Preventive Medicine 91 (2016) 123–131

Contents lists available at ScienceDirect

Preventive Medicine

journal homepage: www.elsevier.com/locate/ypmed

Training fast or slow? Exercise for depression: A randomized controlled trial

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ARTICLE INFO

Article history:
Received 22 March 2016
Received in revised form 3 August 2016
Accepted 6 August 2016
Available online 8 August 2016

Keywords:
Exercise
Depression
Intervention studies
Dose-response

ABSTRACT

Exercise can be used to treat depression but there is a lack of evidence regarding the optimal intensity and mode. Our aim was to compare the effects of different exercise intensities on post-treatment depression severity. People aged 18–67 years with mild to moderate depression (Patient Health Questionnaire-9 score of ≥10) participated in a single-blind, parallel randomized control trial lasting 12-weeks (Sweden 2011–2013). Four treatment arms were included: treatment as usual (TAU) ($n = 310$), light exercise (yoga or similar $n = 106$), moderate exercise (aerobic conditioning, $n = 105$) and vigorous exercise (aerobic conditioning, $n = 99$). Depression severity was measured at baseline and post-treatment using the Montgomery-Åsberg Depression Rating Scale (MADRS). Differences between the groups in depression severity at post-treatment were analysed using linear regression. Differences in exercise intensity were confirmed by heart rate monitoring. At post-treatment, the light (−4.05 Confidence Interval (CI) = −5.94, −2.17), moderate (−2.08 CI = −3.98, −0.18) and vigorous exercise groups (−3.13 CI = −5.07, −1.19) had reduced their MADRS scores significantly more than TAU. No significant differences were found between the exercise groups, and no significant interaction effect was observed between group and gender. In conclusion, exercise, whether performed at a low (yoga or similar), moderate or vigorous intensity (aerobic training) is effective in treating mild to moderate depression and is at least as effective as treatment as usual by a physician.

1. Introduction

Studies have demonstrated associations between physical activity and mental health (Harvey et al., 2010; Mammen and Faulkner, 2013; Song et al., 2012; Teychenne et al., 2008). Recently, exercise has emerged as a popular alternative treatment for mild to moderate depression (Parker and Crawford, 2007). The advantages of exercise include ease of access, low cost, lack of stigma and few side effects (Khawam et al., 2006; Vogel et al., 2007). A Cochrane review concluded that the effects of exercise were small to moderate but could be equally effective as medication or psychological therapy (Cooney et al., 2013).

Important research questions remain concerning the optimal dosage (mode/type, intensity, duration and frequency) of exercise required to achieve clinically relevant improvements. Two recent systematic reviews were unable to draw conclusions about the effects of different exercise characteristics on depression as study protocols varied, results were inconsistent and small sample sizes were common (Perraton et al., 2010; Stanton and Reaburn, 2014). Reviews that have examined exercise intensity have produced mixed results. Some have been inconclusive due to inadequately controlled comparison groups (Carek et al., 2011; Mead et al., 2009), while others have found some indications that higher intensities are better than lower (Rethorst et al., 2009). Reviews focusing solely on finding the exercise parameters that are more effective conclude that moderate aerobic exercise, performed three times a week for at least 8–9 weeks can be recommended, but this is based largely on evidence from trials that have used moderately intense exercise in their interventions, without comparisons to other intensities (Perraton et al., 2010; Stanton and Reaburn, 2014).

Dunn et al. (2005) found that an exercise dose equivalent to minimum physical activity recommendations (17.5-kcal/kg/week) was more effective than a lower dose, and that the effect did not vary with frequency (3 versus 5 times a week) (Dunn et al., 2005). Another study examining exercise in combination with pharmacological treatment also found that a higher dose (16 kcal/kg/week, walking at approximately 4.0 mph for 210 min per week) was associated with larger improvements in depression compared to a lower dose (4 kcal/kg/week, walking at approximately 3.0 mph for 75 min per week) (Trivedi et al., 2011). However, both studies were efficacy trials on dose rather than intensity and were conducted in supervised laboratory settings; effectiveness trials examining the relationship between exercise intensity and depression in community-based interventions remain scarce.

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http://dx.doi.org/10.1016/j.ypmed.2016.08.011
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A systematic review found that yoga could have a positive effect on depression (Pilkington et al., 2005) and yoga has been shown to perform better than aerobic exercise in a meta-analysis but only two studies were included and these were of low quality (Cramer et al., 2013).

The relationship between exercise and depression is a complex one and it is of interest to explore differences between men and women in treatment response. Differences could potentially be due to preference which would lead men and women to respond differently to different intensity levels or be due to biological mechanisms (Jovanovic et al., 2008; Yuan et al., 2015).

1.1. Aims of the study

To examine dose-response relationships between exercise performed at three levels of intensity with similar frequency and duration, and post-treatment depression severity. Secondary aims were to examine the effects of exercise mode (yoga or similar versus aerobic conditioning) on depression severity, and to explore gender differences.

2. Methods

2.1. Study design

'Regassa' is a single blind, parallel, multicentre randomized controlled trial (RCT) conducted in six Swedish counties and regions (Stockholm, Kronoberg, Blekinge, Skåne, Västra Götaland and Västmanland). The aim was to evaluate the effectiveness of three treatments for mild to moderate depression: exercise, Internet-Based Cognitive Behavioural Therapy (ICBT) and Treatment As Usual (TAU). In the present study, only the exercise ($n = 310$) and TAU ($n = 310$) arms were included. Results from the main RCT have been published (Hallgren et al., 2015). The study was re-registered with the German Clinical Trial Register (DRKS study ID: DRKS00008745). The study was approved by the Stockholm regional ethical review board (Dnr: 2010/1779-31/4).

2.2. Randomization

Assignment of participants was computer generated and conducted externally; making it impossible to obtain group placement until all baseline evaluations had been recorded. The randomization was done in blocks of 36 to ensure an even distribution. Participants were first randomized to one of the three primary treatment arms, and then randomized a second time (no blocks) into one of three exercise intensity groups, making the ratio of participants per group 3:1:1:1 (TAU, light exercise, moderate exercise, vigorous exercise). Further details are available Fig. 1.

2.3. Participants

Participants were recruited through primary health care centres and advertisements between February 2011 and January 2013. Inclusion criterions were 18–67 years and scoring ≥10 points on the Patient Health Questionnaire (PHQ-9). Exclusion criteria were a primary diagnosis of alcohol or drug dependency, serious somatic disorder, or requiring specialist psychiatric treatment.

2.4. Treatment groups

Participants in TAU received standard treatment for depression administered by their primary care physicians. In most instances, this involved CBT with a clinical psychologist or supportive counselling. One-third of all patients were taking anti-depressant medication during the trial, and 27% of usual care patients reported no psychological treatment.

The three exercise groups were 1) light exercise consisting of classes incorporating yoga-based stretching and balance exercises, (mindfulness i.e. self-regulated attention on immediate experience (Bishop et al., 2004) was not an active component of the yoga classes in this trial); 2) moderate exercise consisting of an intermediate-level group aerobics class; and 3) vigorous exercise, consisting of a more strenuous group aerobics class. The sessions were calibrated to ensure that the intensity differed between groups. Participants were asked to join supervised pre-existing group classes (corresponding to their assigned intensity level) lasting 55 min, three times per week for 12-weeks. Although specific exercise classes were recommended, the patients could chose to participate in alternative exercise classes or self-directed activities such as walking that might be more convenient to them. They were however asked to keep deviations from the protocol to a minimum. Importantly, these alternative options were of similar intensity and duration (e.g. walking rather than yoga). All exercise sessions (including the alternative classes) were completed at a modern fitness centre with locations throughout Sweden. Membership was provided free to all exercise participants and they met one-on-one with a member of the study personnel once per week. The personnel gave advice about exercise if requested, but were instructed not to discuss depressive symptoms as they were not trained psychologists or counsellors. Instead, most were general nurses, personal trainers or physiotherapists. The main purpose of these meetings was gathering the heart rate data (discussed below) and record attendance.

2.5. Heart rate data

Heart rate (HR) was recorded using pulse watches. Two models were used: Polar RS400 or Activio BM-SWIEU. Information from the watches was downloaded once a week by the study personnel. As some participants did not always wear the watches, or because of malfunction, the final registered number of exercise sessions was based on either the number of recorded sessions (78%), or in the absence of these data, the number of self-reported exercise sessions (22%). The protocol used to process the HR data is discussed in Appendix A.

The data for each session was compared with the calculated max heart rate (MHR) for each participant (220 minus age). Three variables were calculated using the HR data: the average heart rate per session as a percentage of MHR, and the average number of minutes per session spent ≥60% and ≥80% of the calculated MHR.

2.6. Depression severity and diagnosis

The primary outcome was depression severity measured by the Montgomery-Åsberg Depression Rating Scale (MADRS) (Montgomery and Asberg, 1979) at baseline and post-treatment (12 weeks). The scale has 10 items (apparent sadness, reported sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, inability to feel, pessimistic and suicidal thoughts) scoring from 0 to 6, with higher scores indicating more severe depression. Snaith and colleagues suggest cut-offs for the MADRS: 7–19 points for mild severity and 20 or higher for moderate severity (Snaith et al., 1986). MADRS was designed to be sensitive to change, has shown good sensitivity and validity (Khan et al., 2002; Montgomery and Asberg, 1979) and was completed face-to-face by the study personnel at baseline before treatment allocation. Personnel were blind to the participant's treatment group at the post-treatment assessment. To maximize post-treatment response rates, a mixture of face-to-face and telephone interviews (one-third) were conducted. The second item of the MADRS ("apparent sadness") was not scored in the telephone interviews; instead, item 1

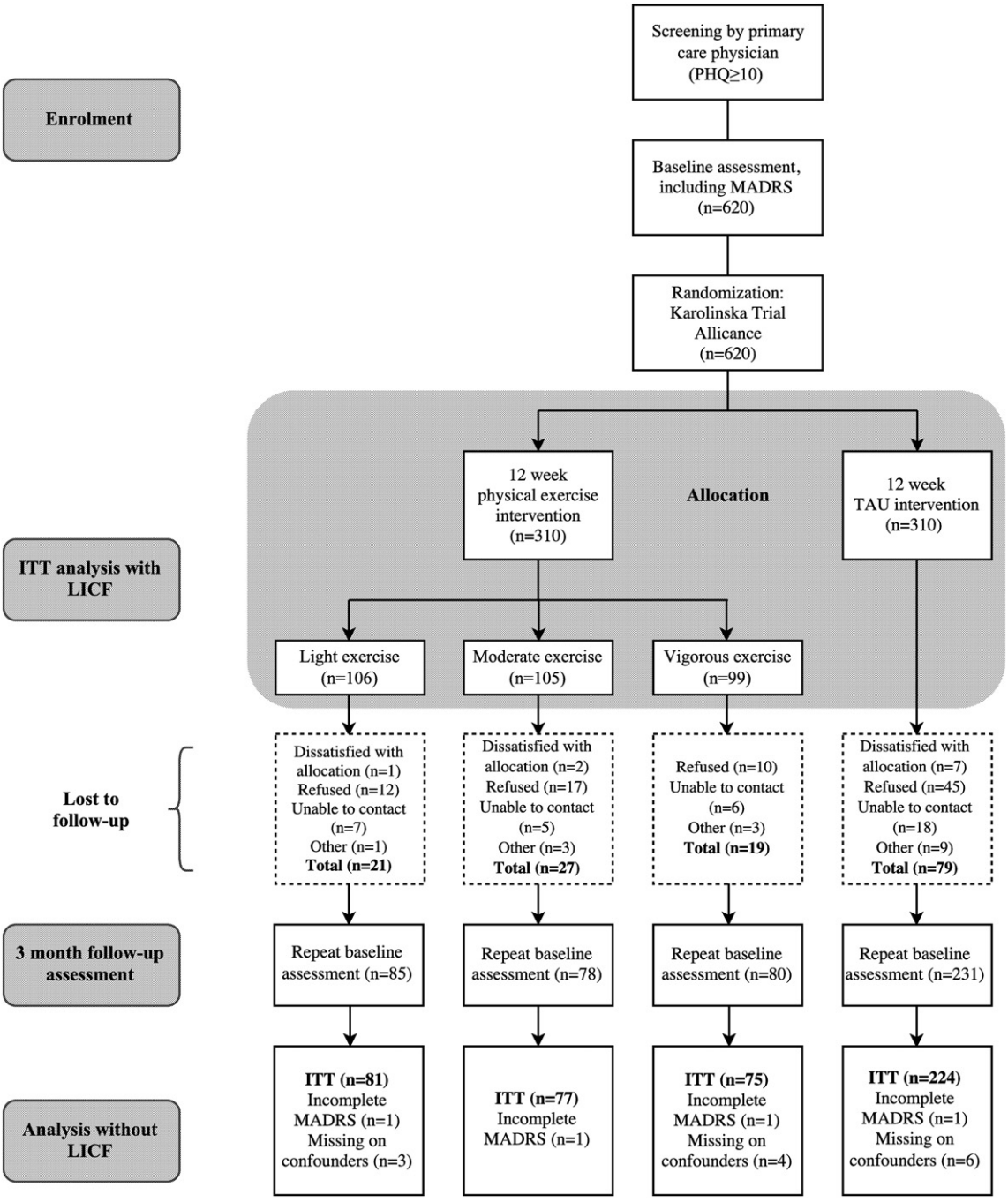

Fig. 1. Flow chart of the Regassa study (Sweden 2011–2013).

(reported sadness) was imputed from the same time point. These two items were highly correlated ($r = 0.568$, $p < 0.001$). As there was some loss to follow-up for the MADRS post-treatment (23.5%), we used the last item carried forward method (LICF) to be able to analyse the full sample (intention-to-treat analysis).

All participants were also interviewed at baseline using the Mini International Neuropsychiatric Interview MINI (Sheehan et al., 1998); a short, structured clinical interview based on the DSM-IV. Following the MINI assessment, patients received a diagnosis of depressive disorder, anxiety disorder or concomitant disorders.

2.7. Other measures

Before randomization, additional participant information was gathered using a questionnaire including age, gender, health status (number of somatic disorders), height and weight. Standard body mass index (BMI) categories for overweight (25–29.9 kg/m^2) and obesity (≥30 kg/m^2) were used but the BMI categories of underweight (<20 kg/m^2) and normal weight (20–24.9 kg/m^2) were analysed together as very few individuals belonged to the underweight category. Leisure time physical activity habits were measured with a question (Ekblom-Bak et al., 2011), with six response alternatives ranging from

almost no physical activity to regular exercise at high intensity. We collapsed these alternatives into three categories: inactive, light physical activity (PA), and moderate to vigorous PA. Education was categorized as tertiary education (≥2 years of university) or less; hazardous alcohol use was measured using the Alcohol Use Disorders Identification Test (AUDIT), where those that scored ≥8 (men) or ≥6 (women) were classified as hazardous drinkers (Bador et al., 2001). Participants were asked to list their current medication use, which was reviewed by a psychiatrist. Approximately one-third of participants were taking anti-depressants (primarily SSRI's). The proportion of participants using other medications (e.g. contraceptives, statins, and thyroid drugs) during the trial was minimal. All participants provided written informed consent and agreed to participate voluntarily.

3. Statistical analysis

As noted, the current paper is part of a larger study comparing exercise, TAU and ICBT. Consequently, no power calculations were performed specifically for this study, though the power calculations for the larger study can be found in the protocol of the Regassa study which is available online (http://www.regassa.se/sv/Om-Regassa/Protocol-REGASSA-studien/).

The distribution of characteristics and heart rate data across groups was tested with Chi^2-tests (categorical variables) and one-way analysis of variance (ANOVA) (continuous variables). The Welch correction was used when the Levene's test for homogeneity of variance showed unequal variances (applied to both variables depicting minutes spent above 60% and 80% of the maximum HR, respectively). This correction did not affect the significance of the results. Post hoc tests (Bonferroni) were applied to test for differences between groups.

Multiple linear regression models were used to calculate changes in mean MADRS scores from baseline to post-treatment with 95% Confidence Intervals (CI) and to test the post-treatment differences between groups. The MADRS was modelled as the difference between post-treatment and baseline scores. The analysis was stratified by gender, and a separate interaction analysis between gender and treatment group was performed by entering an interaction term into the model. Additionally, the effect of treatment group on depression severity was analysed using per protocol analysis. Here the exercise 'compliers' in each group (defined as those attending ≥12 exercise sessions), were compared the TAU group. A cut-off of 12 sessions was chosen as this frequency of training is what might reasonably be expected of patients in this context. Sensitivity analyses were performed, restricting to 1) those who answered MADRS at follow-up, 2) those who received a depression diagnosis according to the MINI, 3) those who were inactive or lightly physically active at baseline, and 4) only those moderately or vigorously active at baseline. All models were adjusted for antidepressant use which was unequally distributed between groups ($p = 0.038$). Significance was set at $\alpha = 0.05$ and all tests were two tailed. All analyses were performed using Stata 14.1.

4. Results

4.1. Characteristics of the study participants

The characteristics of the study population at baseline are displayed in Table 1. The majority of the study participants were women (73.7%, see Table 1); mean age was 42.6 years (SD = 12.0) and the majority were diagnosed with both depressive and anxiety disorders.

4.2. Exercise treatment

In the exercise group, 32.3% of the participants completed at least 12 sessions. Most of the exercise classes performed in the light group consisted of simple yoga (51.3%), or balance classes (19.9%). The

Table 1
Distribution of participant characteristics across treatment groups, displayed as percentages and means with standard deviations (Sweden 2011–2013).

	All N = 620		Treatment as usual N = 310		Light exercise N = 106		Moderate exercise N = 105		Vigorous exercise N = 99		p
Age											
18–34 years	30.8		28.7		35.8		28.6		34.3		0.682
35–49 years	37.4		37.7		36.8		36.2		38.4		
50–67 years	31.8		33.5		27.4		35.2		27.3		
Women	73.7		76.8		71.7		68.6		71.7		0.340
BMI											
<25	50.7		52.3		48.6		45.7		53.5		0.247
25–29.9	34.2		31.8		39.0		33.3		37.4		
≥30	15.1		15.9		12.4		21.0		9.1		
Health status											
0 somatic disorders	57.6		58.7		59.4		51.4		58.6		0.853
1 somatic disorder	25.5		25.8		23.6		27.6		24.2		
≥2 somatic disorders	16.9		15.5		17.0		21.0		17.2		
Reported physical activity											
Inactive	16.0		15.3		12.3		17.1		21.2		0.648
Light PA	47.9		49.7		50.0		43.8		44.4		
Moderate to vigorous PA	36.1		35.1		37.7		39.0		34.3		
Tertiary education	59.4		61.2		61.3		54.8		56.6		0.608
Hazardous drinker	16.5		15.5		16.3		18.1		18.4		0.879
On antidepressants	25.3		21.6		22.6		34.3		30.3		0.038
MINI diagnosis											
Depression only	9.0		9.4		10.4		4.8		11.1		0.152
Anxiety only	19.2		20.7		19.8		13.3		15.6		
Depression and anxiety	67.1		63.9		64.2		80.0		66.7		
Subthreshold affective disorder	4.7		6.1		5.7		1.9		2.0		
MADRS at baseline (mean ± SD)	21.5	±7.1	20.9	±7.1	21.3	±7.1	22.8	±6.9	22.4	±6.8	0.055
MADRS post-treatment (mean ± SD)	14.6	±8.9	15.6	±8.8	11.9	±8.4	15.3	±8.6	13.8	±9.4	0.001

All measurements taken at baseline unless otherwise specified.

Table 2
Measured intensity of sessions and number of sessions across exercise groups (Sweden 2011–2013).

	Light exercise $N = 71$ Mean (95% CI)	Moderate exercise $N = 55$ Mean (95% CI)	Vigorous exercise $N = 48$ Mean (95% CI)	p*
% of max heart rate (average across sessions)	54.1 (52.2, 56.0)	70.3 (68.1, 72.3)	76.2 (73.9, 78.6)	<0.001
Minutes spent in 60% or more of max heart rate (average across sessions)	12.5 (9.9, 15.1)	32.2 (29.6, 34.7)	35.8 (33.9, 37.7)	<0.001
Minutes spent in 80% or more of max heart rate (average across sessions)	1.5 (0.6, 2.4)	9.3 (7.1, 11.4)	16.8 (13.7, 19.9)	<0.001
	$N = 106$ Mean (95% CI)	$N = 105$ Mean (95% CI)	$N = 99$ Mean (95% CI)	
Number of sessions (recorded or reported)	10.3 (8.2, 12.5)	7.8 (5.7, 9.9)	7.5 (5.4, 9.7)	0.121
% attending 12 sessions or more (recorded or reported)	38.7 (29.4, 48.0)	27.6 (19.1, 36.2)	30.3 (21.3, 39.4)	0.210

* p: statistical significance of the overall effect (F-test).

majority of the moderate exercise sessions were the intended classes (66.5%) or similar aerobic activities (24.5%). In the vigorous group, 62.9% of the exercises completed were the recommended classes, and 25.9% were other types of aerobic activities.

The three exercise groups significantly differed on measures of average MHR (Table 2), both regarding overall effect ($F(2, 171) = 119.6$, $p < 0.001$) and differences between the groups ($p < 0.01$). Although the overall model for minutes spent in ≥60% of MHR was significant ($F(2171) = 107.5$, $p < 0.001$), only the light group statistically differed from the other two groups ($p < 0.001$). Finally, the overall effect for average minutes spent ≥80% of MHR was significant ($F(2171) = 57.8$, $p < 0.001$); each of the three groups significantly differed from each other ($p < 0.001$). No significant differences were found between the groups regarding number of exercise sessions or proportion of compliers i.e. attending 12 sessions or more.

4.3. Change in depression severity

Fig. 2 shows the changes in MADRS scores from baseline to post-treatment (adjusted for antidepressant use). All four groups significantly reduced their MADRS scores from baseline to post-treatment. Reductions in the three exercise groups were similar (7.4 to 9.4 points), and all three were larger than the reduction seen in TAU; 5.4 points.

Compared to TAU, mean MADRS scores in the light group reduced by 4.1 points more ($p < 0.001$), the vigorous group had reduced by 3.1 points more ($p = 0.002$) and scores in the moderate group reduced by 2.1 points more ($p = 0.032$) than the TAU (Table 3). No significant differences were found between the exercise groups, though the difference between the moderate and light group approached statistical significance ($p = 0.095$) with the light group reducing their scores by almost two points more than the moderate group.

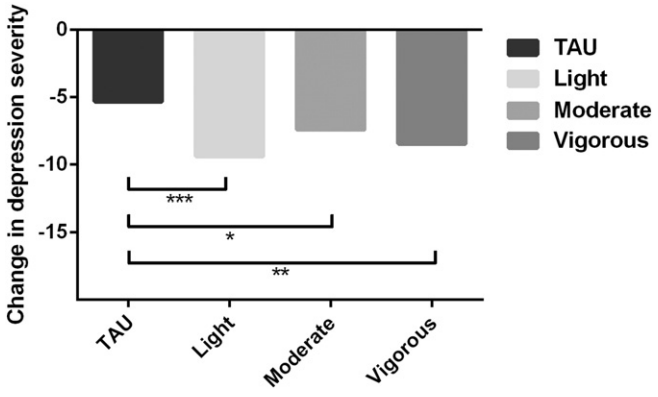

Fig. 2. Adjusted change in depression severity (MADRS scores) between baseline and post-treatment (Sweden 2011–2013). Comparisons between groups: $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$.

4.4. Gender differences

We stratified by gender while controlling for baseline antidepressants use (Table 3, baseline characteristics by gender: Table A.1). Among men, all exercise groups had significantly larger reductions in MADRS scores than the TAU group ($p < 0.05$). In women, the light and vigorous groups had significantly larger reductions than TAU ($p = 0.005$ and $p = 0.016$). No significant differences were found between the three exercise groups for either men or women. The interaction term between gender and treatment group was not significant ($p = 0.156$).

4.5. Per-protocol analysis

As shown in Table 3, results of the per-protocol analysis were similar to the primary intention-to-treat analysis, though the effect sizes were slightly larger for the per-protocol analysis.

4.6. Sensitivity analysis

We performed a sensitivity analysis (Table A.2) based on only those participants with sufficient MADRS data at post-treatment revealing comparable results to the primary analyses. We also analysed separately data only from participants diagnosed with depressive disorders or concomitant depressive and anxiety disorders. Again, results were similar to the main analysis though the effect sizes were slightly smaller for the vigorous group and only the light group was significantly different from the TAU ($p < 0.001$). Finally we ran the analysis using only those that were inactive or lightly physically active at baseline ($n = 395$). Effect sizes were almost identical across all exercise groups compared to the TAU, though all were significantly different from TAU. When we restricted to those that were already moderately or vigorously active at baseline ($n = 223$), the effect was largest in the light exercise group. The interaction between group and physical activity level at baseline was significant ($p = 0.001$).

5. Discussion

In this large randomized controlled trial conducted in a naturalistic setting, all exercise groups had larger reductions in depression scores post-treatment compared to treatment as usual (TAU). The changes were clinically meaningful; all groups (including TAU) reduced their

Table 3
Adjusted associations between depression severity (MADRS) and exercise intensity (Sweden 2011–2013).[a]

Groups	n	Mean change from baseline to post-treatment (95% CI)	Mean difference from reference group			
			TAU as reference β (95% CI)	Light as reference β (95% CI)	Moderate as reference β (95% CI)	Overall group effect p
All						
TAU	310	−5.34 (−6.30, −4.39)***	1			<0.001
Light exercise	106	−9.40 (−11.03, −7.77)***	−4.05 (−5.94, −2.17)***	1		
Moderate exercise	105	−7.43 (−9.07, −5.79)***	−2.08 (−3.98, −0.18)*	1.97 (−0.34, 4.29)	1	
Vigorous exercise	99	−8.48 (−10.16, −6.79)***	−3.13 (−5.07, −1.19)**	0.92 (−1.42, 3.27)	−1.05 (−3.40, 1.30)	
Men						
TAU	72	−3.27 (5.25, −1.29)**	1			<0.001
Light exercise	30	−10.06 (−13.13, −6.99)***	−6.79 (−10.44, −3.14)***	1		
Moderate exercise	33	−8.16 (−11.10, −5.21)***	−4.89 (−8.45, −1.32)**	1.90 (−2.37, 6.17)	1	
Vigorous exercise	28	−7.81 (−10.98, −4.63)***	−4.54 (−8.29, −0.79)*	2.25 (−2.17, 6.67)	0.35 (−3.98, 4.67)	
Women						
TAU	238	−5.98 (−7.06, −4.89)***	1			0.011
Light exercise	76	−9.17 (−11.09, −7.26)***	−3.20 (−5.40, −1.00)**	1		
Moderate exercise	72	−7.05 (9.02, −5.07)***	−1.07 (−3.33, 1.19)	2.13 (−0.63, 4.88)	1	
Vigorous exercise	71	−8.76 (−10.75, −6.77)***	−2.78 (−5.05, −0.52)*	0.41 (−2.35, 3.18)	−1.71 (−4.51, 1.09)	
Per protocol analysis						
TAU & non-compliers	310	−5.32 (−6.20, −4.45)***	1			<0.001
Light exercise	41	−12.25 (−14.65, −9.69)***	−6.93 (−9.49, −4.37)***	1		
Moderate exercise	29	−10.75 (−13.61, −7.88)***	−5.42 (−8.42, −2.42)***	1.50 (−2.25, 5.25)	1	
Vigorous exercise	30	−9.39 (−12.21, −6.58)***	−4.07 (−7.02, −1.12)**	2.85 (−0.85, 6.56)	1.35 (−2.66, 5.37)	

[a] Adjusted for antidepressant use at baseline.
* $p < 0.05$.
** $p < 0.01$.
*** $p < 0.001$.

depression severity from moderate to mild (Snaith et al., 1986). Importantly, TAU was not a control group equivalent, but an active treatment group in which most patients received face-to-face CBT or supportive counselling, sometimes in addition to medication. Thus, the favourable results of exercise participation were not uniquely attributable to greater 'support' or monitoring within the exercise intervention.

Although there were no statistically significant differences between the exercise groups at post-treatment, the light exercise group reduced their MADRS scores by almost 2 points more than the moderate group ($p = 0.095$). Gender did not appear to be an effect modifier for the association.

Currently, the evidence base for the prescription of different exercise intensities for depression is weak, although one study has found that a dose (intensity, duration, frequency) equivalent to public health guidelines was associated with a larger effect than a lower dose of exercise (Dunn et al., 2005). The present study revealed no clear dose-response for exercise *intensity* (duration and frequency were constant), yet there were indications that light exercise was more beneficial than moderate exercise. One explanation could be that those with mild to moderate depression find lighter exercise, in this case yoga, more enjoyable as it is easier to perform leading to greater self-esteem and feelings of mastery. Previous research has demonstrated positive associations between yoga and specific health outcomes, including depression (Cramer et al., 2013), anxiety and stress (Kohn et al., 2013). This could be due to a mindfulness component, though this was minimal in our yoga classes, or instructions on how to focus on your breathing which is an important component of yoga.

Our finding could also reflect individual variation in the preference for exercise intensity. Affective responses to acute bouts of exercise have been shown to vary widely between individuals, but highly vigorous exercise tends to be associated with displeasure, especially among non-regular exercisers (Ekkekakis et al., 2011; Hallgren et al., 2010). When people are unsupervised, they tend to self-select exercise intensity below their ventilatory threshold (Ekkekakis, 2009), and in studies of acute exercise, self-selected exercise intensities are associated with greater pleasure than exercise that is prescribed (Ekkekakis et al., 2011; Williams, 2008).

A plausible explanation for the non-significant differences between the exercise groups could be that the participants changed their total physical *activity* behaviour differentially. This could have led to the overall energy expenditure being similar; for example, the light group might have decreased their sedentary time by increasing light activity (such as walking) while the higher intensity groups might have increased sedentary time. Increasingly, research is focusing on the mental health effects of sedentary time. In a meta-analysis Zhai et al. (2014) found that sedentary behaviour was significantly associated with risk of depression (Zhai et al., 2014).

Current physical activity guidelines from the American College of Sports Medicine suggest at least 150 min of moderate-intensity aerobic exercise per week (Garber et al., 2011). Our recommendations to the moderate and vigorous exercise groups could be classified as at least fulfilling the above criteria but our light exercise group cannot. As we found no differences between the three groups, we feel that for the purposes of reducing depression, yoga or other low impact activities can be a viable option.

6. Strengths and limitations

To our knowledge, this is the largest RCT examining the effects of exercise intensity on depression. The large participant sample, external randomization procedure, and blinded follow-up assessments are methodological strengths.

Compliance in the exercise groups was sub-optimal as 31.7% attended no exercise sessions at all, though 39.6% attended 12 or more sessions. However, given the nature of the trial and population involved, this result is not unexpected; other trials report similar non-compliance issues (Oeland et al., 2010). A promising observation is that clinically

meaningful reductions in depressive symptoms were achieved despite relatively low compliance.

The supportive approach adopted for this trial (i.e., free gym-memberships and weekly meetings) might not be feasible in all contexts, although it is entirely feasible in Sweden and may be possible elsewhere. The fitness centres were relatively inexpensive and the weekly meetings could be offered via the internet to further reduce costs.

The exercise groups differed with regard to the type of exercise performed, and some participants reported performing exercise that slightly different from what was prescribed. However, with objective assessments of exercise, we confirmed that the three exercise groups differed with regards to exercise intensity. We considered prescribing other types of exercise in the light condition, such as walking as then all the exercise groups would have been aerobic. However, other important differences would have been unavoidable. Walking is usually performed outside, alone, and without an instructor. Group walking was not offered by the fitness centre; neither were pure 'stretching classes' which were also considered but dismissed as they would have minimal impact on participant's heart rate. It could be argued that light exercise, by definition, invites a more 'mindful' approach to training, regardless of the specific mode.

Care providers declined to keep records of how many people were offered to participate in the study but declined, which makes assessing external validity of the trial problematic. However, the selection of participants from different geographic areas, varying in population density and composition helped to maximize the external validity of the findings.

7. Conclusions

In conclusion, the results indicate that exercise, whether performed at a light, moderate or vigorous intensity, can be at least equally effective in the treatment of mild to moderate depression compared to treatment as usual by a physician. The findings have clinical implications and support previous research (Williams, 2008) indicating that exercise can be prescribed for depression at different intensity levels depending on the individual characteristics of the patient, including fitness level, motivation and readiness to change their behaviour. This conclusion is supported by our sensitivity analyses, which showed almost identical effect sizes when the analyses were restricted to patients that were inactive or lightly active at baseline.

Funding

This work was supported by: the LJ Boethius Foundation, the Vårdal Foundation (RS2009/27) , the Brain Foundation Sweden (Hjärnfonden), and the six Swedish counties and regions involved in the study.

Conflicts of interest

All authors declare no conflicts of interest.

Acknowledgements

We would like to thank Elisabet Erwall for organizing the collection of the data, Zangin Zeebari for statistical advice and Cecilia Kullberg for auditing the data. All authors declare no conflicting interests.

Appendix A. Heart rate data protocol

Heart rate data from each recorded session was summarized according to the following protocol: 1) If multiple zeros occurred in the recording, indicating that the pulse band had lost contact, the zeros were deleted to avoid faulty data; 2) Multiple files on the same day and occurring consecutively were assumed to be from the same session and were therefore merged; this could be due to the participant turning the watch on and off due to poor functioning, or uncertainty about how it should be operated; 3) The first 2 min of the recording were not used and only the minutes up to and including minute 45 were used, in total max 43 min for each session; 4) Each session needed to be ≥30 min to be included.

Table A.1
Baseline characteristics by gender.

	Men	Women	p
Age			
18–34 years	33.0	32.9	0.425
35–49 years	41.8	35.2	
50–67 years	25.3	32.0	
BMI			
<25	44.4	51.1	0.522
25–29.9	41.1	34.7	
≥30	14.4	14.2	
Health status			
0 somatic disorders	67.0	52.1	0.043
1 somatic disorder	20.9	26.9	
≥2 somatic disorders	12.1	21.0	
Reported physical activity			
Inactive	19.8	15.5	0.608
Light PA	42.9	47.5	
Moderate to vigorous PA	37.4	37.0	
Tertiary education	31.9	44.8	0.036
Hazardous drinker	37.4	9.3	<0.001
On antidepressants	25.3	30.6	0.347
MINI diagnosis			
Depression only	12.1	7.3	0.101
Anxiety only	68.1	71.2	
Depression and anxiety	19.8	16.9	
Subthreshold affective disorder	0.0	4.6	
MADRS at baseline (mean ± SD)	22.6 ± 6.9	22.0 ± 7.0	0.446
MADRS post-treatment (mean ± SD)	13.8 ± 9.8	13.6 ± 8.5	0.827

Table A.2
Adjusted associations[a] between depression severity (MADRS) and exercise intensity (Sweden 2011–2013).

			Mean difference from reference group			
		Mean change from baseline to post-treatment	TAU as reference	Light as reference	Moderate as reference	Overall group effect
Groups	n	(95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	p
Complete MADRS at follow-up						
TAU	309	−7.10 (−8.23, −5.96)***	1			<0.001
Light exercise	105	−11.85 (−13.73, −9.98)***	−4.76 (−6.95, −2.56)***	1		
Moderate exercise	104	−10.00 (−11.97, −8.03)***	−2.90 (−5.18, −0.62)*	1.85 (−0.88, 4.58)	1	
Vigorous exercise	98	−10.45 (−12.39, −8.51)***	−3.35 (−5.60, −1.11)**	1.40 (−1.30, 4.11)	−0.45 (−3.20, 2.30)	
Diagnosed with Depression (MINI)						
TAU	227	−6.05 (−7.21, −4.90)***	1			0.003
Light exercise	79	−10.25 (−12.21, −8.30)***	−4.20 (−6.47, −1.93)***	1		
Moderate exercise	89	−7.84 (−9.69, −6.00)***	−1.79 (−3.97, 0.39)	2.41 (−0.28, 5.09)	1	
Vigorous exercise	77	−7.86 (−9.84, −5.88)***	−1.81 (−4.10, 0.49)	2.39 (−0.39, 5.17)	−0.01 (−2.72, 2.69)	
Physically inactive or light physical activity						
TAU	200	−5.25 (−6.46, −4.04)***	1			0.003
Light exercise	66	−8.59 (−10.69, −6.49)***	−3.34 (−5.76, −0.92)**	1		
Moderate exercise	64	−8.46 (−10.60, −6.32)***	−3.21 (−5.68, 0.74)*	0.13 (−2.88, 3.13)	1	
Vigorous exercise	65	−8.64 (−10.76, −6.52)***	−3.39 (−5.84, −0.94)**	−0.05 (−3.04, 2.93)	−0.18 (−3.18, 2.82)	
Moderate to vigorous physical activity						
TAU	108	−5.74 (−7.31, −4.17)***	1			0.008
Light exercise	40	−10.75 (−13.33, −8.17)***	−3.34 (−5.76, −0.92)**	1		
Moderate exercise	41	−5.78 (−8.32, −3.23)***	−3.21 (−5.68, −0.74)*	4.98 (1.35, 8.60)**	1	
Vigorous exercise	34	−8.11 (−10.92, −5.32)***	−3.39 (−5.84, −0.94)**	2.63 (−1.17, 6.44)	−2.34 (−6.13, 1.44)	

*p < 0.05, **p < 0.01, ***p < 0.001.
[a] Adjusted for antidepressant use at baseline.

Appendix B. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.ypmed.2016.08.011.

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