REVIEW

A Systematic Review of Cardiorespiratory Fitness Testing in Major Depression

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ABSTRACT

Background: Depression is associated with physical inactivity, low cardiorespiratory fitness (CRF), and poor physical health compared with the general population. Various protocols are employed to determine CRF studies of people experiencing depression, but standardized methods are absent from the literature. Thus, the aim of the present review is to systematically examine the protocols reported to determine CRF in patients with major depressive disorder (MDD).
Methods: Replicating a previously published search strategy, the present review sourced relevant studies from PubMed, PsycInfo, Embase, CINAHL, MEDLINE, Psychology and Behavioural Sciences Collection, and SPORTDiscus from August 2015 to February 2021. Details of CRF testing protocols were extracted into a preprepared form for analysis.
Results: Twenty-three studies met the inclusion criteria, including those from a previous review of CRF in people with MDD. Twelve included studies employed maximal testing protocols, while 11 studies reported using submaximal testing protocols. Cycle ergometry was the most used protocol, followed by treadmill and walk tests. Notably, complete descriptions of the test protocols to facilitate test replication were frequently absent.
Conclusions: Cycle ergometry is commonly used to assess CRF in people with MDD, but protocol details are lacking, making replication difficult. Efforts to standardize protocol descriptions are warranted. *J Clin Exerc Physiol*. 2022;11(3):103–114.

Keywords: fitness, mental illness, assessment, aerobic capacity

INTRODUCTION

Depression is a leading cause of disability worldwide, impacting up to 14.6% of people globally (1). People with depression often exhibit poor health behaviors such as low physical activity (PA), have poorer cardiometabolic health, and subsequently die earlier compared with the general population (2,3). PA is a modifiable behavior able to positively impact a variety of health outcomes, leading to significant interest in the role PA and exercise may play in the treatment of patients with depression, including those with major depressive disorder (MDD) (4).

There is growing evidence for aerobic exercise (AE) in the treatment of depression. A recent Cochrane review reported AE has a moderate effect on reducing depressive symptoms (5). More recent reviews further support the antidepressant properties of AE (6–8), with significant effects in both inpatient and outpatient settings and with group and individual interventions (9). Considering the strength of evidence supporting the role of AE in the treatment of depression, many global treatment guidelines now recommend AE as one avenue of preventing and treating MDD.

For instance, the European Psychiatric Association concluded that moderate-vigorous intensity, supervised PA improves quality of life and depressive symptoms in patients with MDD (10). Both the Canadian Network for Mood and Anxiety Treatments and the Royal Australian College of General Practitioners consider PA as a safe, efficacious nondrug intervention for MDD, and both organizations have published guidelines for prescribing PA in patients with depression (11,12). While most guidelines include advice on exercise duration, frequency and type, exercise intensity often lacks sufficient detail to fully inform practitioners on

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exercise prescription (13). Lack of guidance here is potentially problematic since high-intensity exercise may induce negative affective responses (14), leading to poor uptake and adherence to exercise (15). One way in which to accurately prescribe exercise intensity and determine exercise capacity is through the initial assessment of cardiorespiratory fitness (CRF), using valid and reliable measures (16).

Recent reviews suggests that CRF is inversely related to severity of depressive symptoms (17) and that low CRF is a risk factor for the onset of depression (18). More recent longitudinal studies suggest higher CRF is strongly associated with a reduced risk of depression over time which is independent of baseline PA (19). Furthermore, low CRF has been more strongly associated with depressive symptoms than weight status, suggesting that targeting CRF would likely yield greater benefits in terms of treating MDD than focusing on body composition (20). In addition to guiding exercise prescription, CRF is a valuable predictor of health outcomes in the general population (21) and a marker of habitual PA (22). However, despite frequent recommendations to assess CRF (23), it remains largely absent in mainstream clinical practice (21).

Completion of some CRF testing protocols is acknowledged as requiring high levels of motivation (24), and completing a maximal test to objective exhaustion is associated with negative affective responses (25). In fact, Evans et al. (25) suggest test protocols be modified when potential negative affective responses of the participant are considered important. Given that exercise motivation and intentions to exercise are lower in those with depression (26), it appears likely that the presence of MDD may impact individuals' ability to exert themselves on an exercise test, especially a maximal test, which may impact test validity. Hence, it becomes important that CRF protocols for people with mental health conditions such as MDD are at least mental health informed. That is, test choice and protocol are underpinned by an understanding of the differential motivations and goals experienced by this cohort.

To date, only a few reviews could be identified that analyzed the relationship between CRF and depression in exercise interventions (27–29). Of these, only Stubbs et al. (27) focused entirely on depression, rather than depression in conjunction with other mental health disorders, concluding AE interventions resulted in statistically significant improvements in CRF. However, a limitation of current reviews is inadequate consideration of CRF test protocols. To the best of our knowledge, no guidelines on measuring CRF in patients with depression have been published, despite evidence supporting the validity and reliability of some protocols for the assessment of CRF in people with mental illness (30). Both an absence of standardized methods and insufficient description of CRF assessment protocols in peer-reviewed literature can be problematic, as this limits replicability of study protocols and thus between-studies comparisons. Therefore, the aim of this review is to systematically examine the protocols reported to determine CRF in patients with MDD. Important for practitioners, the present review is not focused on the outcomes of CRF assessment (magnitude of CRF), rather on the types of tests used and the degree of detail reported regarding the CRF assessment protocol in the included studies.

METHODS

This review follows the PRISMA statement (31), using a predetermined but unpublished protocol.

Inclusion Criteria

Articles included in this review were identified using criteria adapted from Stubbs et al. (27), specifically randomized controlled trials (RCTs) with (a) adult participants (18 years and older) with a diagnosis of MDD by either established criteria (e.g., Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition [DSM-V] (32)) or a validated screening measure (e.g., Beck Depression Inventory, Second Edition [BDI-II] (33)). (b) The primary diagnosis of participants was MDD which was not secondary to chronic illness. (c) CRF was objectively measured or predicted using either maximal or submaximal exercise tests.

Information Sources and Searches

First, articles included for analysis in a recent review on CRF in MDD were sourced from Stubbs et al. (27). The search criteria for were based on a previous Cochrane review (5), which is one of the most comprehensive reviews of exercise and depression to date. Since the present review is focused on RCTs and protocols used for the assessment of CRF, search terms used by Stubbs et al. (27) relating to resistance training were removed, and the final search strategy included the following terms as author keywords: (exercis* OR aerobic* OR running OR jogging OR walk* OR hiking OR swim* OR aquatic* OR cycling OR bicycl* OR activit* OR fitness OR train* OR "physical medicine") AND (depression OR dysthymia). These search criteria were applied in the following databases: PubMed, PsycInfo, Embase, CINAHL, MEDLINE, Psychology and Behavioural Sciences Collection, and SPORTDiscus. Searches were date limited from August 2015 to February 2021 to avoid duplication of studies already included in the review of Stubbs et al. (27). Reference lists of all included articles were screened for potential additional papers meeting the inclusion criteria.

Study Selection

In the first stage of screening, 1 author screened the title and abstract of references cited by Stubbs et al. (27). In the next stage, after removing duplicates, the same author retrieved potentially eligible articles from each database and screened for inclusion based on article title and abstract. Included articles were checked by the second author with disagreements resolved by discussion. Where consensus could not be reached, resolution was achieved by consultation with an expert colleague. The full texts of remaining articles were then screened by the first author, and a final list of eligible articles was reached through consensus. In the event of 2 or

more articles being based on the same dataset, only the earliest publication was included to avoid overrepresentation of methods used to assess CRF.

Outcomes

The primary outcome was the protocol used in the objective measurement of CRF.

Data Extraction

Once a list of eligible full-text articles was finalized, relevant data were extracted using a predetermined data extraction form. This extraction form included participant characteristics (gender, mean age, mean body mass index [BMI], primary diagnosis, diagnostic tool used, percent taking antidepressants, and inpatient/outpatient status), the method by which CRF was determined, criteria for attainment of Vo_{2max}/Vo_{2peak}, and the criteria for test termination.

Data Synthesis

The present review describes the published protocols employed in studies assessing CRF in people with depression rather than the objective CRF outcome (e.g., Vo_{2max} or Vo_{2peak}). Additionally, given that this review was concerned with the explicit reporting of CRF assessment protocols, authors of included articles were not contacted for unpublished information.

RESULTS

Search Results

In the first stage of the search strategy, 8 articles from the review of Stubbs et al. (27) met the inclusion criteria for the present review. Six of these (34–39) were included in the analysis of Stubbs et al. (27), and 2 were obtained from the reference list of the same review (40,41). In the second stage (database searches), after removal of duplicates, 971 potentially eligible articles were screened for inclusion. Twenty-two articles were identified as meeting the inclusion criteria for the present review with a further 5 articles identified via searching of reference lists. After full-text screening, 12 articles were subsequently excluded, leaving a total of 8 from the review of Stubbs et al. (27) and 15 from the search conducted by the reviewers of the present review, leaving 23 papers in total. Flow through of articles for inclusion including reasons for exclusion are shown in Figure 1. No discrepancies were recorded between reviewers regarding inclusion of manuscripts for this review.

Since the inclusion criteria for the present review differed slightly from that of Stubbs et al. (27), not all studies were eligible for the present review. Only 1 arm of the trial conducted by Krogh et al. (37) was included in the present review, and the paper by Blumenthal et al. (42) was excluded based on the participant's diagnosis of depression being secondary to heart failure. Two articles retrieved from the reference list of Stubbs et al. (27) not included in the analysis undertaken by the authors were included in the present review, as both met the inclusion criteria (40,41).

Overall, 23 RCTs which included 1549 participants (1051 females) that measured CRF in patients with MDD were included for analysis. The mean age of participants was 45.5 years (range = 18.8 (39) to 76.5 (43)). The average gender distribution across all studies was 65% female (range = 29% (44) to 100% (34,39,45)). Six interventions took place in an inpatient setting, 16 were conducted in an outpatient setting, and 1 study included both inpatients and outpatients. Details of included studies are shown in Table 1.

Twelve included studies (52%) used a maximal testing protocol, while 11 (48%) studies used a submaximal protocol. Overall, the most used procedure to assess CRF was cycle ergometry ($N = 12$; 52%), followed by treadmill tests ($N = 6$; 26%), walk tests ($N = 4$; 17%), and step tests ($N = 1$; 4%). Regarding test protocols, an unspecified cycle ergometer test was most referred to ($N = 6$), followed by a Balke treadmill protocol ($N = 3$). Of included RCTs that conducted maximal tests, 73% used cycle tests ($N = 8$), while the use of submaximal tests was equally distributed between cycle ergometry ($N = 4$; 36%) and walk tests ($N = 4$; 36%). Frequent gaps in the reporting of testing protocols beyond the types of test instrumentation used were identified, notably in the lack of description of criteria for test termination and reporting of failure to reach Vo_{2max}/Vo_{2peak}. Details of the described protocols for maximal and submaximal tests of CRF, stratified by setting, are shown in Tables 2 and 3, respectively.

DISCUSSION

To our knowledge, this review is the first to examine protocols reported in RCTs assessing the CRF of people with MDD. We show that, although cycle ergometry is favored in this population, complete description of test protocols is often absent, making replication difficult. These findings make a significant contribution to our understanding of CRF assessment in people with MDD and will guide future studies in protocol selection and reporting.

Across both maximal and submaximal tests, cycle ergometer tests were most used, with 26% of all RCTs reporting an unspecified cycle ergometer protocol, while a further 26% referred to specific cycle ergometer tests (e.g., Astrand-Rhyming cycle test (35,55) or YMCA submaximal cycle test (39,51)). Compared with other test instrumentation, cycle ergometer tests are easy to administer, portable, and allow for the selection of precise workloads in small increments (58). Compared with treadmills, cycle ergometers are low cost, easy to calibrate, permit blood pressure measurements more easily, and require less familiarization (16,58). A disadvantage of cycle ergometry is the potential for localized muscle fatigue, which may lead to earlier test termination than otherwise expected (59,60). Studies report that both Vo_{2max} and Vo_{2peak} values are 10% to 28% higher in treadmill tests compared with cycle tests in both active and sedentary populations (61,62), perhaps due to the comparatively low prevalence of cycling as routine exercise in the general population compared with walking.

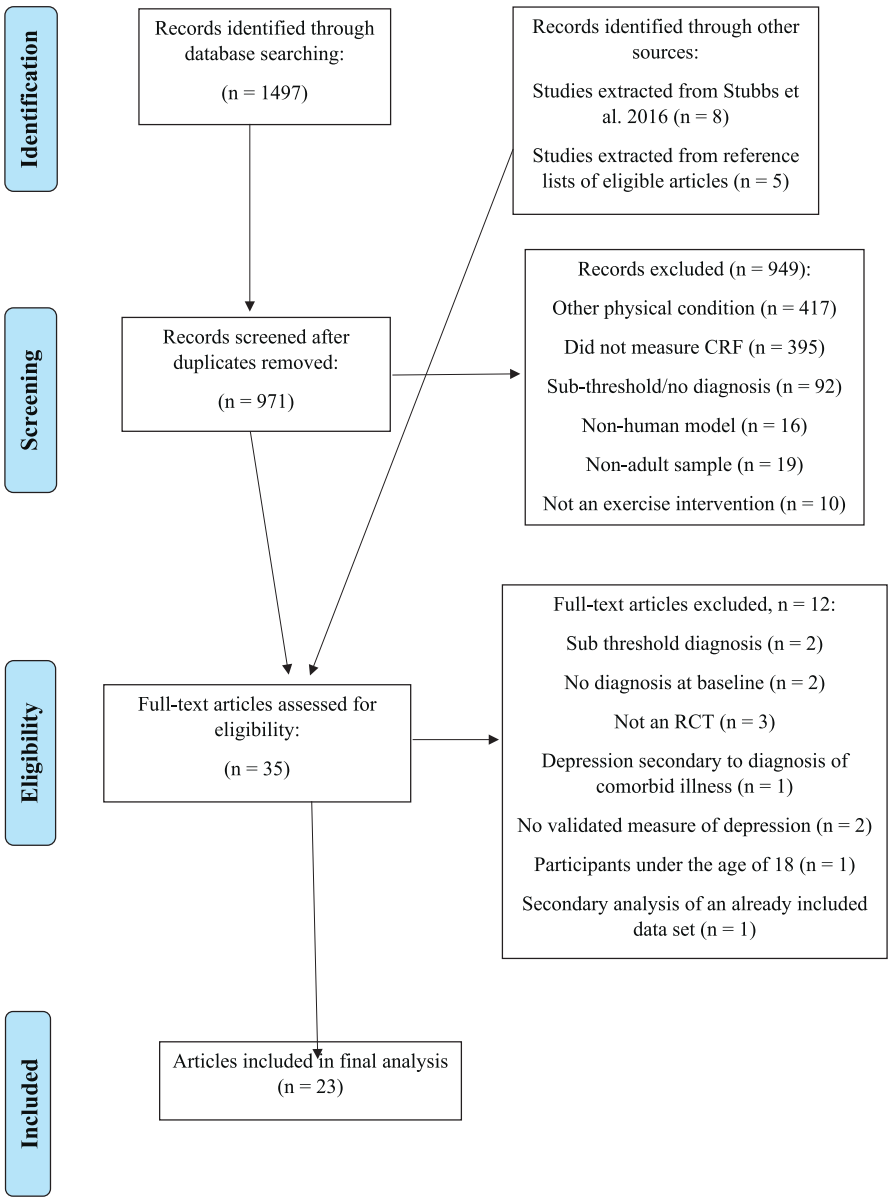

FIGURE 1. Flow through of papers.

Despite variance between cycle ergometry tests and treadmill tests, test-retest reliability for both maximal (63) and submaximal (64) cycle ergometry protocols has been consistently rated as excellent in both active and sedentary populations. This is supported in a recent systematic review showing the validity and reliability of a range of fitness testing protocols in people with mental illness (30). Although CRF values obtained from treadmill tests and cycle ergometry are likely to be different, their ease of use, accessibility, and portability suggest cycle tests are likely to be suitable for determining CRF in patients with MDD; however, caution should be used when comparing CRF measured using differing modalities or test protocols.

Despite their relatively low usage, the utility of submaximal walk tests to estimate CRF in patients with MDD is worthy of mention. Field tests like the 2-minute walk test (2MWT) and 6-minute walk test (6MWT) can be used to evaluate CRF in populations in which ergometer or treadmill tests could not feasibly be applied, such as older adults or those with otherwise limited functional capacity (16,58). In fact, of the 4 included studies that used walk tests, 2 were in community-dwelling adults with an average age above 70.0 (43,65). While distance walked in a 6MWT appears to be only modestly correlated with Vo_{2max} measured from maximal testing (66), walk tests are considered a valid representation of capacity to perform submaximal, everyday tasks (67) and allow participants to control their pacing in a manner not possible during treadmill tests (67). Moreover, brief tests such as the 2MWT are shown to be reliable in patients with MDD, minimizing participant burden (68).

Across all RCTs, submaximal and maximal tests were used almost equally. Unsurprisingly, most inpatient studies used submaximal protocols, requiring only heart rate (HR) response to workload be recorded. In contrast, maximal

TABLE 1. Description of included studies.

Author(s)	Partici-pants (*N*)	Country of Study	% Female	Mean Age	BMI	Diagnosis	Diagnostic Tool	Setting	% Taking Anti-depressants
Blumenthal et al. (46)	202	USA	76	52.0 ± 8.0	30.0 ± 7.3	MDD	DSM-IV + BDI-II	Outpatient	24
Blumenthal et al. (47)	156	USA	72	57.0 ± 6.5	N/R	MDD	DSM-IV + HAM-D	Outpatient	100
Boettger et al. (40)	44	Germany	32	37.0 ± 12.7	23.9 ± 4.2	MDD	DSM-IV	Outpatient	86
Carneiro et al. (45)	19	Portugal	100	50.2 ± 12.1	29.3 ± 5.7	Depressive episode moderate (5%), recurrent depressive disorder (21%), or dysthymia (74%)	ICD-10 + psychiatrist confirmation	Outpatient	89
Chu et al. (34)	54	USA	100	25.9 ± 6.1	24.1 ± 3.9	Mild to moderate depressive symptoms (BDI-II 14–28)	BDI-II	Outpatient	39
Danielsson et al. (35)	62	Sweden	77	45.5 ± 13.3	25.1 ± 4.4	MDD	DSM-IV + MINI	Outpatient	100
Doose et al. (48)	46	Germany	63	47.9 ± 10.5	25.4 ± 4.4	Major depressive episode	ICD-10	Outpatient	59
Gujral et al. (49)	15	USA	N/R	N/R	N/R	MDD	PRIME-MD	Outpatient	100
Herbsleb et al. (44)	34	Germany	29	39.2 ± 11.9	21.8 ± 2.8	MDD	DSM-V + HAMD-21 + BDI	Outpatient	94 (patients)
Huang et al.(43)	57	Taiwan	53	76.5 ± 5.9	N/R	Mild to moderate depressive symptoms (GDS-15 score ≥ 5)	GDS-15	Outpatient (community dwelling)	0
Imboden et al. (50)	34	Switzerland	50	38.9 ± 11.3	24.7	MDD	ICD-10	Inpatient	100
Jaworska et al. (51).	13	Canada	46	21.5 ± 1.5	30.35 ± 18.4	MDD	MINI + HAMD	Outpatient	0
Kerling et al. (36)	42	Germany	38	42.6 ± 10.2	26.8 ± 5.0	MDD	DSM-IV + standardized clinical interviews	Inpatient	76
Knubben et al. (52)	38	Germany	55	49.5 ± 13.0	N/R	MDD	DSM-IV + BRMS	Inpatient	85
Krogh et al. (37)	165	Denmark	74	38.9 ± 9.46	26.5 ± 5.4	Unipolar depression	ICD-10 + professional referral	Mixed	69
Krogh et al. (38)	115	Denmark	67	41.6 ± 11.25	26.4 ± 6.0	Major depression	DSM-IV + MINI	Outpatient	0
Makizako et al. (53)	89	Japan	51	73.1 ± 5.5	N/R	Mild to moderate depressive symptoms (GDS-15 score ≥ 5)	GDS-15	Outpatient (community dwelling)	0
Minghetti et al. (54)	60	Switzerland	78	36.0 ± 11.0	23.9 ± 3.9	MDD	BDI-II	Inpatient	88
Nabkasorn et al. (39)	49	Thailand	100	18.8 ± 0.7	N/R	Mild to moderate depressive symptoms	CES-D	Outpatient	0
Rahman et al. (55)	110	Sweden	68	41.9 ± 11.5	24.7 ± 3.8	Mild to moderate depression	MADRS-clinician rated	Outpatient	24
Shachar-Malach et al. (56)	12	Israel	75	43.4 ± 16.1	N/R	MDD	DSM-IV	Inpatient	100
Voderholzer et al. (41)	102	Germany	45	(Dprs) 49.0 ± 11.4 (Cntrl) 48.0 ± 12.1	(Dprs) 26.5 ± 5.0 (Cntrl) 25.1 ± 4.1	Depressive disorder	ICD-10	Inpatient	82
Zanetidou et al. (57)	121	Italy	71	75.0 ± 6.0	25.9 ± 3.6	MDD	DSM-IV + HAM-D	Outpatient	100

BDI = Beck Depression Inventory; BDI-II = Beck Depression Inventory, Second Edition; BMI = body mass index; BRMS = Bech-Rafaelsen Melancholy Scale; CES-D = Center for Epidemiologic Studies Depression Scale; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; DSM-V = DSM, Fifth Edition; GDS-15 = Geriatric Depression Scale (Short Form); HAM-D = Hamilton Depression Rating Scale; HAMD-21 =Hamilton Depression Rating Scale; ICD-10 = International Classification of Diseases – 10th Revision; MADRS = Montgomery-Asberg Depression Rating Scale; MDD = major depressive disorder; MINI = Mini International Neuropsychiatric Interview; N/R = Not reported; PRIME-MD = Primary Care Evaluation of Mental Disorders

TABLE 2. Summary of protocol details for maximal tests of CRF.

Author(s)	Fitness Test Type	Reference Provided for Test	Key CRF Measurement	Criteria for Attainment of Vo_{2max}/Vo_{2peak} Details	Criteria for Test Termination Details	How Was the Key Measurement Determined? (Details)	Setting
Kerling et al. (36)	Incremental cycle ergometer test—start at 20W, regular increase of 10W/min	Y	Vo_{2peak}	When a patient could no longer continue based on peripheral muscle fatigue and/or dyspnoea + rating on Borg scale (6–20; specific Borg score not stated)	When a patient could no longer continue based on peripheral muscle fatigue and/or dyspnoea + rating on Borg scale (6–20)	Measured (subjective exhaustion and workload at anaerobic threshold)	Inpatient
Shachar-Malach et al. (56)	Graded exercise training on a treadmill with Bruce protocol	N	Vo_{2max}	Not reported	Not reported	Estimated (implied)	Inpatient
Minghetti et al. (54)	Incremental cycle ergometer test—start at 25W, regular increase of 10W/min	N	Vo_{2peak}	Subjective perceived exhaustion (BORG10) was reached	Participant rated perceived exhaustion at BORG10	Estimated (highest oxygen uptake averaged over 30 s; facemask measured respiratory gas exchange every 10 s)	Inpatient
Voderholzer et al. (41)	Standardized incremental cycle ergometer test—starting workload adjusted for individual capacity, increased every 3 min	N	Lactate concentration	Subjects instructed to cycle at a steady rate and continue until subjectively feeling exhausted	Subjective exhaustion	Measured (subjective exhaustion and workload at anaerobic threshold)	Inpatient
Blumenthal et al. (46)	Graded treadmill exercise test—workload increased at 1 metabolic equivalent per min	Y	Vo_{2peak}	Analysis of expired air; samples collected at 20 s intervals; peak values determined from an average obtained during the last 60 s	When exhaustion was reached or other standard endpoint (chest pain, decreasing blood pressure)	Measured (average O_2 consumption during last 60 s of test)	Outpatient
Blumenthal et al. (47)	Symptom-limited graded treadmill test with modified Balke protocol—workload increased at 1 metabolic equivalent per min	Y	Vo_{2peak}	Analysis of expired air; samples collected at 15 s intervals; peak values determined from an average obtained during the last 60 s	When exhaustion was reached or other standard endpoint (chest pain, decreasing blood pressure)	Measured (average O_2 consumption during last 60 s of test)	Outpatient
Chu et al. (34)	Balke treadmill protocol	N	Vo_{2peak}	Subjective exhaustion (not explicitly stated)	Not reported	Estimated (equation including time taken to complete the test; not explicitly stated)	Outpatient
Herbsleb et al. (44)	Cycle ergometer with 15W/min intervals until subject reached limit of tolerance	Y (protocol paper)	Vo_{2max}	1. Plateau in O_2 uptake with increase in power output. 2. Attainment of RERmax. 3. Maximal Borg rating of RPE (>18). Exhaustion occurred when patient could no longer maintain required power output (encouraged to give maximal effort)	Once objective exhaustion measures had been met (including max lactate levels, highest HR and O_2 uptake plateau)	Measured (by reaching maximal exertion through objective measures)	Outpatient
Krogh et al. (38)	Andersen maximal cycle protocol—in initial 5 min of test, 100W for men and 75W for women; increased by 25W/min until exhaustion	Y	Vo_{2max}	Subjective perceived exhaustion (BORG15) was reached	Voluntary termination based on RPE	Measured (based on RPE (BORG15))	Outpatient

TABLE 2. Continued.

Author(s)	Fitness Test Type	Reference Provided for Test	Key CRF Measurement	Criteria for Attainment of Vo_{2max}/Vo_{2peak} Details	Criteria for Test Termination Details	How Was the Key Measurement Determined? (Details)	Setting
Zanetidou et al. (57)	Cycle ergometer with breath-by-breath expired gas analysis—duration of 12 min, 3-min warmup with regular increase of 10W/min (women) or 15W/min (men)	Y (protocol paper)	Vo_{2max}	Full duration of 12 min or voluntary termination	The test was interrupted earlier than 12 min in the following conditions: muscular exhaustion, refusal of the patient to continue, respiratory quotient >1.03, reaching the plateau of oxygen consumption. The test was suspended, and the participant excluded on appearance of signs of atrial fibrillation or other arrythmias	Measured (breath-by-breath expired gas analysis (if 12 min reached), exhaustion, refusal to continue, plateau of oxygen consumption)	Outpatient
Boettger et al. (40)	Incremental cycle ergometer test—starting at 25W, increasing by 25W every 3 min until exhaustion. Cool-down protocol included	N	Vo_{2peak}	Highest O_2 uptake at the end of the test	When objective exhaustion was reached (O_2 output, lactate concentrations)	Measured (face mask)	Outpatient
Krogh et al. (37)	Andersen maximal cycle protocol—in initial 5 min of test, 100W for men and 75W for women; increased by 25W/min until exhaustion	Y	Vo_{2max}	Subjective perceived exhaustion (BORG15) was reached	Voluntary termination based on RPE	Measured (based on RPE (BORG15))	Mixed

CRF = cardiorespiratory fitness; HR = heart rate; RERmax = Respiratory Exchange Ratio; RPE = Rating of Perceived Exertion

testing using expired gas analysis requires highly specialized equipment and trained technicians (58). Additionally, since physical health comorbidities are common in people with MDD (69), submaximal tests may offer a lower risk alternative for CRF assessment.

Unfunded studies or those with limited resources such as those conducted in community or outpatient settings may be forced to use lower-cost, more convenient submaximal cycle or walk tests. In contrast, well-funded studies conducted in inpatient settings may have access to exercise laboratories and staff capable of conducting and interpreting maximal fitness tests. Another important consideration in test choice is participant motivation. High levels of motivation are usually required to complete a maximal exercise test (24), and exercise motivation is generally lower in those with depression (26), suggesting that maximal exertion may be more difficult to achieve in patients with MDD. Considering the generally low levels of PA and CRF in people with depression, submaximal test protocols appear well justified in patients with MDD.

Although evidence supports the validity and reliability of fitness testing in people with mental illness (30), a primary factor limiting the validity of submaximal CRF testing in patients with MDD could be concerns about sensitivity to measure change (24). Given that CRF estimated from submaximal testing is usually calculated using submaximal HR response, proper control of environmental, dietary, and behavioral factors is essential (58). Failure to control for these variables during repeated tests may affect HR response to exercise, potentially reducing the reliability of CRF values estimated from submaximal tests (58). This may be especially relevant in longitudinal studies; hence, the selection of test protocols must consider sensitivity to measure change of time and determination of a minimal detectable change in an MDD population must be established.

The relatively low usage of maximal CRF protocols could be due to concerns related to failure to reach an oxygen plateau, that is, where an increase in workload does not result in an increase in oxygen consumption, along with angina or anginalike symptoms, or excessive rise in blood pressure (systolic pressure >250 mm Hg and/or diastolic pressure >115 mm Hg) is a key criterion for test termination (58). Of the 5 RCTs that conducted maximal fitness testing and measured Vo_{2max}, only 1 study (40) acknowledged this limitation, stating that 15% of participants did not reach objective exhaustion due to either hypertension or discomfort. Furthermore, despite using a submaximal protocol, Rahman et al. (55) stated that valid Vo_{2max} could not be

TABLE 3. Summary of protocols for submaximal tests of CRF.

Author(s)	Fitness Test Type	Ref. Provided for Test	Key CRF Measurement	Criteria for Attainment of Vo_{2max}/Vo_{2peak} Details	Criteria for Test Termination Details	How Was the Key Measurement Determined? (Details)	Setting
Imboden et al. (50)	Queens College Step Test	Y	Vo_{2max}	Reference provided but not explicitly stated	Upon 3 min of stepping up and down	Estimated (heart beats are counted for 15 s from 5 to 20 s of recovery)	Inpatient
Knubben et al. (52)	Modified Bruce treadmill test—begin at 3 km/h and continue until 80% of age expected maximal HR	N	Vo_{2max}	When a patient reached 80% of expected maximal HR	HR 80% of max	Estimated (using HR and lactate concentration in blood)	Inpatient
Carneiro et al. (45)	6MWT	N	Distance walked (m)	N/A	Not reported	By measuring meters walked	Outpatient
Danielsson et al. (35)	Astrand-Rhyming submaximal exercise test	Y	Vo_{2max}	Estimated based on HR adjusted for age	After 6 min or if patient could not complete 6 min	Estimated (Vo_{2max} predicted using age-based HR formula)	Outpatient
Doose et al. (48)	UKK 2-km walk test—walk for 2 km with instruction to go as fast as possible without running. Participants also gave Borg RPE rating of 6–20 after each lap	Y	Vo_{2max}	Calculated using recorded lap time, BMI, HR during last 30 s of walking, age and gender	Not reported	Estimated (Vo_{2max} calculated using recorded lap time, BMI, HR during last 30 s of walking, age and gender)	Outpatient
Gujral et al. (49)	Modified Balke treadmill protocol—constant speed with 2% grade increments every 2 min	N	Vo_{2peak}	Estimation	When subjects HR reached 85% of age-based max, volitional fatigue or RPE ≥ 15	Estimated (using time to complete the test)	Outpatient
Jaworska et al. (51)	YMCA submaximal bicycle ergometer protocol	Y	Vo_{2max}	HR response to workload increments	When HR plateaued	Estimated (predicted based on HR response to submaximal workloads)	Outpatient
Rahman et al. (55)	Åstrand-Rhyming submaximal cycle ergometry test—ride for 6 min at 50 rpm with HR between 120 and 150 bpm	Y	Vo_{2max}	Estimated based on HR adjusted for age	After 6 min or if patient could not complete 6 min (due to tiredness or fatigue)	Estimated (VO_{2max} predicted using age-based HR formula)	Outpatient
Nabkasorn et al. (39)	Multistage YMCA submaximal bicycle ergometer protocol	N	Vo_{2peak}	HR response to workload increments	Not reported	Estimated (predicted based on HR response to submaximal workloads)	Outpatient
Huang et al. (43)	6MWT	N	Distance walked (m)	Walk accompanied back and forth along a marked 50 m hallway for 6 min	Not reported	By measuring meters walked	Outpatient (community dwelling)
Makizako et al. (53)	2MWT	Y (protocol paper)	Distance walked (m)	Not reported	Not reported	By measuring meters walked	Outpatient (community dwelling)

2MWT = 2-minute walk test; 6MWT = 6-minute walk test; BMI = body mass index; CRF = cardiorespiratory fitness; HR = heart rate; N/A = Not available; RPE = Rating of Perceived Exertion; UKK = Urho Kaleka Kekkonen

predicted for 38% of participants due to influenza, dizziness, or fatigue. This is not an uncommon phenomenon, with 1 study of college athletes reporting 80% of participants did not reach an oxygen plateau (70). Of the RCTs included in this review, 30% (6 maximal and 1 submaximal protocol) did not report criteria for test termination. Generally, studies reporting maximal testing protocols described criteria for test termination in detail.

Two key findings of the present review are the heterogeneity of protocols used to assess CRF in people with MDD and the limited reporting of protocol details. While protocol papers were often cited, reference to earlier precedents was found in only 1 article (54), and 43% of included RCTs provided no reference describing the method used to determine CRF. Additionally, 50% of all cycle ergometry protocols used were unspecified and had no cited protocol. While some protocols were described in detail, including comprehensive information about criteria for test termination and the exact methods used to estimate/determine Vo_{2max} or Vo_{2peak}, a lack of standardization makes between-studies comparisons difficult. Moreover, the level of detail given to describe each unspecified protocol was not consistent across all RCTs. This lack of detailed reporting is problematic both for the replication of existing studies and to provide guidance for future investigations. To encourage complete and detailed description of exercise interventions, Slade et al. (71) developed the 16-item Consensus on Exercise Reporting Template (CERT). The CERT aims to assist in the interpretation, replication, and translation to practice of complex exercise interventions and provides guidance on key items to report when describing an exercise program (e.g., "detailed description of the qualifications, expertise and/or training," "detailed description of how exercises are tailored to the individual") (71). While guidelines for CRF testing in healthy and clinical populations exist and are widely accessible (58), the complete reporting of protocol details in studies examining CRF in people with MDD is generally poor.

To achieve standardized reporting of CRF protocols, a modified version of the CERT instrument could be developed based on a Delphi approach or through expert consensus of exercise physiologists, mental health clinicians, researchers, and those with lived experience of mental illness. This unified approach could be adopted by journals and by peak mental health research bodies to facilitate adoption of standardized protocols, making between-studies comparisons possible. Moreover, a consensus on CRF protocol for people with mental illness could be translated to clinical practice through peak exercise professional bodies.

Strengths and Limitations of Review

The present review is the first to synthesize the CRF assessment protocols used in RCTs examining CRF in people with MDD. A strength of the review is the use of an established search protocol and inclusion criteria. A further strength is the detailed extraction of CRF assessment components across different testing modes and settings. However, the review was limited to RCTs published in English, used only a selection of the available databases, and included only studies of people with MDD, not subthreshold symptoms, and exercise-based assessments of CRF. The latter point is important since CRF can be estimated from nonexercise data such as demographic and PA status data or from using specific PA surveillance tools such as the International Physical Activity Questionnaire (72). Although previously noted as a strength of this review, the use of an established search protocol may be considered a limitation resulting in some relevant manuscripts being missed.

Clinical Implications

Although maximal and submaximal tests are used in almost equal proportions, the findings of the present review highlight the lack of standardized use and reporting of CRF assessment protocols in people with MDD. To combat this issue, formation of a modified CERT (71) to describe CRF testing protocols is recommended as well as the adoption of standardized reporting in journals and mental health research bodies. Test choice should be mental health informed to accommodate levels of exercise motivation of people with MDD which may impact validity and reliability of test outcomes. Self-selected test protocols and prediction algorithms for CRF assessment warrant further research in this population.

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