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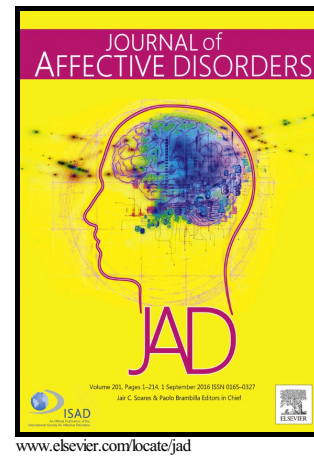
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Physical activity and sedentary behavior in people with major depressive disorder: A systematic review and meta-analysis

Felipe Schuch, Davy Vancampfort, Joseph Firth, Simon Rosenbaum, Philip Ward, Thaís Reichert, Natália Carvalho Bagatini, Roberta Bgeginski, Brendon Stubbs



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**Physical activity and sedentary behavior in people with major depressive disorder: A
systematic review and meta-analysis**

Felipe Schuch ^{a,b,c*}, Davy Vancampfort ^{d,e}, Joseph Firth ^f, Simon Rosenbaum ^{g,h}, Philip Ward ⁱ, Thaís Reichert ^b, Natália Carvalho Bagatini ^b, Roberta Bgeginski ^j, Brendon Stubbs ^{k,l}

^aUnilasalle, Canoas, Brazil

^bEscola de Educação Física, Fisioterapia e Dança, Porto Alegre, Brazil

^cHospital de Clínicas de Porto Alegre, Porto Alegre, Brazil

^dKU Leuven – University of Leuven, Department of Rehabilitation Sciences, Leuven, Belgium

^eKU Leuven – University of Leuven, University Psychiatric Centre, Leuven-Kortenberg, Belgium

^fInstitute of Brain, Behaviour and Mental Health, University of Manchester, Manchester, UK

^gDepartment of Exercise Physiology, School of Medical Sciences, University of New South Wales, Liverpool NSW 2170, Sydney, Australia

^hThe Black Dog Institute, University of New South Wales, Hospital Road, Prince of Wales Hospital, Randwick, 2031, NSW, Australia.

ⁱSchool of Psychiatry, UNSW Australia, Sydney and Schizophrenia Research Unit, Ingham Institute of Applied Medical Research, Liverpool, NSW Australia

^jObstetrics and Gynecology Department, Universidade Federal do Rio Grande do Sul, Rio Grande do Sul, Brazil

^kPhysiotherapy Department, South London and Maudsley NHS Foundation Trust, London, UK

^lHealth Service and Population Research Department, Institute of Psychiatry, Psychology and Neuroscience, King's College London, De Crespigny Park, London, UK

* Corresponding author at: Unilasalle, Canoas, Brazil Tel: +55 51 3476 8500; Fax: +55 51 3476 8500. E-mail address: felipe.schuch@ufrgs.br (Felipe Barreto Schuch).

Abstract*Background:*

Low levels of physical activity (PA) and sedentary behavior (SB) are independent risk factors for cardiovascular disease and premature mortality in people with major depressive disorder (MDD).

Aims:

Investigate levels of PA and SB and their predictors in people with MDD.

Methods:

Electronic databases were searched from inception till 04/2016 for articles measuring PA and SB with a self-report questionnaire (SRQ) or objective measure (e.g. accelerometer) in people with MDD. Random-effects meta-analyses and meta-regression analyses were conducted.

Results:

Twenty-four eligible studies were identified including 2,901 people with MDD (78.4% female, mean age=54 years; range: 21 to 77 years). People with MDD spent 126.0 min (95%CI=91.9-160.1) per day engaging in all types of PA and spent 8.5 hours (95%CI=7.51-9.62) during their waking day being sedentary. Compared to controls, people with MDD spent less time in total PA (SMD=-0.25, 95%CI=-0.03-0.15) and moderate to vigorous PA (SMD=-0.30, 95%CI=-0.40-0.21) and engaged in higher levels of SB (SMD=0.09, 95%CI=0.01-0.18). The proportion of people with MDD not meeting the recommended PA guidelines was 67.8% (n=13 studies), which was higher in studies relying on objective versus self-report measures (85.7% v 62.1%, p=0.04). People with MDD were less likely than controls to meet recommended PA guidelines (OR=-1.50, 95%CI=-1.10--2.10).

Limitations:

Heterogeneity was evident in most analyses.

Conclusions:

Adults with MDD engage in low levels of PA and high levels of SB. PA and SB are independent predictors of mortality, therefore, future lifestyle interventions targeting both the prevention of SB and adoption and maintenance of PA are warranted.

Keywords: physical activity, exercise, sedentary behavior, depression, major depression, depressive symptoms, psychiatry

Introduction

People with major depressive disorder (MDD) are at increased risk of premature mortality (Cuijpers et al., 2014) with 10 year lower life expectancy compared to the general population (Laursen et al., 2016). Recent research suggests that cardiovascular and metabolic disease are major factors contributing to this premature mortality (Charlson et al., 2013). In the general population, there is good evidence that physical activity and exercise can attenuate rates of cardiovascular disease and mortality (Naci and Ioannidis, 2013). However, people with MDD experience a range of barriers to engaging in physical activity such as depressive symptoms, higher body mass index, physical co-morbidity and lower self-efficacy (Vancampfort et al., 2015c).

The relationship between physical activity and depression seems to be bidirectional. Depressed people are typically less active (De Moor et al., 2006), whilst lower levels of physical activity increase the risk of depression (Mammen and Faulkner 2013). In addition, physical activity and exercise (i.e. structured physical activity) can improve depressive symptoms (Schuch et al., 2016a) and quality of life among people with depression (Schuch et al., 2016b; Schuch et al., 2015). Despite the benefits of physical activity for people with depression, it remains unclear how much physical activity people with depression engage in and what influences physical activity participation. While public health physical activity recommendations exist, such as achieving 150 minutes of moderate to vigorous PA (MVPA) per week (O'Donovan et al., 2010), it remains unclear how many people with MDD achieve this target.

Recently, interest has grown in the importance of preventing prolonged periods of sedentary behavior in order to tackle cardiovascular disease and mortality. Sedentary behavior is defined as an energy expenditure ≤ 1.5 metabolic equivalents of task (METs), while in a sitting or reclining posture during waking hours (Sedentary Behaviour Research, 2012). A

large meta-analysis in the general population demonstrated that sedentary behavior is associated with an increased risk of developing cardiovascular disease, type 2 diabetes, cardiovascular and all-cause mortality (Biswas et al., 2015). People with depression are known to experience high levels of diabetes (Vancampfort et al., 2016a; Vancampfort et al., 2015b). However, it remains unclear exactly how much sedentary behavior people with depression engage in.

When considering physical activity and sedentary behavior levels, many studies appear to have relied on self-report questionnaires (SRQ) rather than relying on objective measures such as accelerometers, which provide more accurate measurements (Soundy et al., 2014). Previous meta-analyses in schizophrenia (Stubbs et al., 2016a; Stubbs et al., 2016b) and bipolar disorder (Vancampfort et al., 2016b) have suggested that significant differences in physical activity and sedentary behavior levels exist between self-report and objective measures. It remains unclear if this extends to people with depression. A number of previous narrative reviews have examined the relationship between physical activity and sedentary behavior among people with depression (Hallgren et al., 2016; Lopresti et al., 2013; Teychenne et al., 2008). However, a comprehensive systematic review and meta-analysis of PA and sedentary behavior levels and predictors among people with MDD is lacking.

The aims of the present systematic review were to: (1), establish the mean amount of physical activity and sedentary behavior per day among people with MDD, (2) investigate predictors of physical activity and sedentary behavior through meta-regression analyses, (3) establish the proportion of people with MDD that meet the guideline recommendation of 150 minutes of MVPA per week (4) explore differences in physical activity and sedentary behavior in people with MDD versus age- and gender matched healthy controls. (5) evaluate differences between physical activity and sedentary behavior measured using SRQs and objective measures.

Methods

This systematic review was conducted according the MOOSE guidelines (Stroup et al., 2000) and the PRISMA statement (Moher et al., 2009).

Inclusion criteria

We included studies that: (1) involved adult participants with a diagnosis of MDD according to established criteria (e.g., DSM-IV (American Psychiatric Association, 2013), or ICD-10 (Organization, 1993). (2) Measured physical activity and sedentary behavior with either a validated SRQ (e.g. IPAQ, (Craig et al., 2003)) or objective measure (e.g. accelerometer). Physical activity was defined as any bodily movement produced by skeletal muscles which requires energy expenditure (Caspersen et al., 1985) while sedentary behavior is defined as an energy expenditure ≤ 1.5 metabolic equivalents of task (METs), while in a sitting or reclining posture during waking hours (Cart, 2012). (3) Were interventional (RCTs, CCTs) and observational (prospective or cross sectional) studies conducted in any setting (inpatients or outpatients). (4) Were published in an international peer-reviewed journal. If we encountered studies that included samples with MDD and other mental illness or with people with depressive symptoms (with a formal diagnosis of MDD), we contact the authors four times over a one month period to acquire the relevant data for our analyses.

Exclusion criteria

Exclusion criteria were: (1) non-quantitative studies, (2) studies not including people with MDD or not reporting the data for those with MDD in mixed sample studies, (3) no valid measure of physical activity or sedentary behavior (i.e. no mean time (minutes) per day/week engaged in physical activity) or sedentary behavior.

Search strategy

Four independent authors (FS, RB, NB, TR) searched PubMed, PsycINFO, SPORTDiscus, and EMBASE without language restrictions from inception till April 1st 2016, using the following keywords: 'Physical activity[MESH]' OR exercise[MESH] OR 'leisure time' OR 'sitting OR 'lying' OR 'screen time') AND (Depression[MESH] 'OR Major depressive disorder[MESH]' OR 'depressive disorder').

Study selection

After removal of duplicates, one author screened titles (FS) and abstracts of all potentially eligible articles. Three other authors (RB, NB, TR) reviewed the included studies to develop a final list.

Outcomes

The primary outcome was the mean time (minutes) per day that people with MDD engaged in physical activity (total, light, moderate, moderate to vigorous or vigorous) or were sedentary. If possible, we collected separate data for light, moderate and high intensity physical activity. Wherever possible, we collected data on physical activity behavior among healthy controls. Finally, we collected any reported data on the proportion of people with MDD that achieved the recommendation of 150 minutes of PA per week.

Data extraction

One author (FS) extracted data using a predetermined data extraction form, which was subsequently validated by a second author (BS). The data extracted included first author, country, setting, population, number of studies and participants included in the article (including mean age, % female), physical activity and sedentary behavior assessment method (objective or self-report), and the primary outcomes. If the study did not indicate the mean and SD values of PA or sedentary behavior levels, and the authors did not reply our emails, we attempted to extract the data from figures using the software Digizelt version 2.2.2.

Meta-analysis

Due to the anticipated heterogeneity across studies, we conducted a random effects meta-analysis with Comprehensive Meta-Analysis software (CMA, Version 3). The meta-analysis was conducted in the following sequence. First, we calculated the mean number of minutes spent in light, moderate, vigorous and total physical activity per day, the mean number of hours spent in sedentary behavior per day, and the proportion of people with MDD that achieved 150 minutes of PA per week, together with the 95% confidence intervals (CI). Second, we calculated the subgroup differences in physical activity and sedentary behavior according to the measurement type (self-report versus objective measurement) and study setting (living in community, outpatients, inpatients/hospitalized or mixed). Third, we investigated potential moderators of physical activity and sedentary behavior with meta-regression analyses. The potential moderators of interest were mean age, % of females, BMI and severity of depressive symptoms. Fourth, we conducted a comparative meta-analysis investigating differences in physical activity and sedentary behavior between MDD patients and healthy controls, calculating the standardized mean difference (SMD) and the 95% CI for the effect size. In addition, we calculated the mean difference in minutes per day together, with the 95% CI in levels of physical activity and sedentary behavior. All comparative analyses were performed using random effects models. We assessed heterogeneity using the I^2 statistics for each analysis (Higgins, 2011) and the publication bias with the Begg-Mazumdar Kendall's tau (Begg and Mazumdar, 1994). Trim and fill analyses were conducted (Duval and Tweedie, 2000) to remove the most extreme small studies from the positive side of the funnel plot, and recalculated the effect size at each iteration, until the funnel plot was symmetric about the (new) effect size.

Results

Search results

The initial search yielded 8,103 results. After removal of duplicates and exclusion during the title and abstract level review, 481 full texts remained. Following the application of the eligibility criteria, 24 articles were included (see Figure 1 for search results). At the full text review stage, seven of 32 research groups contacted provided additional data (see acknowledgements). Overall, 24 articles, were eligible for inclusion (Appelhans et al., 2012; Belvederi Murri et al., 2015; Bernard et al., 2015; Boettger et al., 2009; Combs et al., 2014; Correia and Ravasco, 2014; Craft et al., 2007; Da Ronch et al., 2015; de Wit et al., 2011; Donath et al., 2010; Forlenza and Miller, 2006; Garcia-Toro et al., 2012; Helgadóttir et al., 2015; Hoogendijk et al., 2008; McKercher et al., 2013; Mota-Pereira et al., 2011; Pfaff et al., 2014; Rahe et al., 2014; Stanley et al., 1999; Stavrakakis et al., 2015; Vancampfort et al., 2015a; Weinstein et al., 2010; Wielopolski et al., 2015; Zanco et al., 2016).

Study and participants' characteristics

Across the 24 unique studies, there were 2,901 (78.4% female) individuals with MDD (mean age=54 years; range: 21-77 years). The sample size of people with MDD ranged from 10 (Stavrakakis et al., 2015) to 840 (Rahe et al., 2015). Most of the included studies were conducted in Europe (n=15), 5 were conducted in North America, 3 in Oceania and 1 in South America (full details in table 1). Eleven studies were conducted in an outpatient setting (MDD n=1,543), seven in a community setting (MDD n=654), three in a mixed setting (MDD n=507) and one in an inpatient setting (n=19). Overall, 18 studies provided data on specific intensities of physical activity (MDD=2,036). Of those, 9 provided data on total physical activity (MDD n= 848), whilst 6 provided data on light (MDD n=610), 6 on moderate (MDD n= 1,411), 11 on moderate to vigorous (MDD n= 1,605) and 7 on vigorous (MDD n=1,463) physical activity. Twelve studies utilized SRQs to assess physical activity (MDD n=1,906) and 6 reported data with objective measures (e.g. accelerometers) (MDD n=101). Six studies provided data on overall sedentary behavior (MDD n=1,057), of which 4 (MDD n=1,006)

used a SRQ and 2 (MDD n=51) used an objective measure, and three studies provided data on sitting time, all using SRQs (MDD n=627). Ten studies reported data from control participants without a diagnosis of MDD. In total 3,783 (63.18% female) controls were included (mean age=48.5 years). Further details of the included studies are summarized in Table 1.

Meta-analysis of physical activity

Meta-analyses results are summarized below with full details displayed in Table 2.

Total physical activity

Nine studies including 1,192 participants with MDD were pooled, and showed that people with MDD spent a total time of 126.0 (95%CI 91.9 to 160.4) minutes per day engaged in physical activity. There was no evidence of publication bias (Kendall's tau with continuity correction=0.22, P=0.49).

Subgroup analyses of total physical activity

Subgroup analyses suggested that people living in the community (27.2 min) spent significantly less time ($P<0.0001$) engaged in total physical activity than inpatients (149.1 min), outpatients (119.0 min) or studies that evaluated people living in mixed settings (401.0 min). Objective measures showed a greater time spent in total physical activity than SRQ (144.2 versus 98.0 min, $P=0.03$) (details in table 2).

Meta regression of total physical activity

Age or gender did not predict the total level of physical activity. Meta-regression analyses results are presented in table 3.

Light physical activity

Six studies demonstrated that people with MDD spent 139.9 (95%CI 90.6 to 189.3) minutes per day in light physical activities. Whilst some publication bias was identified (Kendall's tau with continuity correction=0.66, P=0.03) the trim and fill test did not change the values.

Subgroup analyses of light physical activity

SRQ reported less time spent in light intensity physical activities than objective measures (84.8 vs 246.0 min, P=0.001).

Meta regression of light physical activity

Age or gender did not predict the engagement in light physical activity (see table 3).

Moderate physical activity

Six studies (n=1,411) demonstrated that patients with MDD engaged in a mean of 61.3 (95%CI 42.7 to 79.8) minutes per day in moderate intensity physical activity. There was no publication bias (see table 2).

Subgroup analyses of moderate physical activity

There was some suggestion that outpatients engaged in less (23.9 min) moderate intensity physical activity than people living in the community (67.1 min) or mixed settings (226.00). There was no significant difference between objective measure and SRQ (P=0.8).

Meta regression of moderate physical activity

Older age was inversely associated with moderate intensity physical activities (n=6, $\beta = -2.91$, 95%CI -5.82 to -0.0109, p=0.04 $R^2=0.20$).

Moderate to vigorous physical activity

Eleven studies (n=1,778) demonstrated that patients with MDD spent a mean of 37.6 (95%CI 27.4 to 47.9) minutes per day engaged in moderate to vigorous physical activity. There was no publication bias (see table 2).

Subgroup analyses of moderate to vigorous physical activity

There was some suggestion that people living in mixed setting (outpatients and inpatients) engaged in more (230.0 min) moderate to vigorous physical activity compared to people living in the community (29.2 min) or outpatients (27.1 min). No difference was observed in MVPA using SRQ and objective measures.

Meta regression of moderate to vigorous physical activity

Female gender was inversely associated with time spent in moderate to vigorous physical activities (n=10, $\beta = -1.30$, 95% CI -1.8 to -0.76, $P < 0.001$).

Vigorous physical activity

Seven studies (n=1,463) revealed that patients with MDD spent a mean of 5.3 (95%CI 2.5 to 8.1) minutes per day in vigorous physical activity. There was some publication bias (Kendall's tau with continuity correction=0.47, $P=0.04$). The amount of vigorous physical activity was unchanged by the trim and fill test.

Subgroup of vigorous physical activity

SRQ studies tended to report higher amounts of time engaged in vigorous physical activity compared to objective measures (7.7 versus 1.0 min, $P < 0.001$).

Meta regression of vigorous physical activity

Age or gender did not predict the engagement in vigorous physical activity.

Sedentary behavior

Across 6 studies, 1,057 participants spent 8.5 (95%CI 7.4 to 9.6) hours per day in sedentary behavior. There was no publication bias (see table 2).

Subgroup analyses of sedentary behavior

Participants living in the community spent significantly ($P<0.001$) more time in sedentary behavior (9.9 hours) than outpatients (7.6 hours) or mixed setting (6.6 hours). Studies using objective measures demonstrated an increased time spent in sedentary behaviors compared to those employing SRQs (9.9 versus 7.7 hours, $P<0.001$).

Meta regression of sedentary behavior

Age or gender was not associated with the amount of time spent in sedentary behavior.

Sitting time

Across 3 studies, 627 participants spent 3.9 (95%CI 3.5 to 4.9) hours per day sedentary sitting. There was no publication bias (table 2).

Subgroup analyses of sitting time

There was no significant difference between patients living in community or in a mixed setting.

Meta regression of sitting time

No moderator was identified.

Proportion of people with MDD who do not meet recommended PA guidelines?

Data from 13 study arms revealed that 67.8% (95%CI 52.1 to 80.3) of people with depression did not comply with the recommendation of 150 minutes of moderate or vigorous physical activity per week. No publication bias was identified (Kendall's tau with continuity correction=0.25, $P=0.24$) and the trim and fill test did not change the results.

Subgroup analyses of proportion of people that do not meet recommended PA

The proportion of people with MDD not meeting the recommended PA guidelines was higher in outpatients (70.9%) than in people living in community (65.3%) or mixed setting (17.4%; $p < 0.001$). A higher proportion of people with MDD did not meet the recommended guidelines when evaluated using objective (85.7%) compared to self-report measures (66.2%, $P = 0.05$).

*Difference in physical activity versus general population controls***Total physical activity**

People with MDD spent significantly less time in total PA ($n=5$, $SMD = -0.251$, 95% CI, -0.3 to -0.1, $P < 0.001$), equating to a mean difference of -11.6 (95% CI -25.7 to 2.6) minutes engaged in physical activities than their non-depressed counterparts. (See figure 2).

Light and moderate physical activity

There was inadequate data to calculate light and moderate PA differences.

Moderate to vigorous physical activity

People with depression spent significantly less time in moderate to vigorous activities ($n=3$, $SMD = -0.30$, 95% CI -0.40 to -0.21, $P < 0.001$), equating to a mean difference of -9.1 (95% CI, -19.7 to -0.8) minutes engaged in moderate to vigorous physical activities than people without depression. (See figure 3).

Vigorous physical activity

There was inadequate data to calculate vigorous PA differences.

Sedentary behavior

People with depression spent significantly more time in sedentary behavior ($n=5$, $SMD = 0.09$, 95% CI 0.01 to 0.18, $P=0.02$), equating to a mean difference of -0.2 (95% CI, -19.7 to 0.8) hours in sedentary behavior than their non-depressed counterparts. (See figure 4).

Sitting time

There was inadequate data to calculate sitting time differences.

People with MDD meeting recommended PA guidelines

People with MDD were less likely to meet the recommended 150 minutes of MVPA physical activity per week ($n=4$, $OR=1.5$, 95% CI 1.1 to 2.0, $p=0.001$).

Discussion

The current meta-analysis is to our knowledge, the first to investigate physical activity and sedentary behavior levels among people with MDD versus controls. Our analyses revealed that during waking hours people with MDD engaged in 139.9 minutes (equivalent to 2.4 hours per day) of light intensity, 61.0 minutes (1 hour per day) of moderate intensity and about five minutes of vigorous intensity physical activity per day. Moreover, people with MDD spent more than 8 hours per day in sedentary behavior, of which at least 4 hours involved sitting (all relying on self-report). The pooled total time spent in physical activity and light physical activities using objective measures was significantly higher than in self-report measures. However, the estimated time spent in vigorous activities was higher using SRQs. Meta-regression analyses demonstrated that older age, and female sex predicted lower

levels of moderate and moderate to vigorous physical activity, respectively. Lastly, people with MDD spent more time in sedentary behavior and less time in total and moderate to vigorous physical activities when compared to controls.

Although several studies have previously indicated that people with MDD engage in low levels of physical activity (Hallgren et al., 2016; Teychenne et al., 2008), this has not been demonstrated with meta-analytic methods until now. Furthermore, we demonstrated that over 65% of people with MDD do not meet the recommended PA guidelines. People with MDD were 50% less likely to meet PA recommendations compared to people without depression. When utilising objective measures, the proportion of people with MDD not meeting the guidelines increases to 88%. Overall, global physical inactivity is estimated as occurring in around 30% of the population (Hallal et al., 2013). It is estimated that a decrease of 10% in the total number of people being sedentary could result in averting 533,000 premature deaths each year (Lee et al., 2012). Increasing physical activity levels should therefore be a priority not only for mental health (Schuch et al., 2016a; Schuch et al., 2016b; Schuch et al., 2015), but also for improving physical health in people with MDD.

The total time spent in physical activity and light physical activities were significantly higher when recorded by objective measures, time spent in vigorous activities were lower when measured using SRQs compared to objective measures, suggesting that SRQs are inaccurate for assessing PA levels in people with mental illness. This result is consistent with previous studies in mental illness showing that the current SRQs are inaccurate tools for measuring physical activity levels (Soundy et al., 2014; Soundy et al., 2013). Thus, our results suggest that current questionnaires do not accurately collate data on physical activity behavior in groups with high levels of sedentary behavior. Some of this may be due to the cognitive deficits associated with depression (Rock et al., 2014). Also clinical variability in mood may influence the ability to accurately complete self-report questionnaires (Pemberton and Fuller Tyszkiewicz, 2016). A new clinical tool aiming to better capture physical activity levels in people with high levels of sedentary behavior is currently being validated (Rosenbaum and Ward).

Time spent in sedentary behavior by people with MDD appears to be one hour lower than in people with bipolar disorders (approximately 10 hours per day; (Vancampfort et al., 2016b) and two hours lower than people with psychosis (approximately 11 hours per day (Stubbs et al., 2016b). However, people with MDD are more sedentary than other groups in the general population, such as older people (about to 5 hours per day) (Harvey et al., 2014). Also, our comparative meta-analysis demonstrated that sedentary behavior levels are higher in depressed people than in their control counterparts. Sedentary behavior is independently associated with increased elevated c-reactive protein (Stubbs et al., 2015) and metabolic syndrome (Vancampfort et al., 2012) and is directly related to short-term all-cause and cardio-metabolic disease-related mortality (Chau et al., 2015). In particular, TV viewing time has been associated with all-cause mortality, including suicide (Keadle et al., 2015). Therefore, strategies seeking to decrease sedentary behavior, including reducing the TV viewing time, in people with depression are required to reduce the elevated rates of cardiometabolic disorders observed in this population (Wijndaele et al., 2010). Some of these pragmatic actions may include: encouraging patients to rise from a chair and move around during television commercial breaks, or adding brief (e.g. less than or equal to five minute) walks throughout the day, for example walking short distances rather than using motorized transport (Vancampfort et al., 2015d). Also, previous research indicated that people with MDD are very sensitive to pressure from their family and friends to be physically active (Vancampfort et al., 2016). It might be that a more therapeutic environment facilitating feelings of autonomy, social relatedness and competence would result in higher physical activity levels (Vancampfort et al., 2016).

Several limitations of this meta-analysis should be noted. First, although we identified 24 studies in the meta-analysis, some of the studies did not report the time spent in each type of physical activity and sedentary behavior, reducing the sample available for these sub-analyses. However, it should be noted that all analysis included considerable sample sizes. For example, the analysis with the smallest sample size included more than 600 participants. Second, most of the included studies assessed physical activity and sedentary behavior with

SRQs, and there were few studies using objective measures. As noted, there are concerns about the accuracy of SRQs (Soundy et al 2014) and our data may be underestimates or overestimates. Also, as indicated, people with depression are known to experience cognitive impairment (Zaninotto et al., 2016) which may make recall less accurate. Those factors may help to explain some of our counterintuitive results such as: 1) people living in the community spent less time in total physical activity than mixed settings, with a difference of more than 300 minutes per day. 2) The finding that approximately 60% of people with MDD not meeting the recommended 150 min/week of moderate to vigorous physical activity, while in those studies providing raw data to calculate the mean minutes was approximately 60 min (equating to considerably more than 150 minutes per week). This discrepancy in the measurement underscores the need for future research to utilize objective PA or standardized self-report measures. In addition, it should be noted that some heterogeneity is expected since the correlation between SRQs and objective measure do not exceed 0.5 (Skender et al., 2016), leading to significant discrepancies in the results of different studies. In fact, we have encountered large heterogeneity for most analyses. Finally, there was inadequate information on psychopathological symptoms, % of participants taking antidepressants, % of participants with clinical psychiatric comorbidities or BMI for each category, thus precluding meta-analytical or meta-regression analysis. Future research is required to explore the impact of different depressive symptoms on physical activity and sedentary behavior in this population.

In conclusion, people with MDD engage in less physical activity and more sedentary behavior versus controls. The proportion of people with MDD not meeting recommended guidelines is high, with objective measures showing that around 80% of people with MDD failed to achieve sufficient amounts of weekly PA. Given the heightened rates of cardiovascular risk, metabolic dysfunction and chronic inflammation associated with MDD, and the potential for physical activity to improve these conditions, interventions which reduce sedentary behavior and increase PA could confer substantial benefits for people with MDD.

Strategies aiming PA increases in daily activities should be incorporated as part of treatment for depression.

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Contributors

FS, TR, NB and RB performed the searches and extracted the data. BS and FS developed the research protocol. All authors wrote and reviewed the manuscript.

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Conflict of interest

FS, BS, RB, NB, JF, TR, DV, PBW and SR report no conflict of interest.

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Table 1. Details of the included studies

Author	Study setting and location	Participants with depression	Assessment method and period	Physical activity (min/day) and sedentary behavior (h/day)	MDD participants that do not meet 150 minutes or more of moderate PA per week or have low level of PA	Controls	Physical activity (min/day) and sedentary behavior (h/day)	control participants that does not meet 150 minutes or more of PA per week or have low level of PA
Appelhaans et al., 2012	Community US	n = 161 (100%female); 45.9 years	24HR, 1 day recall	PAMV = 9.02±11.65	n = 144	None	-	-
Belvedere	Outpatient	Sertraline:	IPAQ, 7	-	Setralin	None	-	-

ri Murri et al., 2015	ents Italy	n = 42 (76%female); 75.6 years Sertraline + NPE: n = 37 (68%female); 75 years Sertraline + PAE: n = 42 (69%female); 75 years	days recall		e: n = 34				
						Sertraline e + NPE: n = 35			
						Sertraline e + PAE: n = 35			
Bernard et al., 2015	Communi- ty Multiple countries in Europe	n = 32 (62.5%female); 47 years	Bodymedia Sensewear Armband , 7 days	SB = 10.3±2.6 PAM = 102.22± 52.34 PAMV = 109.92± 53.15 PAV = 1.69±1.5	-	None	-	-	-
Boettger et al., 2009	Outpatients Germany	n = 22 (68.18%female); 36.9 years	IPAQ, 7 days recall	SB = 7.3±3 PAMV = 60.2±89. 4	-	n = 22 (68.18%female); 37 years	SB = 7.4±2.1	-	-
Combs et al., 2010	Outpatients US	n = 198 (76%female); 52 years	Godin Leisure- Time Exercise Question- naire	PAL = 93.4±17 8.9 PAM = 14.3±37. 8 PAMV = 15.3±38. 1 PAV = 1±6.9 TPA = 108.7±1 87	-	None	-	-	-
Correia et al., 2014	Outpatients Portugal	n = 127 (94%female); 48 years	7 PAR, 7 days recall	-	n = 111	None	-	-	-
Craft et al., 2004	Communi- ty US	Home- based: n = 16 (100%female); 37.4 years Supervised: n = 16 (100%female); 43.4	7 PAR, 7 days recall	Home- based: PAMV = 5.9±4.9 Supervised: PAMV = 5.8±5.7	*	None	-	-	-

Da Ronch et al., 2015	Community Multiple countries in Europe	n = 216 (61.8%female); 72.4 years	IPAQ, 7 days recall	SB = 3.6±1.4 PAL = 51.1±47 PAM = 33.1±45 PAV = 19.3±38	n = 32	n = 1040 (41% female); 73.3 years	SB = 3.6±1.4 PAL = 55.9±52 PAM = 36.5±48 PAV = 26.1±44	n = 145
De Wit et al., 2011	Multiple settings Netherlands	n = 396 (64.9%female); 40.9 years	IPAQ, 7 days recall	SB = 3.9±2.2	n = 69#	n = 652 (61.3% female); 41.1 years	SB = 3.5±1.9	N = 77#(low PA)
Donath et al., 2010	Multiple settings Germany	n = 15 (100%female); 28 years	IPAQ, 7 days recall	SB = 5.0±2.2	-	n = 15 (100%); 38 years	SB = 5.4±1.6	-
Forlenza et al., 2006	Outpatients Canada	n = 84 (81%female); 28.7 years	Paffenbarger Physical Activity Scale 7 days recall	PAMV = 12.8±24.9	-	n = 85 (81.2%); 28.9 years	PAMV = 16.5±24.6	-
Garcia-toro et al., 2012	Outpatients Italy	Active: n = 8 (87.5%female); 53 years Control: n = 7 (84.2%female); 56 years	Actigraph, 14 days recall	Active: TPA = 164.2±74.4 Active: TPA = 131.1±53.1	-	None	-	-
Helgadóttir et al., 2015	Outpatients Sweden	n = 21 (?%female); ? years	Actigraph, 4 days or more recall	SB = 9.6±1.61 PAL = 235.97±62.71 PAMV = 37.75±22.22	n = 18	None	-	-
Hoogendijk et al. 2008	Community Netherlands	n = 26 (80.8%female); 77.7 years	LASA questionnaire, 7 days recall	TPA = 19.4±12.2	-	n = 1087 (47.7%female); 75.1 years	TPA = 20.1±14.8	-
McKercher et al., 2013	Community Australia	n = 173 (69.64%female); 31.4 years	IPAQ, 7 days recall	PAMV = 18.5±28.4	-	None	-	-
Mota-pereira et al., 2011	Outpatients Portugal	n = 29 (65.5%female); 48.4 years	Actigraph, 7 days recall	PAL = 267,9 ±136,5 PAM = 27.7±27 PAMV = 28.00±27.7	-	None	-	-

Pfaff et al., 2014	Outpatients Australia	Control: n = 92 (64.1%female); 60.7 years Intervention: n = 108 (62%female); 61.2 years	Community Healthy Activities Model Program for Seniors (CHAMPS) questionnaire, 7 days recall	PAV = 0.3±2.3 -	Control: n = 40 Intervention: n = 58	None	-	-
Rahe et al., 2015	Outpatients Germany	n = 840 (59.2%female); 49.4 years	IPAQ, 7 days recall	SB = 7.6±2.9 PAL = 37.88±39.47 PAM = 30±37.64 PAV = 12.64±22.47 PAMV = 42.47±46.55 TPA = 80.37±68.37	n = 368	n = 820 (50.5%female); 53.5 years	SB = 7.3±3.0 PAL = 40.22±47.52 PAM = 41.48±43.80 PAV = 18.35±31.6 PAMV = 59.74±59.85 TPA = 99.68±83.88	n = 244
Stravaski et al., 2015	? Netherlands	n = 10 (70%female); 36.4 years	Actical, 7 days recall	PAMV = 11.85±12.7	-	n = 10 (70%female); 36.7 years	PAMV = 19±15.5	-
Ström et al., 2013	? Sweden	n = 46 (83.3%female); 49.2 years	IPAQ, 7 days recall	SB = 9.8±4.9 PAL = 41.7±31.7 PAV = 3.29±7.0	-	None	-	-
Vancampfort et al., 2015	Multiple settings Belgium	n = 96 (65%female); 48.4 years	IPAQ, 7 days recall	SB = 6.6±3.2 PAL = 171±152 PAM = 226±168 PAMV = 230±170 PAV = 4±8 TPA = 401±290	-	None	-	-
Weinstein et al.,	Community	n = 14 (50%female)	Aerobics Center	TPA = 36.7±23.	-	n = 16 (50%female)	TPA = 38.9±25	-

2010	US	e); 41.7 years	Longitudi nal Study Physical Activity Question naire, 7 days recall	81		e); 38.1 years	.9	
Wielopo lski et al., 2015	Inpatien ts Germa ny	n = 19 (47.3%fem ale); 43.3 years	Sensewe ar armband, 1 day recall - data used for T3 extracted from figures DIGIZEL T*	TPA = 149.15± 160	-	n = 19 (47.3%fem ale) 43.0 years	TPA = 228.2±2 62	-
Zanco et al., 2016	Outpati ents Brazil	n = 20 (95%femal e); 74 years	IPAQ, 7 days recall	TPA = 133.97± 74.8	n=9#	n = 17 (85%femal e) 64 years	TPA = 159.31± 64.5	n=4#

24HR = 24 hour physical activity recall, 7PAR = seven day physical activity recall; NOS=not otherwise specified, BMI=body mass index, PAL=Physical activity low intensity, PAM= Physical activity moderate intensity, PAH= Physical activity high intensity, PAMV=Physical activity moderate to vigorous intensity, TPA=total physical activity, IPAQ=International Physical Activity Questionnaire. #data used = low physical activity or insufficiently active.

Table 2. Meta-analytic results of the time spent physically active and sedentary in people with MDD

Analysis	N studies	N participants	Meta-analysis Time per day 95%CI			Between group p value	Trim and fill adjusted ES	I ²
Total PA (min/day)								
Main analysis	8	1,192	126.0 6	91.97	160.1 4		Unchange d	97.7
<i>Setting</i>						<0.001		
Community setting	2	40	27.04	10.02	43.88		Unchange d	84.6
Inpatient setting	1	19	149.1 5	77.20	221.0 9		N/A	0
Outpatient setting	4	1,037	119.0 1	87.57	150.4 5		Unchange d	86.4
Mixed setting	1	96	401 8	342.9	459.0 1		N/A	0
<i>Assessment method</i>						0.03		
Subjective	7	1,367	98.02	67.13	128.9 1		145.63 (95% CI 64.30-	99.1

Objective	2	34	144.2 1	115.5 3	172.8 9	226.95) N/A	0
Light intensity PA (min/day)							
Main analysis	6	610	139.9 1	90.61	189.2 9	Unchange d	98.4
<i>Setting</i>						0.95	
Community setting	2	237	143.0 5	-38.11	324.2 2	N/A	99.4
Outpatient setting	2	235	241.7 2	-48.54	531.9 9	N/A	99.7
Mixed setting	1	96	171.0 0	140.5 9	201.4 0	N/A	0
<i>Assessment method</i>						<0.001	
Subjective	4	559	84.84	53.63	116.0 5	No changes	95.9
Objective	2	51	246.0 2	216.9 5	275.0 9	N/A	26.2
Moderate intensity PA (min/day)							
Main analysis	6	1,411	61.27	42.75	79.79	Unchange d	97.7
<i>Setting</i>						<0.001	
Community setting	2	248	67.10	-0.61	134.8 3	N/A	98.0
Outpatient setting	3	1,067	23.91	12.59	35.24	Unchange d	92.7
Mixed setting	1	96	226.0 0	192.3 9	259.6 0	N/A	0
<i>Assessment method</i>						0.8	
Subjective	4	1,350	58.91	37.67	80.15	Unchange d	98.7
Objective	2	61	64.55	-8.46	137.5 8	N/A	98.1
Moderate to vigorous intensity PA (min/day)							
Main analysis	11	1,728	37.60	27.24	47.97	Unchange d	98.2
<i>Setting</i>						<0.001	
Community setting	4	225	33.57	20.36	46.78	Unchange d	98.6
Outpatient setting	5	1,165	29.79	15.78	43.80	Unchange d	97.1 6
Mixed setting	1	96	230.0 0	195.9 9	264.0 0	Unchange d	0
<i>Assessment method</i>						0.7	
Subjective	6	944	42.54	27.02	58.08	31.87 (95% CI - 1.36- 51.11)	97.6 9
Objective	6	561	37.06	18.97	55.15	17.25 (95% CI - 03.43-	97.6

								37.94)
Vigorous intensity PA (min/day)								
Main analysis	7	1,463	5.37	2.56	8.18		Unchanged	93.0
<i>Setting</i>						0.5		
Community setting	2	248	10.3	-6.94	27.56		N/A	97.8
Outpatient setting	3	1,071	4.61	-1.57	10.80		N/A	99.9
Mixed setting	1	96	4.00	2.41	5.60		N/A	0
<i>Assessment method</i>						0.01		
Subjective	5	1,402	7.69	2.47	12.91		Unchanged	97.9
Objective	2	61	1.03	-0.32	2.39		NA	98.5
Sedentary behavior (h/day)								
Main analysis	6	1,057	8.51	7.40	9.62		Unchanged	94.0
<i>Setting</i>						<0.001		
Community setting	2	51	9.91	9.29	10.52		N/A	18.2
Outpatient setting	2	864	7.59	7.39	7.87		N/A	34.3
Mixed setting	1	96	6.60	5.96	7.24		N/A	0
<i>Assessment method</i>						<0.001		
Subjective	4	1,006	7.66	6.76	8.57		8.14 (95% CI 7.06-9.23)	84.1
Objective	2	51	9.91	9.29	10.52		N/A	18.2
Sitting Time (hours/day)								
Main analysis	3	627	3.94	3.5	4.39			84.3
<i>Setting</i>						0.2		
Community setting	1	216	3.60	3.41	3.78		N/A	0
Mixed setting	2	411	4.54	3.09	6.02		N/A	85.16
% of people with MDD that do not meet PA recommendations								
Main analysis	13	2,275	67.8	52.10	80.30		Unchanged	97.3
<i>Setting</i>						<0.001		
Community setting	3	550	65.30	60.20	70.10		Unchanged	98.6
Outpatient setting	9	1,656	70.90	56.30	82.22		Unchanged	90.5
Mixed setting	1	69	17.40	142.00	21.51		N/A	0
<i>Assessment method</i>						0.04		
Subjective	11	2,257	66.20	49.80	79.42		Unchanged	97.5
Objective	1	18	85.70	63.90	95.30		N/A	0

ES=Effect size, PA= physical activity, N/A=not applicable, *Significant when $P < 0.05$.

Table 3. Meta-regressions of moderators for physical activity and sedentary behavior in people with MDD

Moderator	N studies	β	95%CI	P-value	R^2
Total PA					
Age	8	-0.0371	-2.6388 2.5646	0.9	0.00
% female	8	0.3936	-1.5461 2.3333	0.6	0.00
Light intensity PA					
Age	5	-4.4354	-12.4983 3.6275	0.2	0.00
% female	5	-4.6824	-14.3761 5.0113	0.3	0.00
Moderate intensity PA					
Age	6	-2.9164	-5.8219 -0.0109	0.04	0.00
% female	6	-1.9624	-6.9085 2.9837	0.4	0.00
Moderate/vigorous intensity PA					
Age	11	2.3192	0.8967 4.4038	0.09	0.00
% female	11	-1.1907	-1.7332 -0.6482	<0.0001	0.43
Vigorous intensity PA					
Age	7	0.6690	1.3655 -1.9726	0.08	0.08
% female	7	-0.3505	-0.7323 0.0314	0.07	0.23
Sedentary behavior					
Age	4	0.0754	-0.2073 0.3580	0.6	0.00
% female	5	0.0674	-0.1009 0.2357	0.4	0.00
% of people with MDD that meet PA recommendations					
Age	11	0.0413	-0.0085 0.0911	0.1	0.28
% female	11	0.0302	-0.0298 0.0902	0.3	0.15

PA= physical activity, *Significant when $P < 0.05$.

Figure 1. Flow diagram for the search results

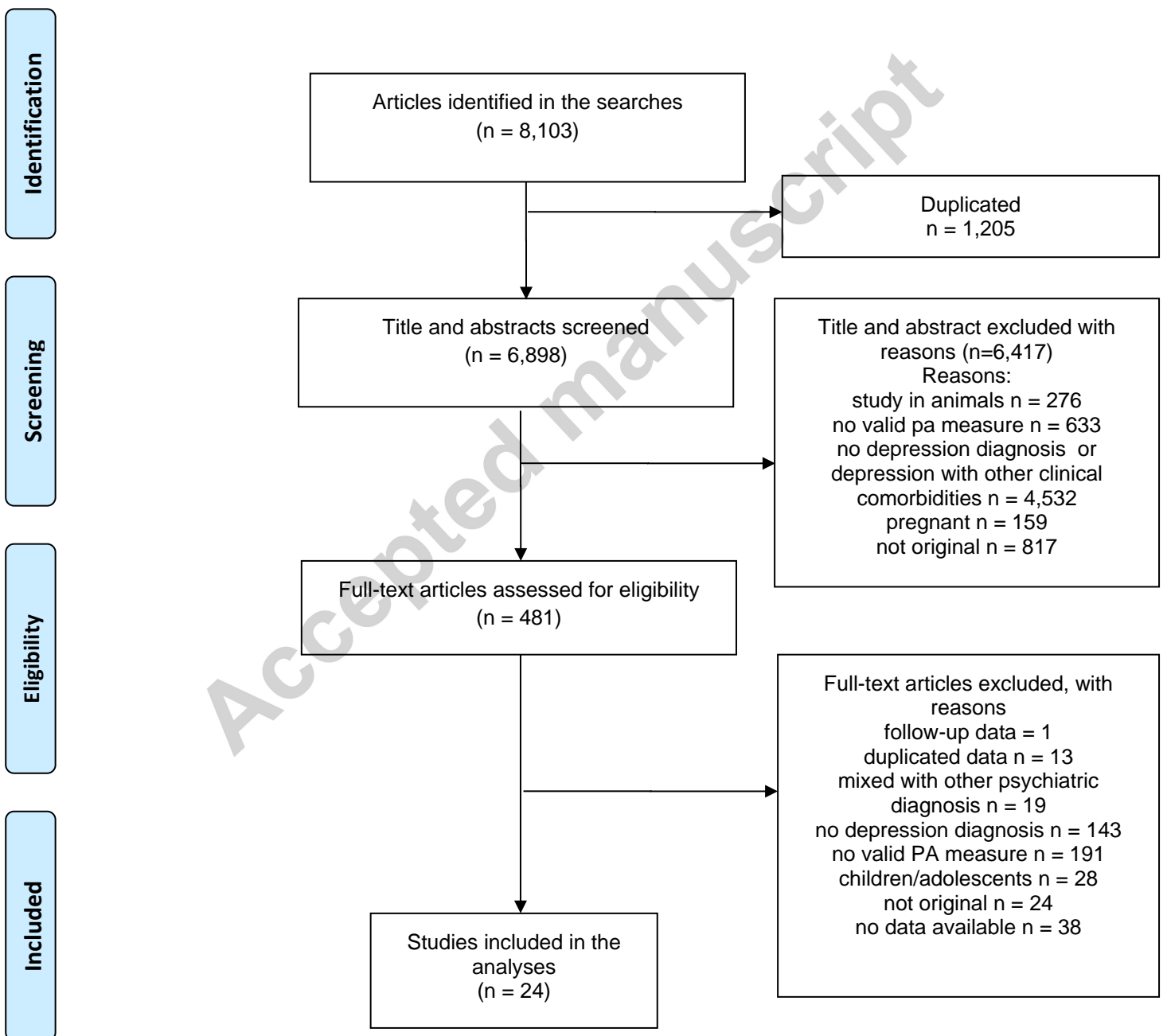


Figure 2. Comparison of total physical activity levels between patients with MDD and matched general population controls

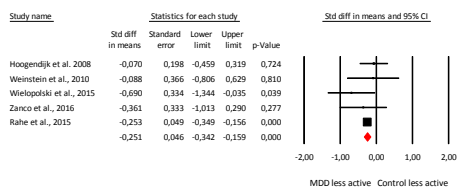


Figure 3. Comparison of moderate to vigorous physical activity levels between patients with MDD and matched general population controls.

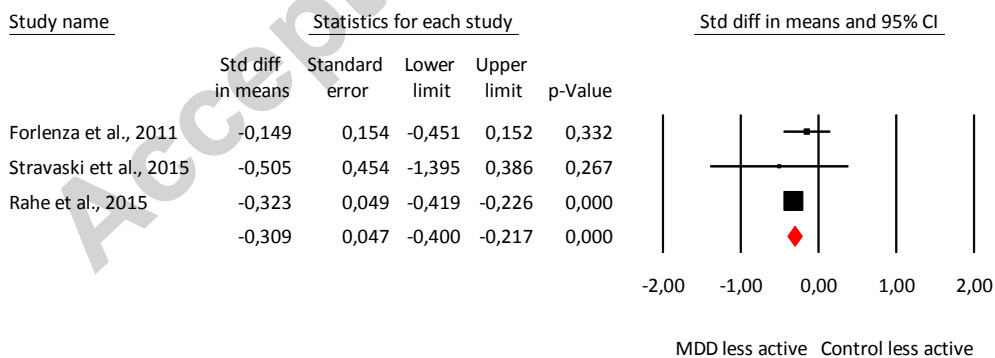
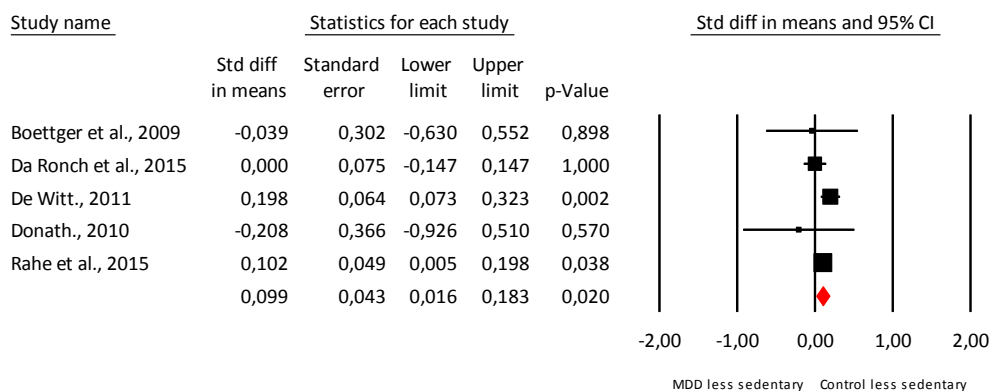


Figure 4. Comparison of sedentary behavior levels between patients with MDD and matched general population controls



Highlights

- People with MDD are less physically active compared to matched controls.
- People with MDD engage in higher levels of sedentary behavior versus controls.
- Approximately two thirds of people with MDD do not meet physical activity recommendations.
- Different estimates of physical activity and sedentary behavior may be obtained using self-report versus objective measures.
- Older age and female gender predict lower moderate and vigorous physical activity in people with MDD.