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Prospective associations between physical activity and clinician diagnosed major depressive disorder in adults: A 13-year cohort study

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ABSTRACT

Regular physical activity (PA) appears to protect against the emergence of depression, but prospective studies linked to clinician diagnoses of major depressive disorder (MDD) remain scarce. It is also unclear whether PA levels recommended for general health are prospectively related to depression onset. We explored these relationships in a cohort of adults followed over 13 years. In total, 43,863 Swedish adults were surveyed in 1997 and responses linked to clinician-diagnosed MDD obtained from specialist medical registers until 2010. Weekly durations of habitual moderate (including walking) and vigorous PA were self-reported. Relationships between total durations of PA, 0–149 ('below'), 150–299 ('achieve'), and ≥300 min ('exceed') with incident MDD were explored using survival analysis with Cox proportional hazards regression. Models were adjusted for relevant covariates. Those with indications of depression at baseline were removed from the primary analyses. Of 25,520 participants with complete data (mean age = 49 years, SD = 16, 65% female), 76% met the recommended weekly duration of PA (≥150 min), and 38% exceeded this duration (≥300 min). During 13-years follow-up 549 MDD cases (1.5%) were identified (incidence rate = 111 cases per 100,000 person-years). Compared to participants who were below, those who exceeded the recommended weekly duration (≥300 min/week) had 29% reduced risk of depression onset (HR 0.71, 95% CI = 0.53–0.96). A non-significant inverse association was observed among those who achieved the minimum duration of 150-min/week (HR 0.86, 95% CI = 0.64–1.14). Habitual PA levels that exceed the duration recommended for general health may reduce the risk of clinician-diagnosed major depression in adults.

1. Introduction

Major depressive disorder (MDD) is a leading cause of disability burden with an estimated global prevalence of between 6 and 20% (Vos et al., 2012). Symptoms include protracted feelings of sadness, decreased motivation, and sustained loss of interest in daily activities. In addition to these psychiatric symptoms, it is well established that high levels of cardiovascular (Correll et al., 2017) and metabolic disease (Vancampfort et al., 2015) contribute to the premature mortality gap of approximately 15 years in MDD compared to the general population (Moussavi et al., 2007). Although effective treatments exist (e.g. counselling, medication), successful treatment and maintenance of treatment response remains sub-optimal. One study reported a 24-month recurrence rate of between 27 and 33% depending on the

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treatment setting (Hardeveld et al., 2013). In the United States, the incremental economic burden of MDD increased from $173 billion in 2005 to $210 billion in 2010, and continues to rise (Greenberg et al., 2015).

Due to the immense personal and socio-economic impact of MDD, there is considerable interest in strategies that may help prevent depression onset. Within this context, physical activity has received considerable attention, both as adjunct treatment (Cooney et al., 2013), and a prevention strategy (Mammen and Faulkner, 2013). A narrative review reported that 25 out of 30 prospective studies demonstrated negative associations between baseline physical activity and risk of subsequent depression (Mammen and Faulkner, 2013). Authors concluded that any level of physical activity, including walking < 150 min per week, can prevent future depression. This finding is relevant from a public health perspective, as the World Health Organization (WHO) guidelines for maintaining health recommend > 150 min of moderate-to-vigorous physical activity (MVPA) per week (WHO, 2010). However, this review only included studies investigating associations with self-rated depression severity, and data were not pooled to determine the overall effect size estimates.

In a recent meta-analysis of prospective studies, Schuch and colleagues examined associations between physical activity and depression, including sub-analyses by activity duration (> 150 min versus less) (Schuch et al., 2018). In total, 49 unique prospective studies were included. Higher levels of physical activity were associated with significantly lower odds of developing depression, and these effects were observed among all age groups (youths, adults, the elderly) and both genders. However, the pooled analyses were based primarily on activity levels defined as 'high' or 'low' by study authors, without specifying the exact duration in minutes. Sub-analyses of eight studies based on clinician ratings of depression indicated non-significant associations between physical activity and major depression (AHR/ARR = 0.87: 95% CI = 0.74, 1.10). By contrast, physical activity was significantly associated with self-rated depressive symptoms in 11 studies (AHR/ARR = 0.84: 95% CI = 0.76, 0.93) (Schuch et al., 2018). These findings are relevant, as they suggest that associations between physical activity and depression may be influenced by both the severity of depression, and whether the outcome is self-reported or clinician-diagnosed. Prospective studies of relationships between physical activity and clinician-diagnosed depression remain scarce, but are needed to reduce the misclassification bias that occurs when depression is self-rated. Moreover, previous studies have frequently included small sample sizes and, to our knowledge, none have examined relationships between physical activity levels recommended for somatic health and depression onset.

To fill this research gap, we explored longitudinal associations between different durations of physical activity (below, achieving, and exceeding WHO recommended levels), with clinician-diagnosed MDD in a large cohort of Swedish adults followed over 13 years.

2. Method

2.1. Participants

Data originate from the Swedish National March Cohort study (SNMC: http://ki.se/en/meb/the-swedish-national-march-cohort-nmc). The National March was a four-day national fundraising event arranged by the Swedish Cancer Society in approximately 3600 Swedish cities and villages in September 1997. In total, 43,863 participants completed a 36-page survey with detailed questions about health behaviours and lifestyle, including specific questions on physical activity habits (type, frequency and duration). Reliability and validity data for the activity questionnaire has been published previously (Lagerros et al., 2006), and the survey has been used extensively (Lagerros et al., 2017). Exclusion criteria included: participants who were younger than 18 years at the beginning of the follow-up (1741), those who emigrated (465) or died (8), or that had a primary diagnosis of any mental disorder (ICD-8: 290-315 ICD-9 290-319 ICD-10 F00-F99) before the beginning of the follow-up. After removing these cases the survey sample consisted of 40,569 participants.

To examine only incident cases, we further excluded 1738 participants with indications of depression at baseline using the question, 'How often do you feed sad, low-spirited, depressed?' where the last two response alternatives (never, sometimes, *often*, *always*) were categorized as 'depressed'. Missing data on the physical activity variable, which comprised three items, described below, was 32%, leaving a final analytic sample of 25,520 participants for the primary analyses, and 27,258 for the sensitivity analyses with depressed cases included. The original study complies with the guidelines of the Declaration of Helsinki. The Research Ethics Vetting Board in Stockholm approved the original study and all subjects gave informed consent. Informed consent was obtained from participants after the procedure was fully explained.

2.2. Primary outcome: major depressive disorder (MDD)

The occurrences of incident MDD (ICD codes: F32.0, F32.1, F32.2, F32.8, F32.9, F33.0, F33.1, F33.2, F33.4, F33.8, F33.9) during the 13-year follow-up to 31st December 2010 were ascertained through linkages to existing nationwide, complete and continuously updated specialist medical registers, including inpatient and outpatient records. Diagnoses were made by a specialist clinician, often a psychiatrist or clinical psychologist. Accurate linkages - and thus essentially complete follow-up were attained using the individually unique National Registration Numbers (NRNs), assigned to all Swedish residents as identifiers both in the baseline questionnaire and in all registers. For this study, we included only the specialist registers. Patients referred to specialist care in Sweden are often moderately to severely depressed, having first attempted a period of treatment in the primary healthcare system. While the total number actually given a questionnaire during the fundraising event could not be assessed, all those who handed in a completed questionnaire consented to follow-up.

2.3. Exposure: habitual physical activity

The average weekly duration of physical activity was estimated by asking participants how much time per week they usually spent in 'exercise, athletics, and sports', including: (1) walking; (2) strenuous exercise (e.g. jogging, swimming); and (3) hard training/competition. The intensity of these activities was not rated; however, the question implied that the activities were performed in a structured or purposeful way. Thus, walking was included in the current definition of MVPA, as previously recommended (WHO, 2010). For each question there were six response alternatives; 0, 0–1, 2; 3; 4, and ≥5 h per week. Ratings were made separately for summer and winter and then averaged. Hours per week were converted into minutes: 0, 30, 120, 180, 240, and 300 min, respectively. Finally, participants were categorized as 'below' (0–149 min), 'achieving' (150–299 min) or 'exceeding' (≥300 min) the WHO recommended levels. The last category is recommended for attaining additional health benefits from physical activity (WHO, 2010), but has rarely been assessed in previous studies. The activity questionnaire has been used extensively and is described in detail elsewhere (Bellocco et al., 2010; Lagerros et al., 2009; Lagerros et al., 2006).

2.4. Covariates

Based on previous prospective studies (Kohler et al., 2018; Schuch et al., 2018), the following variables were included in the statistical models:

Body mass index (BMI): was calculated from self-reported weight and height (kg/m^2) and then categorized according to the WHO's BMI classification for adults; normal weight (< 25), overweight (25– < 30), and obese (≥30). Due to the small number of observation for underweight (BMI < 18.5) (1.3%), this group was collapsed with the first

category.

Occupation: was obtained by a single question '*What is your present occupation*?' Participants were classified into five groups; full-time, part-time, unemployed, retired, and other (including students).

Smoking status: was assessed by asking participants if they had ever smoked cigarettes for six months or more. Those answering yes were coded as 'smokers'.

Comorbidities: were assessed based on the twelve self-reported conditions that were treated by a medical doctor, including asthma, myocardial infarction, hypertension, angina pectoris, claudication, lipid disturbance, stroke, rheumatoid arthritis, tuberculosis, cancer, diabetes, multiple sclerosis. A total score was determined by adding one point ('yes') for each condition.

Self-reported depression: (adjusted models only) assessed at baseline by asking '*How often do you feel sad, low-spirited, depressed*?' The four response alternatives were: never, sometimes, often, and always. The last two categories were coded 'depressed'.

Age and Sex: As previous studies suggest that depression has a non-monotonic distribution across age, i.e. higher prevalence among young people and the elderly (Kessler and Bromet, 2013), age was categorized into three groups based on the distribution; < 45, 46–59 and ≥60 years. Sex was considered a confounder due to the gender difference in depression.

2.5. Statistical analyses

For the primary outcome (MDD) we report the number of cases (n, %), and the incidence rate (total sample and separately by each group of exposure). The incidence rate ratio (IRR) of MDD and associated 95% confidence interval (CI) was calculated by Poisson regression adjusted for survival year. Cox proportional hazard regression models assessed associations between physical activity (below, achieving and exceeding the recommended weekly duration) and MDD. Four models were tested: Crude, Model A (adjusted for sex and age); Model B (further adjusted for occupation and smoking), and Model C (further adjusted for BMI and comorbidities). Hazard ratios (95% CIs) and *p*-values are reported. Before running the models, we used Schoenfeld residuals to test the assumption of proportional hazards for each covariate adjusting for other covariates in the model. There was no evidence for a violation of the assumption. Two sensitivity analyses were then performed. First, as physical activity habits could have changed during the 13-year follow-up (thus violating an assumption of the Cox proportional hazard model), we performed additional analyses with MDD outcomes registered within 6 years. Second, we also performed analyses adjusting for baseline depression using the entire sample (n = 27,258). In the fully adjusted models, potential moderating effects of age and gender were also explored by entering interaction terms into each model. All analyses were performed using STATA v.14.

3. Results

3.1. Participant characteristics

From the primary analytic sample (25,520 participants), 65% were female (mean age = 49.3 years, SD = 15.9), 30% had a tertiary education and 61% were employed. Thirty-nine percent were overweight or obese and 39% indicated having ever smoked cigarettes (≥ six months). Seventy-six percent of participants engaged in ≥150 min of MVPA per week (achieve). Of these, 38% exceeded the recommended weekly level (≥300 min).

Table 1 presents characteristics of participants stratified by physical activity status. Compared to the group that exercised below the recommended level, those who achieved ≥150 min of MVPA per week included more women and elderly adults. They also were more highly educated and likely to be retired. The 'achieve' group was less overweight/obese (40.1% compared to 48.2% in the 'below' group) and were less often smokers (7.8% compared to 12.3%). Compared to the 'achieve' group, those who exercised ≥300 min per week included more men and younger adults with higher levels of education. This group was less overweight/obese (33.3% compared to 40.1% in the 'achieve' group), but smoked as much as the 'achieve' group.

Table 1
Participant characteristics by physical activity level.

Characteristic (n = 25,520)	Physical activity level		
	Below	Achieve	Exceed
Total	(n = 6016)	(n = 9747)	(n = 9757)
Female*; n (%)	3725 (61.9)	6655 (68.3)	6146 (63.0)
Age group*; n (%)			
< 45	2189 (36.4)	3461 (35.5)	3965 (40.6)
45–59	2285 (38.0)	3385 (34.7)	2896 (29.7)
≥60	1542 (25.6)	2901 (29.8)	2896 (29.7)
Educational level*; n (%)			
Compulsory (≤9 year)	2929 (49.1)	4556 (47.1)	4334 (44.8)
Upper-secondary (10–12 years)	1298 (21.8)	1956 (20.2)	2437 (25.2)
Vocational and other	50 (0.8)	81 (0.8)	87 (0.9)
Tertiary	1688 (28.3)	3077 (31.8)	2815 (29.1)
Occupation*; n (%)			
Full-time	2872 (56.7)	4237 (51.6)	3879 (46.8)
Part-time	541 (10.7)	919 (11.2)	754 (9.1)
Unemployed	176 (3.5)	240 (2.9)	249 (3.0)
Retired	1073 (21.2)	2187 (26.6)	2324 (28.1)
Other	402 (7.9)	628 (7.7)	1078 (13.0)
BMI**; mean (SD), median	25.3 (4.0), 24.8	24.6 (3.4), 24.2	24.0 (3.1), 23.6
BMI group*; n (%)			
Normal weight (< 25)	2994 (51.9)	5651 (59.9)	6390 (67.4)
Overweight	2104 (36.5)	3133 (33.2)	2661 (28.1)
Obese (≥30)	673 (11.7)	657 (7.0)	430 (4.5)
Comorbidities**; mean (SD), median	0.46 (0.85), 0	0.43 (0.79), 0	0.37 (0.73), 0
Smokers*; n (%)	2470 (41.5)	3665 (38.0)	3594 (37.3)

Below: < 150 min/week; achieve: 150- < 300 min/week; exceed: ≥300 min/week; *Significant by Chi-squared test (*p*-value < 0.05), **Significant by Kruskal-Wallis test (*p*-value < 0.05). Data collected in September 1997 from approximately 3600 Swedish cities and villages.

3.2. Incidence of MDD

During the 13-year follow-up, 382 cases of MDD occurred which accounted for 1.5% of the total sample. The incidence rate was 114 cases per 100,000 person-years (95% CI = 102.8–125.6). The occurrence rate of MDD was 1.7 times higher among women than men (IRR 0.6, 95% CI = 0.5–0.8). Increasing the duration of MVPA was associated with a downward trend in the risk of MDD. The incidence rate of MDD was 133.9 cases per 100,000 person-years (95% CI = 110.7–162.0) in the 'below' group, 114.0 cases per 100,000 person-years (95% CI = 96.7–133.7) in 'achieve' group, and 101.1 cases per 100,000 person-years in the 'exceed' group (95% CI = 85.1–120.0). Compared to those who did not achieve 150 min of MVPA per week, those who achieved and exceeded these levels had lower risks of MDD (IRR = 0.8, 95% CI = 0.7–1.1, and 0.8, 95% CI = 0.6–1.0, respectively). The incidence rate and IRR for each group of exposure and characteristics can be found in Supplement 1.

3.3. Associations between physical activity levels and incident MDD

Results from Cox proportional hazard regression models are shown in Table 2. We observed a dose-response effect of physical activity on MDD. There was a significantly reduced risk of MDD among those who exceeded the recommended level for MVPA (≥300 min/week) compared to those below 150 min per week. Specifically, engaging in ≥300 min of MVPA per week reduce the risk of depression by 25%

Table 2
Associations between physical activity and incident MDD (depressed cases removed).

	HR	95% CI
Crude model (n = 25,520, cases = 382)		
Below (< 150 min)	1	–
Achieve (150–299 min)	0.85	0.66–1.09
Exceed (≥300 min)	0.75	0.58–0.97
Model A (n = 25,520, cases = 382)		
Below (< 150 min)	1	–
Achieve (150–299 min)	0.83	0.65–1.07
Exceed (≥300 min)	0.75	0.58–0.97
Model B (n = 21,297, cases = 303)		
Below (< 150 min)	1	–
Achieve (150–299 min)	0.85	0.64–1.13
Exceed (≥300 min)	0.69	0.52–0.93
Model C (n = 20,594, cases = 289)		
Below (< 150 min)	1	–
Achieve (150–299 min)	0.86	0.64–1.14
Exceed (≥300 min)	0.71	0.53–0.96

Model A adjusted for sex and age; Model B further adjusted for occupation and smoking; Model C further adjusted for BMI and comorbidities. Data collected in September 1997 from approximately 3600 Swedish cities and villages.

compared to engaging in < 150 min per week (HR 0.75, 95% CI = 0.58–0.97). The trend was observed in all crude and adjusted models, and the hazard ratios did not differ significantly between the models. Age and gender interaction terms entered into the fully adjusted model were not statistically significant (data not shown).

3.4. Sensitivity analyses

Results from the Cox regression using the total cohort (n = 27,258 participants) and adjusting for baseline depression are presented in Table 3. During the 13-year follow-up, 706 MDD cases occurred (1.7%). The associations between physical activity and MDD were all statistically significant for the 'exceed' group only. The number of participants shown in the four models is higher than in Table 2, as these analyses include individuals with indications of baseline depression.

To assess a potential misclassification effect of time, data were also analysed with MDD assessed up to six years after the baseline assessment. In total, 159 people (0.9%) developed MDD during this period. Here also, the direction of the associations favoured higher levels of physical activity, however, only one model (B; adjusted sex, age, occupation and smoking) was statistically significant (see Supplement 2).

Table 3
Associations between physical activity and incident MDD, adjusting for baseline depression severity.

	HR	95% CI
Crude model (n = 27,258, cases = 498)		
Below (< 150 min)	1	–
Achieve (150–299 min)	0.86	0.69–1.07
Exceed (≥300 min)	0.75	0.60–0.94
Model A (n = 27,258, cases = 498)		
Below (< 150 min)	1	–
Achieve (150–299 min)	0.85	0.69–1.06
Exceed (≥300 min)	0.74	0.60–0.93
Model B (n = 22,667, cases = 382)		
Below (< 150 min)	1	–
Achieve (150–299 min)	0.91	0.71–1.17
Exceed (≥300 min)	0.71	0.55–0.92
Model C (n = 21,902, cases = 364)		
Below (< 150 min)	1	–
Achieve (150–299 min)	0.89	0.69–1.15
Exceed (≥300 min)	0.71	0.55–0.93

Crude model adjusted for baseline depression; Model A further adjusted for sex and age; Model B further adjusted for occupation and smoking; Model C further adjusted for BMI and comorbidities. Data collected in September 1997 from approximately 3600 Swedish cities and villages.

4. Discussion

This is one of the first studies to examine prospective associations between recommended physical activity levels and incident MDD. Our findings are presented in the context of rising public and research interest in lifestyle interventions to help reduce depression (Hallgren et al., 2016; HealthDay, 2018). Overall, results indicate that regular physical activity reduces the risk of developing MDD. Exceeding the duration recommended for general health (≥300 min per week, or about 40 min per day) was associated with significantly lower hazards of incident MDD compared to durations falling below the recommended level (< 150 min per week). A dose-response was observed where longer durations of habitual physical activity were associated with lower risk of depression. Neither age nor gender appeared to moderate these associations. The results suggest that regular (i.e. daily) moderate physical activity, which includes walking, can significantly reduce the risk of major depression onset in adults.

Of relevance to the interpretation of these findings, all diagnoses were obtained from specialist inpatient and outpatient registers. In Sweden, treatment within psychiatric care often occurs following a period of treatment in primary care, indicating a high degree of symptom severity in the present cohort. Therefore, the findings may not be directly generalizable to populations exhibiting sub-threshold depression where shorter durations of physical activity could have equivalent protective effects.

A similar prospective design was used in a Danish study involving 18,146 adults aged 20–93 years followed from 1976 to 1994 (Mikkelsen et al., 2010). 'High' levels of physical activity compared to 'moderate' and 'low' levels were associated with reduced risk of MDD (ICD codes F32, F33), but only among women. These results are broadly consistent with the current study, although in the Danish study physical activity levels were defined in hours per week rather than minutes, and without reference to recommended levels of activity. In a recent cohort study (HUNT) involving 33,908 Norwegian adults followed over eleven years, researchers examined associations between different durations of exercise (none, up to 30 min, 31–59 min, 1–2 h, 2–4 h, 4+ hours) and the occurrence of self-reported depression (Harvey et al., 2018). Results showed that relatively small amounts of exercise (1 h per week) can provide significant protection against future depression, and this effect was seen equally across all groups, regardless of the intensity of exercise (Harvey et al., 2018). Unlike the HUNT study, we observed a significantly reduced risk of MDD at higher durations of physical activity. One explanation for the disparate results may relate to the outcomes used, where the current study included only cases of MDD diagnosed and treated in specialist care. These cases could be more severe than self-reported cases of depression and require longer average durations of physical activity to 'protect' vulnerable individuals.

As noted, we did not observe a statistically significant association between the recommended minimum weekly duration of physical activity (150 min) and depression. This could partly be explained by the use of self-report instruments which are known to over-estimate activity levels compared to objective assessments (Adams et al., 2005; Prince et al., 2008). In the current study, 76% of participants reported meeting the recommended activity level, which is 10% higher than a national survey of Swedish adults, also based on self-reported physical activity (WHO, 2014). Thus, activity levels may have been overestimated by some participants, possibly due to the perceived social desirability of exercise (Adams et al., 2005), resulting in an inflated proportion who 'exceeded' the recommended levels (38%). Although normative data on the proportion of adults who exceed the recommended PA levels is not currently available in Sweden, studies that do not include walking in the definition of MVPA may report lower activity durations. Placing our findings in broader context, a recent worldwide study of PA involving

1.9 million adults from 168 countries found that 63% of those from high-income countries were sufficiently active (self-reported), and the highest prevalence was among Finnish adults (83%) (Guthold et al., 2018).

Although not our primary focus, it is relevant to briefly consider plausible mechanisms that could explain these relationships. This question is of theoretical importance to determine whether physical inactivity plays a role in the aetiology of depression. A combination of biochemical and psychosocial factors are likely responsible, including mechanisms through which exercise increases neurogenesis and reduces inflammatory and oxidant markers (Schuch et al., 2016) and activates the endocannabinoid system (Brellenthn et al., 2017). People with depression have reduced hippocampal volumes, fewer markers of neurogenesis (e.g. brain derived neurotophic factor (BDNF)), and increased levels of inflammatory (e.g., interleukin-6) and oxidant markers (Kohler et al., 2017; Lindqvist et al., 2017). Physical activity may regulate these abnormalities, increasing hippocampal volume (Erickson et al., 2014) and neurogenesis levels (Kerling et al., 2017), while adjusting the imbalance between anti- and pro-inflammatory and oxidant markers (Toups et al., 2014). An improved level of fitness also leads to both subjective and objective improvements in physical health status (Cairney et al., 2009). Some studies suggest that higher 'doses' of physical activity may be needed to elicit these biological mechanisms (Chaouloff, 1997; Dishman, 1997), although the optimal duration and intensity of physical activity remains unclear. Regular exercise may also act as a distraction from daily worries and promote self-esteem or perceptions of physical competence.

Our study has notable strengths; baseline surveys were linked to national specialist inpatient and outpatient registers and clinician diagnoses of depression, which reduces the risk of misclassifying the study outcome. The positive predictive value for diagnoses in the Swedish medical registers is very high (85–95%) (Ludvigsson et al., 2011). The cohort was large and the follow-up period (13 years) long enough to observe a sufficient number of incident cases, enabling relevant associations to be explored with adequate statistical power. Several limitations are also acknowledged. As noted, the exposure was self-reported which may have overestimated activity levels generally; an observation also made in studies of healthy populations, and among those with serious mental illness (Suetani et al., 2016; Suetani et al., 2017). However, as the outcome could not be predicted at baseline, overestimation of physical activity was likely to be equally distributed between cases and non-cases. Non-differential misclassification of the exposure could dilute the reported associations. Despite this possibility, a favourable dose-response was still observed. An assumption of the regression model concerns proportionality of the hazard rates and it remains possible that activity levels changed during the follow-up period, which would lead to misclassification over time. However, sensitivity analyses based on outcomes registered after six years indicated a similar, though non-significant trend. The cohort displayed some characteristics which may not reflect the general Swedish adult population. For example, participants smoked less, but were more overweight than adults surveyed in national health surveys (Lagerros et al., 2017). Finally, the study could underestimate the true incidence of MDD in the Swedish adult population because the outcome was retrieved from specialist medical registers only. Cases of depression diagnosed by physicians in primary healthcare were not included.

In conclusion, regular moderate-to-vigorous physical activity can help prevent major depression onset in adults. Achieving the recommended duration of 150 min per week could have beneficial somatic effects, but exceeding this level with at least 300 min per week, including walking, significantly reduces the risk of being diagnosed with major depression. Future prospective studies should replicate these findings focusing on patients diagnosed with sub-threshold depression in primary healthcare settings.

Conflict of interest

Authors declare no conflict of interest regarding to either this project or this article.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ypmed.2018.10.009.

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