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Review article

Dropout from exercise randomized controlled trials among people with anxiety and stress-related disorders: A meta-analysis and meta-regression

Davy Vancampfort [a,b,*], Carlos Pelayo Ramos Sánchez [a], Mats Hallgren [c], Felipe Schuch [d], Joseph Firth [e,f], Simon Rosenbaum [g,h], Tine Van Damme [a,b], Brendon Stubbs [i,j]

[a] KU Leuven Department of Rehabilitation Sciences, Leuven, Belgium
[b] University Psychiatric Center KU Leuven, Leuven, Kortenberg, Belgium
[c] Department of Public Health Sciences, Karolinska Institute, Stockholm, Sweden
[d] Department of Sports Methods and Techniques, Federal University of Santa Maria, Santa Maria, Brazil
[e] Division of Psychology and Mental Health, University of Manchester, Manchester, UK
[f] NICM Health Research Institute, Western Sydney University, Westmead, Australia
[g] School of Psychiatry, University of New South Wales, Sydney, Australia
[h] Black Dog Institute, Sydney, Australia
[i] Physiotherapy Department, South London and Maudsley NHS Foundation Trust, London, UK
[j] Health Service and Population Research Department, Institute of Psychiatry, King's College London, London, UK

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ABSTRACT

Objective: . Exercise has established efficacy in people with anxiety and stress-related disorders. Dropouts from randomized controlled trials (RCT's) pose a threat to the validity of the evidence, with dropout rates varying across studies. We conducted a meta-analysis to investigate the prevalence and predictors of dropout rates among adults with anxiety and stress-related disorders participating in exercise RCT's.

Methods: . Two authors searched major electronic databases up to 07/2020. We included RCT's of exercise interventions in people with anxiety and stress-related disorders that reported dropout rates. A random effects meta-analysis and meta-regression were conducted.

Results: . Fourteen RCT's involving 16 exercise interventions (n=369, mean age 20.7 to 67.7years; 38.4% male) were included. The trim-and-fill-adjusted prevalence of dropout across all studies was 22.4% (95%CI = 15.0% to 32.0%). Applying controlled motivation strategies (P<0.001) predicted higher dropout. Supervision during all sessions and by an expert in exercise prescription and applying autonomous motivation strategies predicted lower dropout (all P<0.001). Dropout was similar in exercise versus control conditions (OR = 0.84, 95%CI = 0.54 to 1.29, p = 0.42, I^2 = 0%; N=16).

Limitations: . Potentially important moderators of dropout, such as the severity of mental health symptoms and illness duration were insufficiently available.

Conclusions: . Exercise is well tolerated by people with anxiety and stress-related disorders and drop out in RCT's is comparable to control conditions. Thus, exercise is a feasible treatment, in particular when autonomous motivation strategies are included and when the intervention is delivered by healthcare professionals with expertise in exercise prescription.

1. Introduction

Although the mental and somatic comorbidity in people with anxiety and stress-related disorders is well known (Rosenbaum et al., 2015b; Saha et al., 2020; Tang et al., 2017; Vancampfort et al., 2017), there are still important health inequalities present in this population (Firth et al., 2019). A primary reason is that, despite empirical evidence for the anxiolytic effects of pharmacotherapy (Jakubovski et al., 2019; Slee et al., 2019), psychotherapy (Carpenter et al., 2018) and exercise (Kandola et al., 2018; Rosenbaum et al., 2015c; Stubbs et al., 2017), a large proportion of people with anxiety and stress-related disorders fail to respond to these treatments (Springer et al., 2018). In

* Corresponding author at: KU Leuven Department of Rehabilitation Sciences, Tervuursevest 101, Leuven 3001, Belgium.
E-mail address: davy.vancampfort@kuleuven.be (D. Vancampfort).

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pharmacological (Pinto-Meza et al., 2011) and psychotherapeutic (Carpenter et al., 2018) interventions, it is not uncommon that the treatment dropout rate exceeds 20%. Dropout represents an important barrier to the achievement of a successful treatment outcome. Patients who drop out generally experience worse clinical outcomes (Zieve et al., 2019). At societal level, dropout from treatment is a major concern as it is associated with greater risk of re-hospitalization and greater resource utilization (Barrett et al., 2008). In research, patients who fail to complete study protocols can affect statistical analyses, study outcomes, and interpretation of results. For example, the current research evidence for exercise in patients with anxiety and stress-related disorders is mainly based on data from participants who completed the intervention (Kandola et al., 2018; Stubbs et al., 2017). This may skew results, favoring individuals who fully engage with exercise, while ignoring those who have been unable or unwilling to take part in the intervention. Some features common to randomized controlled trials (RCT's) investigating exercise in people with anxiety and stress-related disorders, such as the use of pre-determined manualized protocols (e.g., frequency, intensity, time, and type) and participant characteristics (e.g. age, gender), and illness related factors (e.g. the presence of physical or mental co-morbidity) have the potential to affect dropout rates. This suggests the need to consider dropout from RCT's separately from pragmatic or real-world interventions. To date, no meta-analysis has examined the prevalence and predictors of dropout data from exercise RCT's in people with anxiety and stress-related disorders. The current evidence on adherence to physical activity, and its' structured form exercise, in people with anxiety disorders is mainly based on cross-sectional (Vancampfort et al., 2016a) and qualitative research (Cushing et al., 2018; Godfrey et al., 2013; Ley et al., 2018). A barrier that has been consistently associated with lower physical activity participation in cross-sectional studies is a higher level of arousal (Vancampfort et al., 2016a), while qualitative research has identified that the most frequently cited barriers towards participation in exercise for people with people with anxiety and stress-related disorders are a lack of time and lack of motivation (Godfrey et al., 2013). Given exercise has important anxiolytic effects (Kandola et al., 2018; Rosenbaum et al., 2015c; Stubbs et al., 2017) and improves physical health outcomes (Warburton et al., 2006), understanding the prevalence and predictors of dropouts in exercise RCT's for people with anxiety and stress-related disorders is an important research question. Moreover, an empirically derived estimate of typical frequency of dropout from exercise RCT's and an exploration of its moderators would inform the design of new RCT's, in addition to informing clinical practice.

The current meta-analysis had the following aims: (i) to establish the prevalence of dropout in exercise RCT's among people with people with anxiety and stress-related disorders. (ii) To compare the prevalence of dropout from exercise with the dropout in non-active control conditions. (iii) To identify predictors that, based on previous research in people with mental health disorders (Stubbs et al., 2016; Vancampfort et al., 2016b), may influence dropout such as demographic characteristics (mean age, % male, baseline body mass index), illness-related factors (illness duration, level of mental health symptoms, medication use), exercise intervention parameters (e.g. frequency, intensity, time and type, use of add-on motivational interventions), professional qualifications of the person delivering the exercise intervention (experts versus non-experts) and study variables (low versus high risk of bias).

2. Method

This systematic review was conducted in accordance with the Meta-Analysis of Observational Studies in Epidemiology (MOOSE) guidelines (Stroup et al., 2000) and in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Moher et al., 2015).

2.1. Inclusion criteria

RCT's that included adult participants with a primary diagnosis of an anxiety or stress-related disorder according to established criteria, e.g. Research Diagnostic Criteria (RDC) (Spitzer et al., 1978), Diagnostic and Statistical Manual of Mental Disorders (DSM) (American Psychiatric Association, 2013) or International Classification of Diseases (ICD) (World Health Organisation, 1993) or those who have received clinical treatment for an anxiety or stress-related disorder were included in this meta-analysis. For the purposes of this review, eligible disorders included generalized anxiety disorder, posttraumatic stress disorder (PTSD), panic disorder, obsessive-compulsive disorder and social phobia. 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 (Caspersen et al., 1985). These interventions could include aerobic exercise, strength training, yoga, and Tai Chi. Stretching and light physical activity that were included as sham interventions without the purpose of improving health outcomes were considered as control interventions. RCT's had to provide information on dropout rates and needed to be published in an international peer review journal in English language. Multiple exercise conditions within a single RCT were included as long as for every exercise arm dropout rates were reported. For studies reporting follow-up assessments, data collection focused on the active phase of the condition, and as defined by the authors of each publication. We excluded RCT's in patients with subthreshold anxiety symptoms and RCT's exploring acute bouts of exercise (i.e. single sessions).

2.2. Information sources and searches

Two independent reviewers (DV, BS) searched Embase, CINAHL, PsycARTICLES, and Medline without language restrictions from database inception until July 1st, 2020, using the following strategy: (Exercise [Mesh] OR Yoga [Mesh] OR Tai Ji [Mesh] OR Qigong [Mesh] OR Exercise Movement Techniques [Mesh] OR Resistance Training [Mesh] OR Physical Activity [title/abstract] OR Tai Chi [title/abstract]) AND (Anxiety [Mesh] OR Panic [Mesh] OR Anxiety Disorders [Mesh] OR Phobic Disorders [Mesh] OR Obsessive Compulsive Disorder [title/abstract] OR OCD [title/abstract] OR Post Traumatic Stress Disorder [title/abstract] OR PTSD [title/abstract] OR Trauma [title/abstract] OR Social Anxiety Disorder [title/abstract] OR Phobia [title/abstract] OR SAD [title/abstract] OR Generalized Anxiety Disorder [title/abstract] OR GAD [title/abstract]) AND (Randomized Controlled Trial [title/abstract]). Search terms were selected after reaching consensus between both reviewers (DV and BS) and were based on similar meta-analyses exploring dropouts in exercise trials in people with a mental disorder (Stubbs et al., 2016; Vancampfort et al., 2016b) and meta-analyses exploring exercise outcomes in people with anxiety and stress-related disorders (Ashdown-Franks et al., 2020; Aylett et al., 2018; Stubbs et al., 2017). The reference lists of included articles and recent reviews (Ashdown-Franks et al., 2020; Aylett et al., 2018; Stubbs et al., 2017) were also considered for potentially eligible articles.

2.3. Study selection

After removal of duplicates, two reviewers (DV and TV) independently screened the titles and abstracts of all potentially eligible articles. Both reviewers applied the eligibility criteria, and a list of full text articles was developed through consensus. Afterwards, the full texts of included articles and a final list of included articles was reached through consensus. There was no disagreement and no third reviewer was needed.

2.4. Outcomes

The primary outcome was the treatment dropout rate in exercise interventions in people with anxiety disorders. We adopted a definition of dropout consistent with its typical use in RCT's: unexpected patient attrition among individuals who were randomized to a treatment but failed to complete it. This definition included any patient who would be included in intent-to-treat (ITT) 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 non-active control conditions (e.g., wait list conditions, treatment as usual).

2.5. Data extraction

Two authors (DV, TV) 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 exercise interventions were considered experts when they had at a minimum a bachelor-level degree in physical therapy, exercise physiology or a similar degree that included education in exercise prescription and assessment. Providers of yoga interventions needed to have also at a minimum a bachelor-level degree in physical therapy, exercise physiology or a similar that included education in exercise prescription and assessment and should 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, severity of mental health symptoms, and baseline body mass index. Design/implementation variables included type, frequency (per week), intensity level (low, moderate, moderate to high, as defined by the American College of Sports Medicine) (American College of Sports Medicine ACSM, 2017) and duration (in minutes) of the last session, supervision (yes or no), the addition of motivational elements to the intervention (yes or no), and the setting in which the exercise intervention took place (inpatient, outpatient or community, mixed). For the motivational interventions a distinction was made for controlled motivation (e.g., financial compensation) and autonomous motivation (e.g. shared decision making in goal setting, exploring barriers and motives, focusing on social interaction) according to the self-determination framework (Deci and Ryan, 2008).

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 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). 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% 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 (Higgins et al., 2003). Publication bias was assessed with the Begg-Mazumdar Kendall's tau and Egger bias test. Moreover, for the main composite analysis we conducted a trim and fill adjusted analysis to remove the most extreme small studies from the positive side of the funnel plot, and recalculated the pooled drop out prevalence at each iteration, until the funnel plot was symmetric about the (new) pooled drop out prevalence.

3. Results

3.1. Study selection

Following the removal of duplicates, we identified 713 potentially relevant articles from our searches. At the full text review stage, we reviewed 64 articles and excluded 50 with reasons (see Supplementary Material 1). Details of the study selection process are summarized in Fig. 1. Overall, there were 14 unique RCT's, providing dropout data from a total of 16 exercise interventions, included in our review (Abrantes et al., 2017; Broocks et al., 1998; Fetzner and Asmundson, 2015; Gaudlitz et al., 2015; Hall et al., 2019; Herring et al., 2012; Hovland et al., 2013; Jazaieri et al., 2012; LeBouthillier and Asmundson, 2017; Merom et al., 2008; Mitchell et al., 2014; Reinhardt et al., 2018; Rosenbaum et al., 2015a; Van der Kolk et al., 2014).

3.2. Study, participants and providers' characteristics

Across the 16 exercise interventions (see Table 1), 369 people with anxiety disorders were enrolled in the exercise arms of the studies. The mean age of the exercise participants in the studies ranged from 20.7 to 67.7 years) and 38.4% ($n = 143$) were male. Most studies were executed in people with PTSD (N exercise interventions = 6) (Fetzner and Asmundson, 2015; Hall et al., 2019; Mitchell et al., 2014; Reinhardt et al., 2018; Rosenbaum et al., 2015a; Van der Kolk et al., 2014), followed by people with panic disorder ($N = 3$) (Broocks et al., 1998; Gaudlitz et al., 2015; Hovland et al., 2013) and mixed anxiety disorders ($N = 3$) (LeBouthillier and Asmundson, 2017; Merom et al., 2008). One RCT with two interventions arms (Herring et al., 2012) focused on people with generalized anxiety disorder, and one RCT explored exercise in people with obsessive-compulsive disorder (Abrantes et al., 2017) and one in people with social phobia (Jazaieri et al., 2012).

Two RCT's were performed in a veteran population (Hall et al., 2019; Reinhardt et al., 2018) and one in a mixed veteran and civilian population (Mitchell et al., 2014). The other 13 exercise interventions were in civilian populations.

One RCT was performed in an inpatient setting (Rosenbaum et al., 2015a), one in a mixed setting (Hovland et al., 2013), and the other twelve in outpatient or community settings.

Most of the studies investigated aerobic exercise ($N = 8$) (Abrantes et al., 2017; Broocks et al., 1998; Fetzner and Asmundson, 2015; Gaudlitz et al., 2015; Herring et al., 2012; Jazaieri et al., 2012; LeBouthillier and Asmundson, 2017; Merom et al., 2008), two strength training (Herring et al., 2012; LeBouthillier and Asmundson, 2017) and another three mixed strength and aerobic training (Hall et al., 2019; Hovland et al., 2013; Rosenbaum et al., 2015a). Three RCT's explored active body - mind interventions such as yoga or tai chi (Mitchell et al., 2014; Reinhardt et al., 2018; Van der Kolk et al., 2014).

Four RCT's used controlled motivation strategies (Abrantes et al., 2017; Merom et al., 2008; Mitchell et al., 2014; Reinhardt et al., 2018) and seven autonomous motivation strategies (Abrantes et al., 2017; Gaudlitz et al., 2015; Hall et al., 2019; Hovland et al., 2013; Jazaieri et al., 2012; Rosenbaum et al., 2015a; Van der Kolk et al., 2014). One RCT use a mixed controlled and autonomous motivation strategy (Abrantes et al., 2017).

Seven exercise interventions were supervised by exercise experts (Abrantes et al., 2017; Gaudlitz et al., 2015; Hall et al., 2019; Herring et al., 2012; Hovland et al., 2013; Rosenbaum et al., 2015a). Nine interventions were supervised during the entire study period (Fetzner and

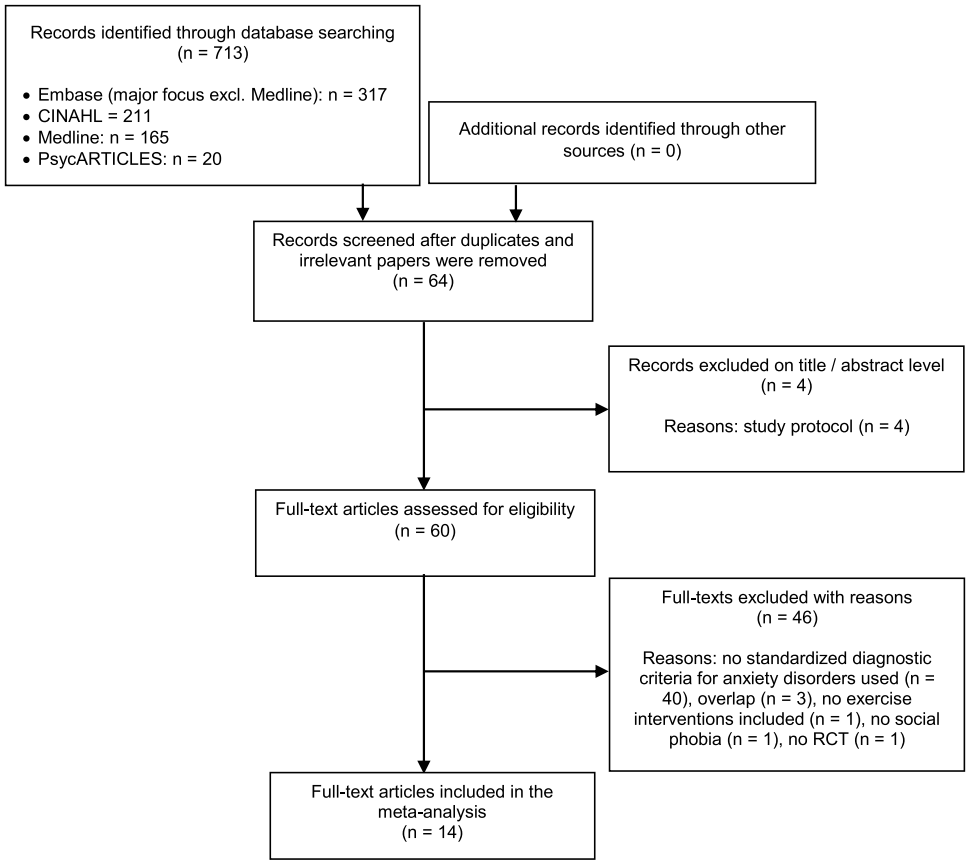

Fig. 1. Flow diagram for the search strategy.

Asmundson, 2015; Gaudlitz et al., 2015; Herring et al., 2012; Hovland et al., 2013; LeBouthillier and Asmundson, 2017; Mitchell et al., 2014; Van der Kolk et al., 2014). The duration of the interventions was on average eight weeks (range = 2 to 12 weeks), and most studies ($N = 8$) adopted a frequency of three sessions per week (range = 1 to 5). The exercise intensity was low in three studies (Abrantes et al., 2017; Reinhardt et al., 2018; Van der Kolk et al., 2014) and in the other interventions moderate-to-vigorous.

3.3. Meta-analysis of dropout rates in exercise RCT's

Across the 16 exercise interventions, the pooled dropout rate was 15.7% (95%CI = 9.9% to 23.9%, $I^2 = 60.3\%$). There was evidence of publication bias (Egger = -3.3, $p < 0.001$; Begg = -50.0, $p = 0.02$) and the trim and fill adjusted dropout rate was 22.4% (95%CI = 15.0% to 32.0%) with five adjusted studies. Full details of all of the subgroup analyses are presented in Table 2. Key findings are highlighted below.

3.4. Exerciser characteristics

There was no significant difference ($P = 0.45$) in dropout rates between people with PTSD (13.0%, 95%CI = 6.0% to 26.1%, $N = 6$), OCD (10.7%, 95%CI = 2.0% to 41.0%, $N = 1$), panic disorder (15.6%, 95%CI = 5.7% to 36.4%, $N = 3$), generalized anxiety disorder (4.5%, 95%CI = 1.0% to 30.5%, $N = 2$) or social anxiety disorder (8.0%, 95%CI = 1.0% to 37.6%, $N = 1$). Dropout rates in studies focusing on veterans (19.4%, 95%CI = 5.3% to 50.9%, $N = 2$) were not significantly ($P = 0.59$) higher than in civilians (14.9%, 95%CI = 9.0% to 28.8%, $N = 13$).

3.5. Design and implementation characteristics

Higher dropout rates were observed in outpatients (17.9%, 95%CI = 11.8% to 26.5%, $N = 14$) versus inpatients (1.2%, 95%CI = 0.0% to 21.9%, $N = 1$) ($P < 0.001$). When looking at differences in exercise types and the exercise intensity, no differences in dropout rates were observed. In contrast, a higher frequency of exercise per week was associated with a higher dropout ($P < 0.001$), while drop-out in sessions of less than 30min were lower than in 30min or above ($P<0.001$). When all exercise sessions were supervised dropout rates were lower ($P < 0.001$) (13.3%, 95%CI = 6.8% to 24.5%, $N = 9$) compared with interventions where part of the sessions were unsupervised (18.2%, 95% CI=9.6% to 31.9%, $N = 7$). When looking at the background of the supervisor, dropout was lower when interventions were supervised by those who had expertise in exercise prescription (7.0%, 95%CI = 3.5% to 13.5%, $N = 7$ versus 25.6%, 95%CI = 18.0% to 34.9%, $N = 6$, $P < 0.001$). Higher dropout rates were also observed when controlled motivation strategies were used (26.9%, 95%CI = 14.6% to 44.1%, $N = 4$ versus 15.3%, 95%CI = 10.7% to 21.5%, $N = 12$, $P < 0.001$) and lower when autonomous motivation strategies were applied (7.2%, 95%CI = 4.2% to 12.3%, $N = 7$ versus 30.4%, 95%CI = 23.6% to 38.2%, $N = 9$, $P < 0.001$).

3.6. Meta-regression of dropout rates

Full details of all of the meta-regression results across all studies are presented in Table 3. No significant participant characteristics were identified. The duration of the overall intervention (weeks) did not predict dropout.

3.7. Comparative dropout rates in exercise versus control groups

A comparative meta-analysis across 16 studies established that dropout from exercise interventions was comparable to the dropout rates observed in the control conditions (OR = 0.84, 95%CI = 0.54 to

Table 1
Participants, providers and exercise characteristics and motivational strategies used in the included randomized controlled trials (n=14 involving 16 exercise interventions).

Study	Participants in the study	Characteristics exercisers	Providers*	Exercise characteristics	Motivational strategies	Dropout rates in exercisers versus controls
Hall 1019	33 (vs. 18 on waitlist) PTSD veterans	67.7±3.2 years; 94% male; community patients	Exercise physiologist (expert)	12 weeks / 3*week / 60-90 min moderate-vigorous aerobic + strength training with also independent exercising	Self-monitoring, mastery experiences, outcome expectations, exploring barriers, modelling, social support	3/54 (5.6%) before start, EX: 2/33 (6.1%) post vs. C: 1/18 (5.6%)
Reinhardt 2018	26 (vs. 25 waitlist /control) PTSD veterans	44.1±14.0 years; 92% male; community patients	Yoga instructor (non-expert)	10 weeks / 2*week / 90 min Kripalu yoga + also exercising outside classes	Monetary compensation for participation (595 USD)	23/74 (31.1%) before randomization EX: 10/26 (38.5%) vs. C: 4/25 (16%)
Abrantes 2017	28 (vs. 28 health education) with OCD	38.8±13.0 years; 36% male; community patients	Exercise physiologist (expert)	12 weeks / 1*week / 60 min moderate-vigorous aerobic exercise + attaining to 150min of physical activity per week	Exploring exercise benefits, goal-setting, time management, exploring barriers AND 5 USD per session + additional compensation for continued attendance (10-50 USD)	1/56 (1.8%) dropped out before randomization EX: 3/28 (10.7%) vs. C: 1/27 (3.7%)
LeBouthillier 2017	23 aerobic exercise and 18 resistance training (vs.15 on waitlist) with anxiety-related disorders	Aerobic exercise = 33.0±8.8 years; 20% male; Resistance training = 31.4±9.2 years; 30% male; community patients	Personal trainer (non-expert)	4 weeks / 3*week / 60min moderate-vigorous	None reported	1/48 (2.1%) before start, aerobic exercise 7/22 (31.8%), resistance training 4/18 (22.2%) vs. C: 4/15 (26/7%)
Fetzner 2015	11 (vs. 11 cognitive distraction and 11 interoceptive prompts) with PTSD	36.9±11.2 years; 24% male; community patients	Personal trainer (non-expert)	2 weeks / 3*week / 20min moderate-vigorous aerobic exercise	None reported	0/33 (0%) before start, EX: 2/11 (18.2%) post vs. C: 4/22 (18.2%)
Gaudlitz 2015	27 (vs. 31 CBT + very low PA / sham intervention) with panic disorder	35.4±12.6 years; 50% male; community patients	(Sports) MDs (expert)	8 weeks / 3*week / 30min moderate-vigorous aerobic exercise on a treadmill in combination with CBT 8 weeks / 2*week / 90min	Motivational support during the intervention	0/47 (0%) before start, EX: 3/27 (11.1%) post vs. C: 8/23 (34.8%)
Rosenbaum 2015	39 (vs. 42 usual care) with PTSD	47.1±11.3 years; 92% male; inpatients	Exercise physiologist (expert)	12 weeks / 1*week supervised and 2*week unsupervised / 30min moderate-vigorous aerobic exercise and strength training	Self-monitoring, goal setting	0/81 (0%) before start, EX: 0/39 (0%) post vs. C: 0/42 (0%)
Mitchell 2014	20 (vs. 18 in assessment control condition) veteran and civilian women with PTSD	44.4±12.4 years; 0% male; community patients	Yoga instructor (non-expert)	12 weekly or 6 twice weekly 75 min Kripalu yoga sessions	Monetary compensation (ranging from 20 to 30 USD) for the assessments + yoga mat + water bottle each session	0/38 (0%) before start, EX: 3/17 (17.6%) post vs. C: 4/16 (25.0%)
van der Kolk 2014	32 (vs. health education) women with PTSD	41.5±12.2 years; 0% male; community patients	Yoga instructor (non-expert)	10 weekly 60 min trauma-informed yoga sessions	Non-controlling language, offering choices	19/83 (22.9%) before start, EX: 1/32 (3.1%) post vs. C: 3/32 (9.3%)
Hovland 2013	17 (vs. 19 CBT) with panic disorder	38.1±8.6 years; 12% male; community patients	Physiotherapist (expert)	12 weeks / 3*week / 90min moderate-vigorous aerobic exercise and strength training	Barriers (e.g. physical sensations) and practical issues were discussed, individual support.	0/36 (0%) before start, EX: 0/17 (0%) post vs. C: 1/19 (5.3%)
Herring 2012	10 aerobic exercise and 10 resistance training (vs.10 on waitlist) with generalized anxiety disorder	Aerobic exercise = 20.7±3.0 years; 0% male; Resistance training = 26.6±7.1 years; 0% male; community patients	Exercise physiologist (expert)	6 weeks / 2*week / 16 min moderate-vigorous	None reported	0/30 (0%) before start, aerobic exercise 0/10 (0%), resistance training 0/10 (0%) vs. C: 0/10 (0%)
Jazaieri 2012	25 (vs. 31 mindfulness) with social anxiety disorder	32.9±8.0 years; 60% male; community patients	None, but gym personnel available (non-expert)	8 weeks / 3*week self-practice in gym moderate-vigorous aerobic exercise, 2 individual and 1 group session	Barriers were discussed, individual and group support.	0/56 (0%) before start, EX: 2/25 (8.0%) post vs. C: 5/31 (16.1%)
Merom 2008	45 (vs. 40 health education and CBT) with anxiety disorders	38.7±11.6 years; 29% male; community patients	Exercise trainer (non-expert)	10 weeks / 5*week / 30 min moderate-vigorous (brisk) walking with CBT 8 weeks / 1*week / 90 min group	Weekly frequency and duration target were set by the exercise trainer.	11/85 (12.9%) before start, EX: 15/38 (39.5%) post vs. C: 16/36 (44.4%)
Broocks 1998	16 (vs. 15 Clomipramine and 15 placebo) with panic disorder	31.8±9.5 years; 37.5% male; community patients	Exercise trainer (non-expert)	10 weeks / 4*week from walking to moderate-vigorous running	None reported	0/31 (0%) before start, EX: 5/16 (31.2%) post vs. C: 4/15 (26.7%)

*Expert if a minimum a bachelor-level degree in physical therapy, exercise physiology or a similar degree that included education in exercise prescription and assessment. Providers of yoga interventions needed to have also at a minimum a bachelor-level degree in physical therapy, exercise physiology or a similar that included education in exercise prescription and assessment and should be certified by an International accepted agency, for example, Yoga Alliance International (http://yogaalliance.in). EX = exercise group, C = control group, CBT = cognitive behavioural therapy, MD = medical doctor, OCD = obsessive compulsive disorder, PA = physical activity, PTSD = posttraumatic stress disorder.

Table 2
Overview of pooled drop-out rates in physical activity interventions (n=16) in people with anxiety and stress-related disorders.

Analysis	Number of study estimates	Meta-analysis Prevalence drop-out	95% CI		Between group P-value	Heterogeneity I^2
Main analysis all interventions	16	15.7%	9.9%	23.9%		60.3%
Type of exercise intervention					<0.001	
Aerobic exercise	8	19.7%	11.2%	32.1%		55.4%
Strength training	2	15.6%	3.8%	46.6%		27.4%
Mixed	3	3.6%	8.4%	14.1%		0%
Mind-body interventions	3	26.0%	15.7%	39.8%		75.5%
Intensity of the intervention					0.10	
Low	3	18.5%	6.4%	43.0%		75.5%
Moderate to high	13	14.6%	8.4%	24.0%		68.6%
Frequency of the intervention					<0.001	
1 / week	2	6.8%	1.6%	25.3%		18.6%
2 / week	3	19.8%	5.9%	49.1%		63.5%
3 / week	8	12.1%	6.1%	22.7%		48.1%
4 / week	1	31.1%	6.7%	74.2%		0%
5 / week	1	39.5%	11.1%	77.1%		0%
Time of an exercise session					<0.001	
16 min	2	4.5%	4.2%	35.0%		0%
30 min	4	16.1%	5.4%	39.0%		75.2%
60min	2	19.8%	5.0%	53.9%		68.4%
90 min	3	14.0%	3.7%	40.4%		80.8%
Supervised exercise sessions					<0.001	
Supervised	9	13.3%	6.8%	24.5%		74.2%
Partially unsupervised	7	18.2%	9.6%	31.9%		30.3%
Health care professional supervising exercise					<0.001	
Expert (physiotherapist, exercise physiologist, MD)	7	7.0%	3.5%	13.5%		0%
Non-expert (nurse, psychologist, personal trainer)	9	25.6%	18.1%	34.9%		49.6%
Autonomous motivational strategies					<0.001	
Autonomous motivation strategies	7	7.2%	4.2%	12.3%		0%
No autonomous motivation strategies	9	30.4%	23.6%	28.2%		16.0%
Controlled motivation strategies					<0.001	
Controlled motivation strategies	4	26.5%	13.8%	44.9%		62.3%
No controlled motivation strategies	12	12.2%	7.1%	20.2%		47.6%
Setting					0.01	
Inpatients	1	1.2%	0.0%	21.9%		0%
Outpatients	14	17.9%	11.7%	26.5%		57.2%
Mixed	1	2.8%	1.3%	39.2%		0%
Diagnosis of the participants					<0.001	
Posttraumatic stress disorder	6	13.0%	6.0%	26.1%		70.7%
Obsessive compulsive disorder	1	10.7%	1.8%	44.2%		0%
Panic Disorder	3	15.2%	5.1%	37.5%		57.3%
Social Anxiety disorder	1	8.0%	1.1%	40.4%		0%
Generalized anxiety disorder	2	4.5%	0.5%	31.2%		0%
Any anxiety disorder	3	31.5%	14.6%	55.2%		0%
Type of participants					<0.001	
Civilians	13	14.1%	7.9%	23.9%		59.3%
Veterans	2	19.4%	5.3%	50.9%		86.2%
Mixed	1	17.6%	2.5%	64.6%		0%

Table 3
Meta-regression of moderators for the drop-out rates in physical activity interventions (n=16) in people with anxiety and stress-related disorders.

Moderator	Number exercise groups	β	95% CI		P-value
Demographical characteristics					
Age (years)	16	-0.02	-0.08	0.04	0.48
Gender (% male)	16	0.001	-0.02	0.02	0.91
Intervention characteristics					
Duration of the intervention (weeks)	16	-0.06	-0.21	0.08	0.37

1.29, $p = 0.42$, $I^2 = 0\%$).

4. Discussion

4.1. General findings

To the best of our knowledge, the current meta-analysis is the first to investigate dropout rates and predictors in exercise RCT's among people with anxiety and stress-related disorders. Our results establish that the prevalence of dropout from exercise is relatively low among people with anxiety and stress-related disorders at 15.7%, adjusted to 22.4% after applying a trim and fill analysis ($N = 16$). Our analyses also suggest that there were no statistical differences between the different diagnostic subgroups, between men and women, across age groups or between civilians and veterans. The current data indicate that there are no

specific demographic subgroups which need additional care in order to reduce exercise dropout. Dropout rates are however lower in inpatient settings. Regarding the delivery of exercise interventions, supervised sessions, those supervised by physiotherapists and exercise physiologists, and applying autonomous motivation strategies resulted in significantly lower dropout rates. Finally, our comparative meta-analysis established that compared to control conditions, exercise results in similar dropout rates. The latter finding is important and suggests that exercise is feasible, well-accepted and tolerated by people with anxiety disorders.

Given the fact that exercise has important anxiolytic effects (Aylett et al., 2018; Kandola et al., 2018; Rosenbaum et al., 2015c; Stubbs et al., 2017) and that dropout can result in worse outcomes (Zieve et al., 2019), our results add further evidence to justify the incorporation of exercise as medicine for people with anxiety and stress-related disorders (Ashdown-Franks et al., 2020; Vancampfort et al., 2015). The pooled dropout prevalence (15.7%) among exercisers with anxiety and stress-related disorders is similar to that reported in a recent meta-analysis investigating dropout from individual psychotherapy in people with anxiety disorders (17.0%) (Gersh et al., 2017). The trim and fill adjusted prevalence of dropout from exercise trials in anxiety (22.4%) is higher than the trim and fill adjusted prevalence in depression (18.1%) (Stubbs et al., 2016), but lower than the trim and fill adjusted dropout rate observed in exercise trials among people with schizophrenia (26.7%) (Vancampfort et al., 2016b).

Specifically, for the first time, we identified moderators that influence dropout rates among people with anxiety and stress-related disorders participating in exercise RCT's. The observation that dropout rates were lowest for inpatient settings, is similar to results in a recent meta-analysis of dropouts in exercise trials in depression (Stubbs et al., 2016) and schizophrenia (Vancampfort et al., 2016b). This may reflect the added structure that is available for exercise trials that are conducted in inpatient settings. Another factor that may contribute to the lower dropout for inpatient trials could be the additional burden for outpatients to travel to the treatment facility to participate in the intervention. However, the findings should be considered with caution as only one inpatient study was included in the dataset.

In order to reduce the impact of dropouts in those with anxiety and stress-related disorders, exercise sessions supervised by physiotherapists and exercise physiologists should lead to lower dropout rates. Therefore, our findings extend recent calls to ensure that health care professionals with expertise in exercise prescription should implement exercise interventions within mental health care settings (Deenik et al., 2019). Given the physical comorbidity among those with diagnosed with anxiety and stress-related disorders including cardiometabolic co-morbidity (Rosenbaum et al., 2015b; Vancampfort et al., 2016c), physiotherapists and exercise physiologists constitute a valuable resource to ensure that people with anxiety and stress-related disorders receive the best care available. However, it should be noted that although mental health training is part of the undergraduate curricula for physiotherapists and exercise physiologists in some countries, this is not the case in all parts of the world (Andrew et al., 2019; Hooblaul et al., 2020; Kleemann et al., 2020; Vancampfort et al., 2018). Therefore, theoretical and practical mental health training is required to ensure that exercise physiologists and physiotherapists are in all parts of the world well equipped to motivate people with anxiety and stress-related disorders to an active lifestyle. Our data demonstrate that in particular implementation of autonomous motivation strategies reduces the drop-out rate. According to the self-determination theory framework (Deci and Ryan, 2008), autonomous motivation can be stimulated by fulfilling three psychological needs, that is the need for autonomy (i.e., experiencing a sense of psychological freedom when engaging in an exercise program), competence (i.e., feeling effective to attain desired exercise outcomes) and relatedness (i.e., being socially connected within the exercise program). Health care professionals can achieve this in exercise interventions by offering clear choices, supporting own initiatives, avoiding the use of external rewards (which is a controlled motivation strategy increasing dropout), and using autonomy supportive language (e.g. "could" and "choose" rather than "should" and "have to") (Deci and Ryan, 2000). Feelings of competence can also be attained when patients experience success while participating in exercise programs. Exercise programs therefore need to be tailored to the capabilities of the patient and sufficient instructions, practice and positive feedback are needed (Deci and Ryan, 2008). Health care professionals need to show enthusiasm and interest. Offering group exercise sessions could increase the feeling of relatedness and decrease the feeling of being isolated (Deci and Ryan, 2000).

4.2. Limitations and future research

Several limitations should be considered when interpreting the current findings. Most limitations largely reflect limitations in the primary studies included. First, potentially important moderators of dropout, such as the level of anxiety and stress-related symptoms, mental and physical co-morbidity, illness duration, body mass index were not or insufficiently available in the dataset. Previous research in depression for example indicated that higher levels of depression were associated with higher dropout rates (Stubbs et al., 2016). Future research should therefore consider the impact of these important moderators. Second, we encountered heterogeneity in some of our analyses. However, our sensitivity analyses were able to explain large proportions of the between-study heterogeneity. Third, we encountered publication bias, but conducted trim and fill analyses to adjust for this. Finally, few of the included studies provided sufficient detailed information on characteristics of dropouts versus completers, thus precluding direct comparative analyses of predictor variables. Future research should explore important characteristics between completers and non-completers of exercise RCT's. Nevertheless, allowing for these caveats, our results provide important data that can guide health care professionals, researchers and policy makers who are seeking to encourage people with anxiety and stress-related disorders to engage in exercise.

In summary, the current systematic review and meta-analysis has demonstrated that exercise is well accepted by participants with anxiety and stress-related disorders with comparable levels of dropout compared to control conditions. Taken together, our results suggest that dropout rates in anxiety and stress-related disorders are lower when delivered by professionals with qualifications to deliver exercise such as physiotherapists and exercise physiologists. Health care professionals supervising exercise programs for people with anxiety and stress-related disorders should consider that dropout is higher when controlled motivation strategies are used but lower when autonomous motivation strategies are applied. Given that exercise is effective in the treatment of anxiety and stress-related disorders, and has a wide range of other health benefits, our results are of interest to health care professionals seeking to engage people with anxiety disorders to exercise. Finally, considering the lower drop rates when physiotherapists and exercise physiologists supervise exercise, these clinicians should be the first choice when considering increasing staff resources to facilitate people with anxiety and stress-related disorders engaging in regular exercise.

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Authors' contribution

DV and BS: Conceptualization, Data curation, Formal analysis, Writing, original draft. CPRS and TVD: Data curation, Formal analysis, Writing - review & editing. MH, FS, JF, SR: Writing - review & editing.

Declaration of Competing Interest

None

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Supplementary materials

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