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Exercise improves physical and psychological quality of life in people with depression: A meta-analysis including the evaluation of control group response

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ABSTRACT

Exercise has established efficacy as an antidepressant in people with depression. However, few meta-analyses have assessed the effects of exercise across different domains of Quality of Life (QoL) in people with depression. Furthermore, there has been no previous meta-analysis of control group response in relation to QoL in exercise trials for depression. Randomized Clinical Trials(RCTs) were initially identified from a Cochrane review, and those including QoL assessments were included in the analysis. Search of major electronic databases were conducted to identify RCTs that compared the exercise effects on QoL versus control condition in people with depression. A random effects meta-analysis was employed to evaluate the Standardized Mean Difference (SMD). Six RCTs were included. Exercise significantly improved physical and psychological domains and overall QoL. Effects on social relationship and environment domains were not significant. No significant control group response was found for any domain or overall QoL. Exercise can be considered as a therapeutic strategy to improve physical and psychological domains and overall QoL of people with depression, with no effect evident across the social and environmental domains. The lack of improvement among control groups reinforces the role of exercise as a treatment for depression with benefits to QoL.

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1. Introduction

Depression is a chronic condition transcending geography, age, ethnic group and sex. In 2010, depressive disorders were the second leading cause of years lived with disabilities, in which major depressive disorder (MDD) accounted for 8.2% and dysthymia for 1.4% of the total years lived with disability in 2010 across all conditions (Ferrari et al., 2013). Depression, even in subsyndromal presentations, often has a marked impact on an individual's mental and physical health leading to considerable impairment in several domains of Quality of Life (QoL), in special at physical, psychological and social QoL (Berlim et al., 2004; Fleck et al., 2005; da Silva Lima and de Almeida Fleck, 2007). QoL is a broad and multifaceted, construct, defined as "an individual's perception of their position in life in the context of the culture and value systems in which they live, and in relation to their goals, expectations, standards and concerns" (The WHOQOL Group, 1995).

Given the association between depression and poor QoL, treatment strategies that address depression are likely to have subsequent implications for QoL (da Rocha et al., 2009). While pharmacological antidepressants are the mainstay of treatment for depression, less than 50% of patients taking antidepressants in an adequate dose experience a meaningful clinical response (Sinyor et al., 2010). Also, some patients stills refer an impairment at physical, psychological and social domains of QoL after full remission of symptoms (Angermeyer et al., 2002; Ishak et al., 2011). Therefore, additional strategies are needed to address impaired QoL in people with depression.

Previous studies have found that exercise (the structured subset of physical activity) can improve physical and psychological domains of QoL in people with severe mental illness (Rosenbaum et al., 2014). In the case of people with MDD, exercise may improve the physical and psychological domains of QoL, showing no significant effects, however, on the social relationships or environmental domains (Schuch et al., 2011b). Also, a previous meta-analysis conducted by the Cochrane collaboration (Cooney et al., 2013), investigated the effects of exercise on physical, psychological, mental, social and environmental QoL domains, yet relied only on the post-intervention outcomes, and not the mean change between the groups, suggesting that exercise improves only the physical domain, with no effect on other domains. The estimation of the effect size based on the mean change, instead the post-intervention outcome only, allow a more accurate assessment of the effect of the intervention since it accounts for any potential differences between the groups at baseline. Therefore, information on the magnitude of the effect of exercise on QoL in people with depression is missing.

Recent research (Stubbs et al., 2015) has demonstrated that control group participants in exercise RCTs experience large improvements in depressive symptoms, making it more challenging for exercise trials to demonstrate the benefits of exercise. However, it remains unclear if participants with depression in exercise RCTs experience control group improvements in QoL domains.

Given the aforementioned, the present review has the following aims: (1) to evaluate the effects of exercise on QoL in people with depression and (2) to evaluate if a control group response occurs (treatment as usual/wait-list) in relation to QoL domains.

2. Methods

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement (Moher et al., 2009) and the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) guidelines (Stroup et al., 2000).

2.1. Inclusion criteria

Included in this meta-analysis were RCTs that: (1) investigated the effects of exercise (defined by Caspersen et al. (1985) as a planned, structured, repetitive and purposive physical activity, in the sense that improvement or maintenance of one or more components of physical fitness is an objective) in the active arm of the trial, on a QoL domain in adults with a primary diagnosis of major depressive disorder (MDD) according to established criteria (e.g., Diagnostic and Statistical Manual of Mental Disorders (DSM) (American Psychiatric Association, 1994, 2013) or International Classification of Diseases (ICD) (World Health Organization, 1993) or those with increased depressive symptoms determined by a validated screening measure (e.g., Hamilton Rating Scale for Depression, (HAM-D), (Hamilton, 1967), Beck Depression Inventory (BDI) (Beck et al., 1961), Geriatric Depression Scale (GDS) (Yesavage, 1988) or other) according to the author's criteria. We also included studies meeting our criteria that included some participants with other related diagnoses, such as dysthymia. This decision was based on the fact that dysthymia is categorized as a chronic and milder disorder within the depressive disorder spectrum (American Psychiatric Association, 2013). (2) Evaluated QoL using a validated instrument (e.g. WHOQOL, SF-36 or other) (Ware and Sherbourne, 1992; Group, 1998). (3) Included a non-active control group such as usual-care/usual-treatment, wait-list control conditions, placebo pills or other social activities.

2.2. Exclusion criteria

Excluded in this meta-analysis were RCTs that: (1) used yoga, tai chi or qigong, since they also comprise a core set of behavioral techniques such as, but not limited to, deep breathing, meditation/mind-fullness and self-awareness (Larkey et al., 2009) that have already demonstrated an influence on depressive symptoms (Goyal et al., 2014). (2) Compared exercise versus any other exercise interventions (such as stretching or low-dose exercise).

2.3. Information sources and searches

Two steps were used to identify studies. First, three authors (BS, FS, SR) reviewed all articles identified (both included and excluded with reasons) by the recent Cochrane review on exercise for depression that evaluated QoL as an outcome (Cooney et al., 2013). Three independent reviewers (BS, FS, SR) subsequently searched Academic Search Premier, MEDLINE, Psychology and Behavioral Sciences Collection, PsycINFO, SPORTDiscus, CINAHL Plus and Pubmed without language restrictions from January 2013 until August 1st, 2015, using the keywords: ((exercis* OR aerobic* OR running OR jogging OR walk* OR hiking OR swim* OR aquatic* OR cycling OR bicycl* OR strength* and activit* OR fitness OR train* OR "physical medicine" OR resistance OR lift*) AND (depression OR dysthymia)). In addition, reference lists of all eligible articles of recent reviews investigating the effectiveness of exercise versus control in QoL were screened to identify potentially eligible articles (Schuch et al., 2011b; Cooney et al., 2013; Rosenbaum et al., 2014).

2.4. Study selection

Three authors (BS, FS, SR) determined potentially eligible articles meeting the inclusion criteria. After removal of duplicates, two independent reviewers screened the potentially eligible articles using titles and abstracts.

2.5. Outcomes

Our main outcome was the mean change in QoL in the exercise intervention group from baseline to post-intervention in comparison with the mean change in the control group, calculated as the SMD and 95% confidence intervals (CIs). We grouped the domains of the studies according to the World Health Organization Quality of Life assessment- Brief version (WHOQOL-BREF) domains: Physical (activities of daily living, dependence on medicinal substances and medical aids, energy and fatigue, mobility pain and discomfort, sleep and rest, work capacity), psychological (bodily image and appearance, negative feelings, positive feelings, self-esteem, spirituality/religion/personal beliefs, thinking, learning, memory and concentration), social (personal relationships, social support, sexual activity), environment (financial resources, freedom, physical safety and security, health and social care: accessibility and quality, home environment, opportunities for acquiring new information and skills, participation in and opportunities for recreation/leisure activities, physical environment [pollution/noise/traffic/climate], transport) and overall QoL (overall perception of QoL). For studies using the instruments derived from the Medical Outcomes Study (MOS), such as the SF-36 (Ware and Sherbourne, 1992), the physical component was grouped with the physical domain and the mental component was grouped with the psychological domain. Instruments that presented only an overall QoL rating were grouped with the overall QoL measure.

2.6. Data extraction

Two authors (FS, SR) independently extracted data using a data extraction form that included: sample (number of participants, % of women, % of participants taking antidepressants, presence), instrument used to assess QoL, setting (outpatient/in-patient), diagnosis of depression (depressive symptoms or MDD), group-based exercise (yes/no) and exercise details (length of the trial, weekly frequency, exercise intensity [according to the American College of Sports Medicine (ACSM) (Garber et al., 2011) classification of intensity]), type of exercise (aerobic/anaerobic/mixed). Lastly, we extracted data (Means and SDs), from both groups, pre- and post-intervention, for the primary outcome (QoL). When not available, we used the mean change and SD from pre- and post-test, if reported within the study.

2.7. Risk of bias and quality assessment

Three authors (FS, JR, BS) assessed the study quality on the presence of a high, low or unclear risk of bias according to the Cochrane Handbook definition (Higgins and Green, 2011). The risk of bias was assessed by considering the allocation concealment, random sequence generation, blinding of those delivering the intervention, blinding of participants, blinding of outcome assessors, incomplete data outcome, selective reporting. To be considered of higher methodological quality, studies had to present 1) adequate presentation of outcome data according to intention-to-treat principles AND 2) allocation concealment. As QoL can only be assessed by self-reported instruments, we decided to consider all studies as presenting a lower risk of bias in the "blinding outcome assessors" criteria.

2.8. Meta-analyses

Due to expected heterogeneity, we performed a random effects analysis. The SMD and 95% confidence intervals (CIs) were used as the effect size measure (ES). The meta-analysis was conducted in the following steps. First, we calculated the SMD statistic together with 95% CIs to establish the effects of exercise on effects of exercise in four domains of QoL (physical, psychological, environment and social) and in the overall QoL across all studies, using Comprehensive Meta-Analysis software (CMA; Version 3, Biostat, Englewood, New Jersey). Further, we evaluated the control group response on each of the different domains of QoL across all reviewed studies. Heterogeneity was assessed with the Cochran Q and I^2 statistics for each analysis (Higgins et al., 2003). Publication bias was assessed with the Begg-Mazumdar Kendall's tau (Begg and Mazumdar, 1994) and Egger bias test (Egger et al., 1997). The publication bias was done using the publication bias option of the CMA. Effect sizes were interpreted according to Cohen's criteria (Cohen, 1988): small (SMD=0.2), medium (SMD=0.5), and large effects (SMD=0.8).

3. Results

3.1. Search results

In the first stage of the search strategy, 8 RCTs were identified from a previous review (Singh et al., 1997, 2005; Brenes et al., 2007; Carta et al., 2008; Chu et al., 2009; Gary et al., 2010; Mota-Pereira et al., 2011; Schuch et al., 2011a). In the second stage, following the removal of duplicates, our search identified 819 potentially relevant articles. At the full-text review stage, we reviewed 49 articles (N=8 from the first stage and 41 from our second stage searches). Of these, 43 were subsequently excluded with reasons. Finally, there were 9 full texts that met the eligibility criteria (Singh et al., 1997, 2005; Brenes et al., 2007; Carta et al., 2008; Chu et al., 2009; Gary et al., 2010; Mota-Pereira et al., 2011; Schuch et al., 2011a; Huang et al., 2015). Of these, six (Brenes et al., 2007; Carta et al., 2008; Gary et al., 2010; Mota-Pereira et al., 2011; Schuch et al., 2011a; Huang et al., 2015) provided complete data and were included in our meta-analysis. Five of the included studies (Brenes et al., 2007; Carta et al., 2008; Gary et al., 2010; Mota-Pereira et al., 2011; Schuch et al., 2011a) were identified from the first stage of the search, being one updated with recent published data (Schuch et al., 2011a, 2015) and only one was from the second stage (Huang et al., 2015) (details summarized in Fig. 1).

3.2. Characteristics of included trials and participants

Across the 6 studies, 198 adults with depression were included, of whom 106 and 92 were randomized to exercise and control conditions respectively. The mean age ranged from 38.8 to 76.4 years and from 41.7 to 75.6 years in exercise and control groups, respectively. Four studies were conducted in a sample exclusively composed of participants with MDD (Carta et al., 2008; Gary et al., 2010; Mota-Pereira et al., 2011; Schuch et al., 2015). One study included participants with depression and participants with additional co-morbid diagnoses, such as cardiovascular diseases (Gary et al., 2010). The measures of QoL used were the WHOQOL (n=3) and SF-36 (n=2). Most of the studies were conducted at outpatient setting (n=5), with a weekly frequency of 3 times per week (n=3), using aerobic exercise interventions (n=4), with light to moderate or moderate intensity (n=3), and supervised by exercise professionals (n=5). Five studies reported data on the physical domain (Brenes et al., 2007; Carta et al., 2008; Mota-Pereira et al., 2011; Huang et al., 2015; Schuch et al., 2015), five on the psychological domain (Brenes et al., 2007; Carta et al., 2008; Mota-Pereira et al., 2011; Huang et al., 2015; Schuch et al., 2015), three on the environmental domain, (Carta et al., 2008; Mota-Pereira et al., 2011; Schuch et al., 2015) three on the social relationship domain (Carta et al., 2008; Mota-Pereira et al., 2011; Schuch et al., 2015) and three on overall QoL (Gary et al., 2010; Mota-Pereira et al., 2011; Huang et al., 2015). Details of included studies are presented in Table 1.

3.3. Risk of bias

Only one study was found to be of higher methodological quality and at lower risk of bias (Schuch et al., 2015) and the remaining 5 were of lower quality (higher risk of bias). Full details of the quality assessment can be seen at the Supplementary Table 2.

4. Main analysis

4.1. Overall QoL

Data pooled from 5 studies showed a statistically significant

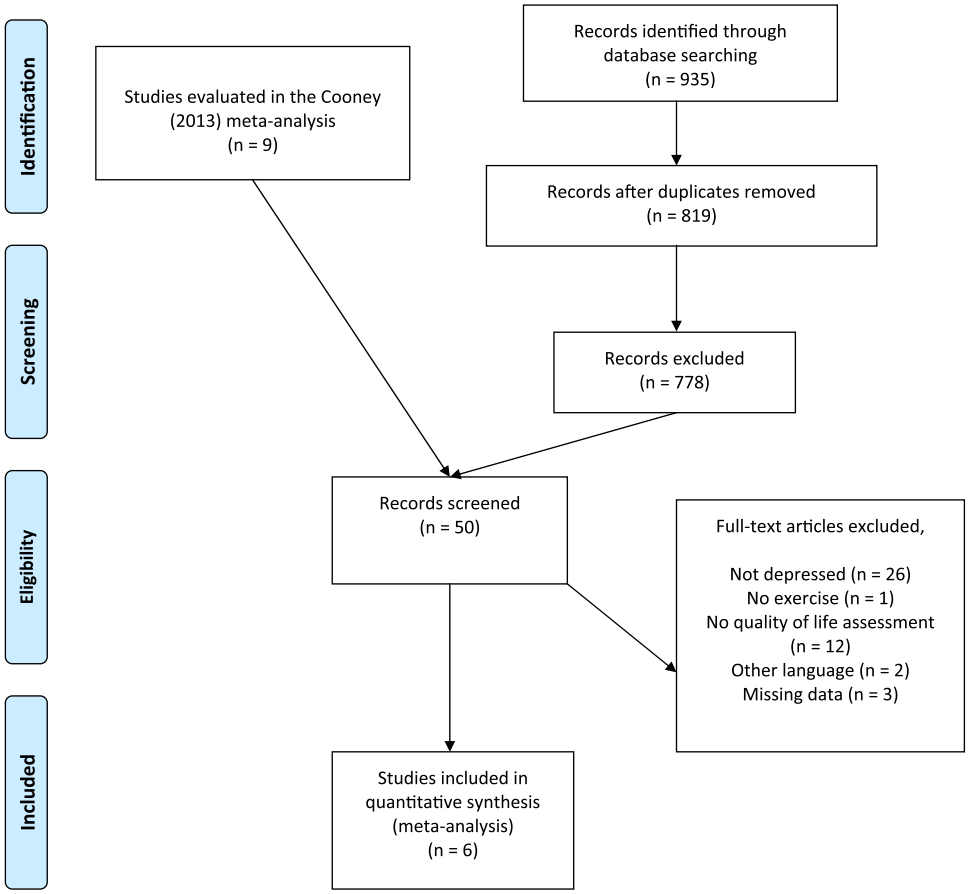

Fig. 1. Flowchart of studies selection.

moderate effect for exercise on the overall QoL (SMD=0.39, 95% CI 0.47–0.74, p=0.002, Q=0.13, I^2=0.0) (Fig. 2e). The Begg test indicated no publication bias (Tau=−0.66, p=0.29) while the Egger test indicated a trend of publication bias (intercept=−1.88, p=0.05).

4.2. Physical domain

Data pooled from 5 studies showed a statistically significant moderate effect for exercise on the physical QoL domain, with zero heterogeneity (SMD=0.53, 95% CI 0.22–0.84, p<0.001, Q=3.74, I^2=00.00) (Fig. 2a). The Begg (Tau=−0.10, p=0.80) and the Egger tests indicated no publication bias (intercept=−2.95, p=0.46).

4.3. Psychological domain

Data pooled from 5 studies showed a statistically significant moderate effect for exercise on the psychological QoL domain (SMD=0.53, 95% CI 0.22–0.85, p<0.001, Q=3.79, I^2=4.89) (Fig. 2b). The Begg (Tau=0.0, p=1.00) and the Egger tests indicated no publication bias (intercept=−1.74, p=0.68).

4.4. Social domain

Data pooled from 5 studies showed a non-statistically significant moderate effect for exercise on the social QoL domain (SMD=0.28, 95% CI −0.13 to 0.71, p=0.18, Q=2.30, I^2=13.04) (Fig. 2c). The Begg (Tau=−0.00, p=1.00) and the Egger tests indicated no publication bias (intercept=2.28, p=0.72).

4.5. Environmental domain

Data pooled from 5 studies showed a non-statistically significant moderate effect for exercise on the environmental QoL domain (SMD=0.36, 95% CI −0.12 to 0.85, p=0.14, Q=2.88, I^2=30.75) (Fig. 2d). The Begg (Tau=0.00, p=1.00) and the Egger tests indicated no publication bias (intercept=2.21, p=0.76).

5. Control group response in Quality of Life

No improvements in control groups were found for the overall QoL (n=2, SMD=−0.04, 95% CI −0.35 to 0.26, p=0.79) and in the physical (n=4, SMD=0.28, 95% CI −0.35 to 0.26, p=0.79), psychological (n=4, SMD=0.27, 95% CI −0.18 to 0.72, p=0.23), social (n=3, SMD =0.08, 95% CI −0.37 to 0.54, p=0.72), and environment QoL (n=3, SMD=0.08, 95% CI −0.11 to 0.28, p=0.38) domains. Full details of control group response analysis are presented in Table 2.

6. Discussion

People with depression often experience a markedly reduced QoL. The present study supports the notion that exercise can significantly improve the physical and psychological domains and overall QoL. No significant effects were found for the social domain. Also, as expected, we did not find any evidence that exercise improves the environmental domain QoL, since this domain is mostly related to non-exercise related elements such as financial sources, home environment, physical environment, and access to

Table 1
Summary of included studies.

Study	Sample size		Age		Gender		Antidepressant use		Outcome	Frequency	Length of the trial	Diagnosis
	Exercise (n=)	Control (n=)	Exercise (mean or range)	Control (mean or range)	Exercise (% females)	Control (% females)	Exercise (% taking)	Control (% taking)	instrument	Times per week	Weeks	MDD or Depressive symptoms
Brenes et al., 2007	14	12	73.5	73.9	64	50	0	0	SF-36	3	16	Depressive symptoms
Carta et al., 2008	10	20	40–60	40–60	100	100	100	100	WHOQOL-BREF	2	32	MDD
Gary et al., 2010	20	15	?	?	?	?	?	?	MLHFQ	3	12	Depressive symptoms
Huang et al., 2015	19	20	76.42	75.85	57.9	55	0	0	SF-36	3	12	Depressive symptoms
Mota-pereira et al., 2011	19	11	48.68	45.33	57.9	80	100	100	WHOQOL-BREF	5	12	MDD
Schuch et al., 2015	25	25	38.8	41.76	72	76	Change during the trial	Change during the trial	WHOQOL-BREF	5	3	MDD

MLHFQ=Minnesota Living with Heart Failure Questionnaire, SF-36=The Short Form Health Survey 36 Items; WHOQOL-BREF=World Health Organization Quality of Life Assessment Instrument.

health services. We also demonstrated in our preliminary analyses that people with depression assigned to control conditions do not appear to experience improvements in QoL. The present findings should be read considering that only one of the 6 studies included were considered of lower risk of bias, however, it is strengthened by the consistency of the exercise effects as seen by the low heterogeneity in all analyses.

Exercise can be used as a treatment strategy for depression (Schuch et al., 2016) and the present study corroborates previous systematic reviews and meta-analyses that found significant effects in the physical domain of QoL (Schuch et al., 2011b; Cooney et al., 2013). Moreover, the magnitude of the effect found in the present study (SMD=0.53) was larger than the effect found in the Cochrane review (SMD =0.45). This novel finding in our review can be attributed to two reasons. First, we included a larger number of data as we reviewed two additional RCTs that were not included in the Cochrane review: one new trial (Huang et al., 2015) and one trial (Mota-Pereira et al., 2011) for which data were obtained from the authors. Secondly, the present review used a different approach to calculating the group differences comparing not only the endpoint of the groups, but using the changes from baseline to endpoint between groups. The use of this approach is relevant since it accounts for potential differences at the baseline between the groups, even for differences that were not detected due the small sample size. For example, in the Mota-Pereira et al., (2011) study, the mean and standard deviation for the psychological domain QoL at baseline were 36.18 (19.15) and 47.92 (19.18) for the exercise and control groups, respectively. At the endpoint, the scores in the psychological domain were 41.45 (19.62) and 43.75 (15.34) for the exercise and control groups, respectively. Assessing the effect size using only the endpoint, the SMD is equal to 0.13 (95% CI −0.49 to 0.75) while using the mean change, the SMD is equal to 0.51 (95% CI −0.25 to 1.28).

The improvement in psychological QoL following exercise treatment differs from the Cochrane study (Cooney et al., 2013). Cooney et al. did not find significant changes in the psychological domain while we found a moderate effect (SMD=0.53). Furthermore, it is important to note that Cooney et al. (2013) analyzed the mental component of SF-36 and the psychological domain of WHOQOL separately, while we pooled the data from both instruments into one single domain. Despite the conceptual and metric differences between the instruments, we believe that the constructs overlap, and can be grouped for analysis. Previous meta-analyses have already used this strategy, using the WHOQOL framework to cluster the domains of different instruments (Gillison et al., 2009; Rosenbaum et al., 2014).

Our results support the notion that exercise interventions do not improve the social and environmental domains of QoL (Schuch et al., 2011b; Cooney et al., 2013) in people with depression and concur with previous studies in healthy people and in people with other chronic conditions (Gillison et al., 2009). This result might, however, be surprising as the social aspect of group exercise and the social support are seen by health professionals as potential mechanisms of the antidepressant effects of exercise (Stathopoulou et al., 2006). A possible reason for the lack of improvement on the social QoL domain in our study is that two of the three reviewed studies employed individualized exercise interventions (Mota-Pereira et al., 2011; Schuch et al., 2015). Although, both studies used supervised interventions, it appears that the supervision of a professional was not able to promote improvements in the social domain. Further studies using a group-based exercise format are therefore required to evaluate if social interactions among the group members potentially influence social QoL ratings.

Overall, additional interventions seeking to improve the QoL of depressed people are essential because despite the potential

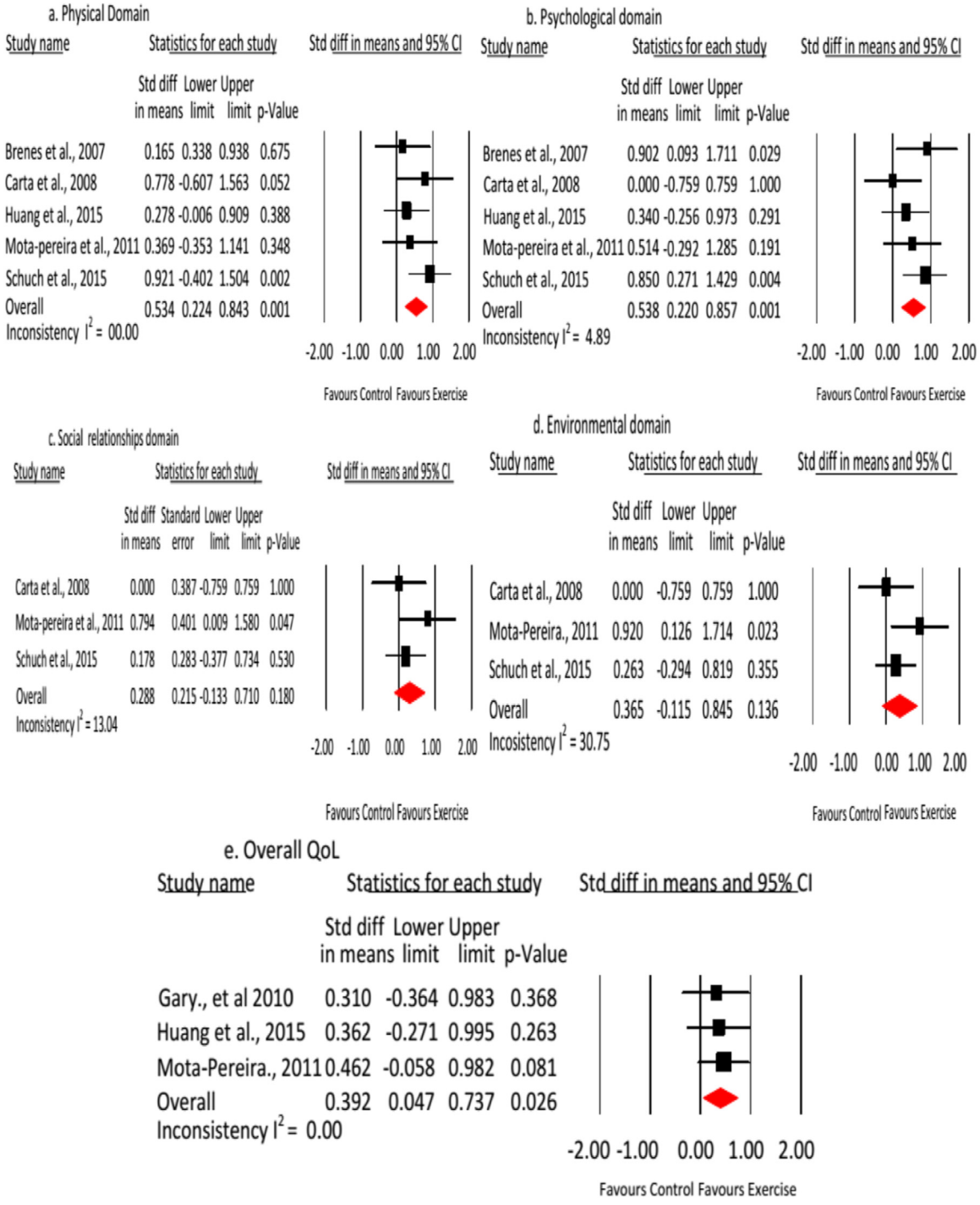

Fig. 2. Forest plot of effects of exercise on quality of Life in people with depression. CI = Confidence interval; QoL = Quality of Life; Std diff = Standardized difference.

Table 2
Control group response in studies evaluating QoL in depression.

Domain	Number of RCTs	Meta-analysis				Heterogeneity
		SMD	95% CI		P value	I^2
Physical	4	0.279	−0.252	0.811	0.3	85.36
Psychological	4	0.271	−0.178	0.720	0.2	80.39
Social relationship	3	0.084	−0.373	0.541	0.7	77.16
Environment	3	0.086	−0.108	0.280	0.3	83.06
Overall QoL	2	−0.410	−0.345	0.264	0.7	0.00

CI = Confidence Interval, QoL = Quality of Life, RCTs = Randomized Clinical Trials, SMD = Standardised mean difference.

overlap between QoL and depression (da Rocha et al., 2009; Ishak et al., 2011), pharmacological treatments are often not sufficient to return the QoL of depressed patients to premorbid levels and some patients still experience impairment in QoL, even after remission of symptoms (Ishak et al., 2011). This notion is supported by the present study; whilst control groups in exercise trials for depressed people experience large improvements in depressive symptoms (Stubbs et al., 2015), the evaluation of the control group response in our study indicated non-significant improvements in any QoL domain, nor overall QoL. This insufficient QoL improvement can be explained by the fact that most of our reviewed studies used antidepressant medication as the comparison treatment (Carta et al., 2008; Gary et al., 2010; Mota-Pereira et al., 2011; Schuch et al., 2015), and the symptom improvements related to antidepressants explain only a small (14–33%) proportion of the overall variance of QoL improvement (Ishak et al., 2011). This finding reinforces the role of exercise, as an important strategy towards the improvement of QOL for people with depression.

The present review has some limitations and our findings should be interpreted with caution. Firstly, only six trials were reviewed, with some sensitivity analyses lying on only three studies. Thus, it was not possible to explore the relationship between exercise prescription variables and QoL improvements. However, it should be highlighted that all analyses presented inconsistency values smaller than $I^2=31$, being $I^2=0$ in physical domain and overall QoL indicating a consistent effect of exercise on QoL improvement. Secondly, only one reviewed trial presented a lower risk of bias. Thirdly, reviewed studies presented their results on a domain basis. Therefore, it is not possible to evaluate the role of specific aspects (facets/sub-domains) in the effects of exercise on QoL in people with depression. Lastly, studies published in languages other than English were excluded from revision; however, we have not encountered an increased risk of publication bias in the analysis of any domain according to the Egger or Begg and Muzandar tests.

7. Conclusion

People with depression experience considerable impairments in QoL and the current meta-analysis demonstrated that exercise appears to be an effective strategy in improving overall QoL and physical and psychological QoL in this vulnerable population. However, further and better designed exercise trials examining the QoL for people with depression are needed in order to evaluate the impact of exercise characteristics (e.g., duration, intensity, modality and group or individualized sessions) and sample characteristics (e.g., age, gender, depression severity) on the overall and domain QoL in comparison to antidepressant medication.

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Conflict of Interest

None to declare from any author.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.psychres.2016.04.054.

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