, Yoga Alliance International (http://yogaalliance.in). Exerciser/participant variables included mean age, % male, duration of illness, baseline body mass index, baseline antipsychotic medication dose (mg/day expressed in chlorpromazine equivalents), baseline total Positive and Negative Symptoms Scale (PANSS) score and negative symptoms PANSS score, and the baseline physical fitness level (expressed as maximal or peak oxygen uptake, $VO_2$ max or peak). Design/implementation variables included type, frequency (per week), intensity level (low, moderate, moderate to high, as defined by the American College of Sports Medicine [38]) and duration (in minutes) of the last session, supervision (yes or no), multimodality (yes or no; yes=inclusion of cointerventions other than usual care), the addition of motivational elements to the intervention (yes or no) and the setting in which the physical activity intervention took place (inpatient, outpatient, community or mixed).

### 2.6. Meta-analysis

Due to the anticipated heterogeneity, we conducted a random-effects meta-analysis with Comprehensive Meta-Analysis software (CMA, Version 3). A random-effects meta-analysis model assumes that the observed estimates of an effect size (in this case, dropout rates) can vary across studies because of (a) real differences in dropout rates in each study and (b) sampling variability (chance) [39]. Under the random-effects model, studies are weighted to account for this variation (heterogeneity). The meta-analysis was conducted in the following steps. First, we calculated the prevalence of dropouts together with 95% confidence intervals (CIs). We examined the funnel plot of the composite outcome searching for extreme outliers and, when appropriate, removed extreme outliers in accordance with best practice. Second, we conducted meta-regression and subgroup analyses with CMA to investigate the potential moderators. For subgroup analyses, we calculated the $z$ statistic and corresponding $P$ value to illustrate between-group differences in dropout rates. Heterogeneity was assessed with the $I^2$ statistics for each analysis, with a value >50% considered as substantial heterogeneity [40]. Publication bias was assessed with the Begg–Mazumdar Kendall's tau [41] and Egger bias test [42]. Moreover, for the main composite analysis, we conducted a trim and fill adjusted analysis [43] to remove the most extreme small studies from the positive side of the funnel plot and recalculated the pooled dropout prevalence at each iteration until the funnel plot was symmetric about the (new) pooled dropout prevalence.

## 3. Results

### 3.1. Study selection

The initial search yielded 7117 hits. After removal of duplicates, 71 abstracts and titles were screened. At the full-text review stage, 47 articles were considered and 28 were subsequently excluded (see Fig. 1 for search results). Overall, 19 unique studies were included in the meta-analysis [44–62]. Four studies included two different physical activity arms. A total of 23 physical activity interventions were included. Full details of the included studies are summarized in Table 1.

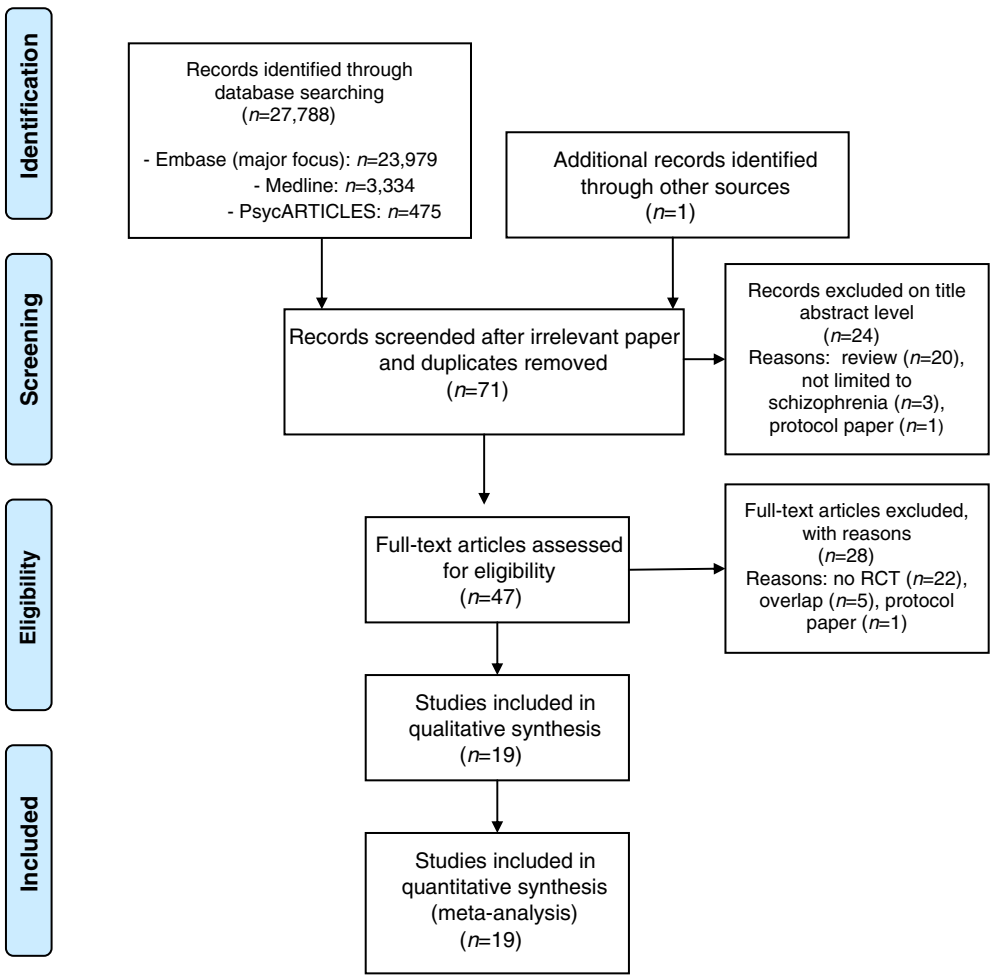


**Fig. 1.** Flow diagram for the search results.

**Table 1**
Study, participants' and providers' characteristics of the included studies ($n$=19 involving 23 physical activity interventions).

| Study | Invited/ dropped out before start | Participants in the study | Characteristics exercisers | Providers | Physical activity characteristics versus controls | Dropout and adherence rates in exercisers versus controls |
|---|---|---|---|---|---|---|
| Beebe 2005 [42] | 26/14 | Outpatients with schizophrenia (DSM-IV); age=52 years | BMI=32.51<br>PANSS total=69.25 | Not specified, no qualified exercise professionals involved | Treadmill walking, 16 weeks, 3/week, 30 min (moderate intensity) versus CAU | 33.3% (2/6) dropped out versus 0% (0/4); 75% attended half of sessions, 50% attended 2/3 |
| Duraiswamy 2007 [43] (yoga) | 61/0 | In- and outpatients with schizophrenia (DSM-IV) | 12/31 male<br>Age=32.53 years<br>Illness $d$=8.25 years<br>PANSS total=58.49<br>PANSS neg=21.31<br>AP dose=469.7 mg/day | Yoga instructor, certified | 16 weeks of which first 3 weeks 5/week, 60-min supervised yoga (low intensity) | 32.3% (10/31) dropped out |
| Duraiswamy 2007 [43] (exercise) | 61/0 | In- and outpatients with schizophrenia (DSM-IV) | 23/30 male<br>Age=31.30 years<br>Illness $d$=6.75 years<br>PANSS total=63.66<br>PANSS neg=22.83<br>AP dose=476 mg/day | No qualification for providing aerobic exercise and resistance training given | 16 weeks of which first 3 weeks, 5/week, 60-min supervised brisk walking, jogging and exercises in standing and sitting postures (moderate intensity) | 33.3% (10/30) dropped out |
| Wu 2007 [44] | ? | Inpatients with schizophrenia (DSM-IV) | 11/28 male<br>Age=42.2 years<br>BMI=30.43 | Physical therapist | 26 weeks, 3/week, 60-min walking/taking stairs+rewards for participation versus CAU (moderate intensity) | No dropouts in both conditions |
| Wu 2008 [45] | 150/22 | Outpatients with first-episode schizophrenia (DSM-IV) | 17/32 male (before start)<br>Age=26.4 years<br>BMI=24.6<br>PANSS total=45.9 | Exercise physiologist | 12 weeks, 7/week, 30 min at 70% HRR walking or jogging on a treadmill (moderate to high intensity) | 0% (0/29) dropped out versus 3.25% (1/32) |
| Marzolini 2009 [46] | 32/19 | Community patients with schizophrenia or schizoaffective disorder (DSM-IV) | Age=44.6 years<br>BMI=27.2 | Cardiac rehabilitation exercise specialist | 12 weeks, 2/week, 90-min aerobic and resistance training up to 80% HR+once per week additional aerobic exercise session individually (moderate to high intensity) or during home visit versus CAU | 0% (0/7) dropped out versus 0% (0/6); mean attendance was 72% (range 54%–87.5%) |
| Pajonk 2010 [47] | 37/13 | Outpatients with schizophrenia (DSM-IV) | 13/13 male<br>Age=35 years | No qualification: one of the investigators | 12 weeks, 3/week, 30-min ergometer cycling: at HR corresponding to blood lactate 1.5–2 mmol/L (moderate to high intensity) versus table top football | 38% (5/13) dropped out versus 27.2% (3/11), average of sessions attended=85% |
| Beebe 2011 [48] | 161/64 | Outpatients with schizophrenia spectrum (DSM-IV) | 51/97 male<br>Age=46.9 years | Not specified, no qualified exercise professionals involved | 16 weeks, 4/weeks, 30-min walking (low intensity)+additional motivational component (WALC-S) | 22.9% (11/48) dropped out versus 14.2% (7/49) |
| Behere 2011 [49] (yoga) | 65/0 | Outpatients with schizophrenia (DSM-IV) | 18/27 male (completers)<br>Age=30.2 years<br>Illness $d$=10.5 years<br>PANSS neg=17.8 | Yoga instructor, certified | 12 weeks (first month supervised), 5/week, 60-min yoga (low intensity) | 20.6% (7/34) dropped out versus 15.4% (4/26) |
| Behere 2011 [49] (exercise) | 65/0 | Outpatients with schizophrenia (DSM-IV) | 14/17 male (completers)<br>Age=31.3 years<br>Illness $d$=7.2 years<br>PANSS neg=14.8 | No qualification for providing aerobic exercise and resistance training given | 12 weeks (first month supervised), 5/week, 60-min brisk walking, jogging, and exercises in standing and sitting postures (moderate intensity) versus waitlist | 45% (14/31) dropped out versus 15.4% (4/26) |
| Methapatara 2011 [50] | 64/0 | Inpatients with schizophrenia (DSM-IV) | 23/32 male<br>Age=43.2 years<br>Illness $d$=14.7 years<br>BMI=28.4 | Physical therapist | 12 weeks, daily pedometer walking, up to 5000–8000 steps/day (low intensity)+motivational interviewing versus CAU | 0% (0/32) dropped out versus 0% (0/32) |
| Visceglia 2011 [51] | 18/0 | Inpatients with schizophrenia (DSM-IV | Age=37.4 years<br>PANSS total=85.1<br>PANSS neg=19.1 | Yoga instructor, certified | 8 weeks, 2/week, 45-min yoga (low intensity) | 0% (0/10) dropped out versus 0% (0/8) |
| Manjunath 2011 [52] (yoga) | 88/0 | Inpatients with schizophrenia (DSM-IV | 26/44 male<br>Age=31.7 years<br>Illness $d$=9.9 years<br>PANSS total=62.5 | Yoga instructor, certified | 6 weeks, 5/week, 600-min yoga (low intensity) | 20.4% dropped out (9/44) |
| Manjunath 2011 [52] (exercise) | 88/0 | Inpatients with schizophrenia (DSM-IV) | 23/44 male<br>Age=31.1 years<br>Illness $d$=8.1 years<br>PANSS total=62.1 | No qualification for providing aerobic exercise and resistance training given | 6 weeks, 5/week, 60-min aerobic and muscle exercises (moderate intensity) | 43.3% dropped out (19/44) |

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**Table 1** *(continued)*

| Study | Invited/ dropped out before start | Participants in the study | Characteristics exercisers | Providers | Physical activity characteristics versus controls | Dropout and adherence rates in exercisers versus controls |
|---|---|---|---|---|---|---|
| Scheewe 2012 [53] | ? | Outpatients with schizophrenia spectrum (DSM-IV) (per-protocol analyses) | 23/31 male<br>Age=29.1 years<br>BMI=6.3 years<br>PANSS total=63.6 | Psychomotor therapist (M.Sc.) | 26 weeks, 2/week, 60-min aerobic and muscle exercises (moderate intensity) versus same amount of occupation therapy (creative and recreational activities). | 42% (13/31) dropped out; exercise adherence was 79%. Control group was occupational therapy. |
| Varambally 2012 [54] (yoga) | 119/0 | Outpatients with schizophrenia (DSM-IV) | 28/47 male<br>Age=32.8 years<br>Illness *d*=10.8 years<br>PANSS total=62.8 | Yoga instructor, certified | 4 weeks, 5/week 45-min yoga (low intensity) | 17.0% (8/47) dropped out versus 2/36 (5.5%) |
| Varambally 2012 [54] (exercise) | 119/0 | Outpatients with schizophrenia (DSM-IV) | 28/37 male<br>Age=30.6 years<br>Illness *d*=7.4 years<br>PANSS total=59.1 | No qualification for providing aerobic exercise and resistance training given | 4 weeks, 5/week 45-min aerobic and resistance training (moderate intensity) | 37.8% (14/37) dropped out versus 2/36 (5.5%) |
| Battaglia 2013 [55] | ? | Community based patients with schizophrenia (DSM-IV) | 12/12 male<br>Age=36 years<br>BMI=28.55 | Exercise physiologist | 12 weeks 2/week, 120-min soccer, mean HR=50%–85% of estimated max HR (moderate to high intensity) versus CAU | 16.7% (2/12) dropped out versus 27.2% (3/11) |
| Jayaram 2013 [56] | 43/0 | In- and outpatients with schizophrenia (DSM-IV) | 12/15 male<br>Age=28.3 years<br>Illness *d*=6 years<br>AP dose=400 mg/day | Yoga instructor, certified | 4 weeks of yoga (low intensity), additional info in appendix not available | |
| Ikai 2014 [57] | 81/31 | Outpatients with schizophrenia or related psychotic disorders (DSM-IV) | 16/25 male<br>Age=53.5 years<br>Illness *d*=25.3 years<br>AP dose=659.3 mg/day<br>BMI=24.6<br>PANSS total=76.3<br>PANSS neg=21.1 | Yoga instructor, certified | 8 weeks, 1/week, 60-min yoga (low intensity) | 28% (7/25) dropped out versus 28% (7/25) |
| Kaltsatou 2014 [58] | 31/0 | Outpatients with schizophrenia (DSM-IV) | 14/16 male<br>Age=59.5 years<br>BMI=24.8<br>PANSS total=86<br>PANSS neg=25 | Physical exercise instructor, with rehabilitation expertise | 8 months, 3/week, 60-min traditional Greek dancing at HR=60%–70% of estimated max HR (moderate intensity) versus CAU | 0% (0/16) dropped out versus 0% (0/15) |
| Oertel-Knöchel 2014 [59] | ? | Inpatients with schizophrenia (DSM-IV) | 3/8 male<br>Age=44.6 years<br>Illness *d*=11 years | Physical exercise instructor with expertise in mental health (2 years) | 4 weeks, 3/week, 45-min cardio+resistance training at HR=60%–70% of estimated max HR (moderate intensity) versus waitlist | 0% (0/8) versus 0% (0/21) |
| Kimhy 2015 [60] | 41/8 | Outpatients with schizophrenia (DSM-IV) | 10/16 male<br>Age=36.6 years<br>AP dose=285.8 mg/day | Bachelor of Science in Therapeutic Recreation | 12 weeks, 3/week, 60-min aerobic training at 75% HR (moderate intensity) max using also video games versus CAU | 21% (3/16) dropped out versus 23.5% (4/17) |

AP=antipsychotic medication; BMI=body mass index; CAU=care as usual; HR=heart rate; HRR=heart rate reserve; neg=negative symptoms; WALC-S=Walk, Address Sensations, Learn About Exercise, Cue Exercise Behavior for schizophrenia spectrum disorders.

### *3.2. Study, participants and providers' characteristics*

Across the 19 unique studies, there were 1177 individuals with schizophrenia invited to participate in physical activity intervention RCTs. Of these 1177, there were 594 exercisers who started the intervention (mean age 37.2 years, 67.5% male, range 37.5%–100%). A range of physical activity interventions was included such as aerobic exercise (including brisk walking) ($n=5$), often combined with other modalities such as resistance training ($n=9$), yoga or tai chi ($n=7$) and other physical activity interventions including performing sports (soccer) and dance activities ($n=2$). The duration of the physical activity interventions ranged from 6 to 34 weeks, the frequency from once per week to daily and the time per session from 30 to 120 min. Fifteen studies included qualified professionals (i.e., providers of exercise intervention were physical therapists, exercise physiologists or those with a similar degree including education in exercise prescription and assessment; yoga instructors should be certified), and 13 studies were supervised for the entire study period. Further details of the included studies are summarized in Table 1.

### *3.3. Meta-analysis of dropout rates in physical activity RCTs*

The pooled physical activity dropout rate across 19 unique studies including 23 physical activity interventions in participants with schizophrenia was 22.1% [95% confidence interval (CI)=16.4% to 28.9%, $P<.001$, $I^2=56.9$; Begg=−0.41, $P=.006$; Egger=−2.42, $P<.001$]. Due to publication bias, we calculated a trim and fill adjusted prevalence, which was 26.7% (95% CI=19.7% to 35.0%, adjusted studies=7).

### *3.4. Comparative meta-analysis of dropout rates in physical activity versus control groups*

The pooled dropout in the nonactive control condition was 12.7% (95% CI=7.7% to 20.2%, $P<.001$, $I^2=63.0$; Begg=−0.20, $P=.24$;

**Table 2**
Subgroup analyses of moderators of dropouts in schizophrenia.

| Analysis | Number of comparisons | Meta-analysis | | | | |
|---|---|---|---|---|---|---|
| | | Dropout prevalence | 95% CI | | Between-group *P* value | $I^2$ | *P* value |
| Physical activity type | | | | | .54 | | |
| Aerobic exercise | 5 | 20.3% | 9.9% | 37.1% | | 61.2 | .035 |
| Aerobic exercise and resistance training | 9 | 26.8% | 17.3% | 39.0% | | 65.0 | .035 |
| Yoga and tai chi | 7 | 20.5% | 12.4% | 31.9% | | 13.5 | .32 |
| Sports and dance | 2 | 10.5% | 2.3% | 37.0% | | 25.3 | .25 |
| Setting | | | | | .41 | | |
| Mixed | 3 | 26.7% | 11.6% | 50.3% | | 42.1 | .18 |
| Inpatients | 6 | 13.8% | 6.5% | 27.0% | | 75.4 | <.001 |
| Outpatients | 12 | 24.6% | 16.3% | 25.3% | | 51.7 | .023 |
| Community patients | 2 | 12.7% | 2.6% | 44.3% | | 0 | .51 |
| Physical activity intensity | | | | | <**.001** | | |
| Low | 9 | 20.2% | 13.9% | 28.6% | | 20.9 | .26 |
| Moderate | 7 | 34.9% | 24.3% | 47.2% | | 50.4 | .059 |
| Moderate to high | 7 | 14.6% | 7.8% | 25.9% | | 42.8 | .10 |
| Additional motivational component | | | | | .18 | | |
| Yes | 4 | 13.4% | 5.6% | 28.7% | | 59.4 | .002 |
| No | 19 | 23.9% | 17.5% | 31.7% | | 55.2 | .06 |
| Supervision the entire study period | | | | | **.04** | | |
| Yes | 13 | 16.2% | 10.2% | 24.8% | | 40.0 | .067 |
| No | 9 | 29.2% | 21.0% | 39.1% | | 61.0 | .008 |
| Certified/qualified providers | | | | | <**.001** | | |
| Yes | 15 | 15.8% | 11.1% | 22.0% | | 43.5 | .036 |
| No | 7 | 36.4% | 27.4% | 46.5% | | 0 | .44 |

Significant when $P<.05$.

Egger=−2.60, $P=.07$). On observation of the funnel plot, one extreme outlier [55] was removed. The prevalence of dropouts was significantly higher in physical activity interventions than in control groups with an odds ratio (OR) of 2.15 (95% CI=1.29 to 3.58, $z=2.93$, $P=.003$; Begg=0.09, $P=.69$; Egger=0.27, $P=.80$).

### 3.5. Subgroup analyses investigating dropout rates in physical activity RCTs

There was no significant difference in dropout rates according to physical activity intervention types. In contrast, we did find a significant difference in dropout rates according to setting with higher dropout in outpatient versus inpatient settings ($z=-4.74$, $P<.001$). Lower dropout rates were found in studies utilizing higher-intensity physical activity interventions versus those including low-to-moderate- and low-intensity interventions ($z=-3.63$, $P<.001$). Similarly, significantly lower dropout rates were found in studies incorporating a motivational component to the intervention, in studies utilizing supervised interventions throughout the entire study period and in studies using adequately qualified professionals. Details of the different subgroup analyses can be found in Table 2.

### 3.6. Meta-regressions investigating moderators of the dropout rates in physical activity RCTs

Separate single meta-regression analyses revealed that dropout rates were not moderated by patient characteristics such as age (years), gender (% male), illness duration (years), baseline body mass index, medication dose (mg/day; chlorpromazine equivalents), PANSS total score and PANSS negative score. There were insufficient data to explore the role of baseline physical activity status.

Physical activity interventions that were supervised ($\beta=-0.71$, 95% CI −1.31 to −0.11, $P=.02$) and provided by an expert professionals ($\beta=-1.00$, 95% CI −1.47 to −0.52, $P<.0001$) significantly predicted lower dropout rates among exercisers. The only intervention characteristic moderating lower dropout was a higher intensity of the physical activity intervention. Meanwhile, the duration (number of weeks) of the physical activity intervention (although trend significant), frequency (number of sessions per week) and time (minutes of the final sessions) did not predict the between-study variance. Details of the meta-regressions are summarized in Table 3.

In a final step, all significant moderators were entered in one multivariate meta-regression model. The qualifications of the professionals

**Table 3**
Meta-regressions of moderators of dropouts in schizophrenia.

| Moderator | Number of comparisons | $\beta$ | 95% CI | | *P* value | $R^2$ |
|---|---|---|---|---|---|---|
| Mean age (years) | 23 | −0.01 | −0.06 | 0.02 | .51 | 0.10 |
| Gender (% male) | 23 | 1.36 | −0.89 | 3.63 | .23 | 0.09 |
| Body mass index (kg/m$^2$) | 9 | 0.07 | −0.25 | 0.4 | .66 | 0.00 |
| Duration of illness (years) | 13 | −0.01 | −0.09 | 0.05 | .60 | 0.11 |
| Medication dose (mg/day)[a] | 5 | 0.001 | −0.002 | 0.005 | .51 | 0.00 |
| PANSS total score | 12 | −0.02 | −0.08 | 0.03 | .41 | 0.15 |
| PANSS negative symptoms score | 9 | −0.05 | −0.15 | 0.05 | .28 | 0.29 |
| Physical activity frequency (*n*/week) | 23 | 0.11 | −0.11 | 0.33 | .33 | 0.23 |
| Physical activity intensity (intercept) | 23 | −1.263 | −1.57 | −0.95 | <**.001** | 1.0 |
| Low moderate vs. high | | 0.77 | 0.32 | 1.22 | **.001** | |
| Low vs. high | | −0.38 | −1.06 | 0.28 | .26 | |
| Physical activity time (min session) | 23 | −0.006 | −0.025 | 0.012 | .52 | 0.00 |
| Physical activity duration (*n* weeks) | 23 | −0.048 | −0.097 | 0.001 | .055 | 0.26 |
| Additional motivational component (yes/no) | 23 | −0.67 | −1.59 | 0.25 | .15 | 0.17 |
| Supervision (yes/no) | 23 | −0.71 | −1.31 | −0.11 | **.02** | 0.39 |
| Expert provider (yes/no) | 23 | −1.00 | −1.47 | −0.53 | <**.001** | 0.88 |

[a] Expressed in chlorpromazine equivalents.

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providing the physical activity intervention ($\beta$=−1.06; 95% CI=−1.77 to −0.35; $z$=−2.96, $P$=.003) remained the only significant predictor, while supervision of physical activity throughout the study ($\beta$=−0.64; 95% CI=−1.29 to 0.01; $z$=−1.92, $P$=.05) showed trend level significance. The model explained the entire proportion of total between-study variance ($R^2$=1.0).

## 4. Discussion

### 4.1. General findings

The current meta-analysis is the first to systematically document dropout rates and predictors in physical activity interventions in people with schizophrenia. Our meta-analysis demonstrated that more than one in four assigned to physical activity arms of RCTs dropped out (26.7%; 95% CI=19.7%–35.0%). The current dropout rates from physical activity interventions in people with schizophrenia seem to be higher than in other vulnerable populations. For example, Umpierre et al. [63] found that, in 19 of 24 structured exercise RCTS in people with type 2 diabetes, dropout rates were less than 20%, while Rethorst et al. [64] found a mean dropout rate of 14.6% in 16 exercise RCTS in people with clinical depression. Our higher rates point to the need for additional resources to deal with dropout from physical activity interventions in people with schizophrenia.

In an attempt to address this need, our results suggest that physical activity programs delivered by a qualified professional and/or supervised throughout the duration of the intervention appear to be associated with significantly lower dropout rates. Future RCTs and clinical physical activity interventions should explore which, or which combination of, characteristics should be addressed in order to minimize risk of dropouts. Our data confirm the recent findings of Ward et al. [65] who concluded in their qualitative review of reviews focusing on nonpharmacological interventions for obesity and related cardiometabolic risk factors that interventions with multiple components and that are personalized, with a longer duration, more frequent face-to-face contact and trained treatment providers are associated with better outcomes.

We additionally found that the mean rate of dropout was more than 10% higher in outpatients than inpatients. A factor accounting for the higher dropout in outpatient trials could be the additional burden of having to travel to the treatment facility to participate in the intervention. Moreover, previous qualitative research [65] has illustrated that people with schizophrenia can feel a sense of anxiety at utilizing community facilities along with the general public. Interventions delivered in inpatients settings may offer more social support and cohesion and therefore increase physical activity intervention attendance [66,67].

Interestingly, none of the characteristics of the patients allocated to physical activity interventions (age, gender, illness duration, baseline body mass index, baseline symptomatology) predicted dropout rate. Of the physical activity intervention characteristics, intervention intensity explained the variance in dropout rates. A lower rate of dropout was observed in interventions incorporating higher-intensity physical activity. An additional analysis comparing the rate of dropout before randomization in studies ($N$=4) using higher intensities versus those studies ($N$=15) incorporating activities at the low to moderate spectrum revealed that the dropout rate before randomization was higher in the former studies (29.6% versus 9.1%, $z$=−2.29, $P$=.022). This might indicate that studies incorporating physical activities with a higher intensity might apply stricter selection criteria (e.g., regarding physical comorbidities as contraindications), but more research explaining this lower dropout in high-intensity physical activity studies is needed. Also, supervision throughout the study period and adding a motivational component to the intervention (e.g., multimodal interventions such as the Walk, Address, Learn and Cue Intervention [44]; providing rewards [46]; motivational interviewing [52] or adding attractive, active video games into the set of offered physical activities [62]) significantly reduced the dropout rate.

The most important predictor of the dropout rates was the qualification of the professionals providing the physical activity interventions. Our meta-analysis showed that studies involving certified yoga instructors and, for aerobic and resistance training, physical therapists and exercise physiologists (or health care professionals with a similar degree involving qualification in exercise prescription and exercise assessment) showed the lowest dropout rates after adjusting for other moderators. The current findings support previous calls [68–73] for certified and qualified physical therapists and exercise physiologists to prescribe exercise to people with schizophrenia. While this is standard practice in nonmental high-risk populations, the potential role of these specialized health care professionals is still widely unappreciated in mental health care settings and multidisciplinary treatment guidelines [74,75]. Given the burden of physical health comorbidity and physical pain in people with schizophrenia [76,77], physical therapists or exercise physiologists should be utilized as part of the multidisciplinary mental health team in order to identify high-risk persons via standardized screening procedures prior to prescribing an individualized and supervised physical activity intervention [78].

### 4.2. Limitations and future research

Several limitations should be considered when interpreting our findings. First, our inclusion criteria limited this meta-analysis to RCTs investigating physical activity in people with schizophrenia. RCTs have been the focus of considerable research [23], and it is likely to remain a relevant topic in the literature for the foreseeable future, as major questions remain about longevity of effects and mechanisms of action [79]. We have to acknowledge as well several limitations which are inherent to the RCT literature and meta-analytic research in general. These include the inability to draw conclusions about patients' specific reasons for dropout and underreporting of potentially valuable information regarding patient and study characteristics (e.g., ethnicity, socioeconomic status, education status, mental and physical comorbidities, other unhealthy lifestyle choices). Some of the potential moderators were also limited to a small number of studies, which is not ideal for detecting effects through meta-regression analyses [80]. Additionally, meta-regression techniques are only able to detect whether a variable is associated with dropout across studies. Few of the included studies provided sufficient detailed information on characteristics of dropouts versus completers in order to conduct separate comparative analyses of predictor variables. It is evident that future research will be enhanced by improved consistency in reporting of differences between completers and noncompleters. Future large-scale systematic reviews and meta-analyses at the patient level might also assist in the identification of factors associated with dropout.

## 5. Conclusions

The current systematic review and meta-analysis demonstrated that, in particular, intervention factors (provision of supervision and delivery by qualified professionals) predicted the dropout of people with schizophrenia in physical activity intervention trials. Budget holders and policymakers should make the inclusion of qualified professionals such as physical therapists and exercise physiologists a priority in order to improve adherence among people with schizophrenia. The quality of clinical physical activity programs provided to people with schizophrenia should be at least equivalent with those provided to other high-risk populations.

## Declaration of interests

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