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Cross-sectional and prospective relationships of passive and mentally-active sedentary behaviours and physical activity with depression

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ABSTRACT

Background: Sedentary behaviour (time spent sitting, as distinct from lack of physical activity) can be associated with poor mental health, but it remains unclear whether all types of sedentary behaviour have equivalent detrimental effects. Prospective studies utilizing clinician-diagnoses of depression can reduce such misclassification bias, but are scarce. The primary aim was to model the potential impact on depression of replacing passive (e.g., TV-viewing) with mentally-active sedentary behaviours (e.g., desk-based office work), and with light and moderate-to-vigorous physical activity. An additional aim was to explore these relationships using both self-report data and clinician-diagnoses of depression.

Method: In 1997, 43,863 Swedish adults were initially surveyed and their responses linked to patient registers until 2010. The isotemporal substitution method was used to model the potential impact on depression of replacing 30-minutes of passive sedentary behaviour with equivalent durations of mentally-active sedentary behaviour, light physical activity, or moderate-to-vigorous physical activity. The outcomes were self-reported frequent symptoms of depression (cross-sectional analyses) and clinician-diagnosed incident major depressive disorder (MDD; prospective analyses).

Results: Of 24,060 participants with complete data (mean age=49.2 years, SD=15.8, 66% female), 1,526 (6.3%) reported having frequent symptoms of depression at baseline. There were 416 (1.7%) incident cases of MDD during the 13-year follow-up. Modelled cross-sectionally, replacing 30-minutes/day of passive sedentary behaviour with 30-minutes/day of mentally-active sedentary behaviour, light physical activity, and moderate-to-vigorous activity reduced the odds of having frequent symptoms of depression by 5% (OR=0.95, 95% CI=0.94-0.97), 13% (OR=0.87, 95% CI=0.76-1.00) and 19% (OR=0.81, 95% CI=0.93-0.90), respectively. Modelled prospectively, substituting 30-minutes/day of passive with 30-minutes/day of mentally-active sedentary behaviour reduced the risk of MDD by 5% (HR=0.95, 95% CI=0.91-0.99); no other prospective associations were statistically significant.

Conclusions: Substituting passive with more mentally-active sedentary behaviours, light activity or moderate-to-vigorous activity may reduce the risk of depression in adults.

Declaration of interest: None.

Keywords: Sedentary behaviour, physical activity, depression, isotemporal substitution modelling.

Relevance statement (93/100 words):

Practicing psychiatrists require updated information concerning factors that may be considered when dealing with patients suffering from depression. Large amounts of time spent sitting and physical inactivity are attributes of depression. Our new findings highlight potentially clinically-relevant relationships of passive and mentally-active sitting time and physical activity with depression. Specifically, they suggest that treatment outcomes for depression may be enhanced by encouraging patients to replace periods of time spent in passive sedentary behaviours (such as TV-viewing) with mentally-active sedentary behaviours (e.g., reading) and preferably with physical activity of a light or moderate intensity.

1. INTRODUCTION

Low levels of physical activity are consistently associated with an elevated risk of depression,[1] while structured forms of physical activity and exercise programs can be effective in the treatment of mood disorders.[2] When adults are not being physically active, they can spend a great deal of their time in sedentary behaviours (sitting). Those with depression spend significantly more time sitting than do their non-depressed counterparts.[3] Conceptually and practically, sitting time may be considered to be distinct from being physically inactive (i.e., engaging in less than 150 minutes of moderate-intensity physical activity per week), with the term sedentary behaviour referring to any waking activity characterized by an energy expenditure of ≤1.5 metabolic equivalents in a seated or reclining posture.[4] Examples of these ubiquitous daily behaviours include TV-viewing, office work, driving, etc. Extended periods of time spent in sedentary behaviour have been linked to increased risk of diabetes, cardiovascular disease, and premature mortality,[5, 6] and these associations have been observed after controlling for time spent in leisure-time moderate-to-vigorous physical activity.[7] There are also relationships of sedentary behaviour with adverse mental health outcomes. In a meta-analysis, the risk of depression from sedentary behaviour was 31% higher over 13 cross-sectional studies, and 14% higher over 11 prospective studies.[8] Two recent trials demonstrated that experimentally-induced sedentary behaviour can have adverse effects on mood and depression.[9, 10] In one trial, a 32 minute/day increase in sedentary behaviour over two weeks resulted in mood disturbances that were independent of changes in physical activity.[10]

However, it remains unclear whether all types of sedentary behaviour can have equivalent detrimental effects on mental health. Some sedentary behaviours are characterized by cognitive effort (e.g., desk-based office work), whereas others primarily involve more-passive mental activity (e.g., TV-viewing). This distinction has been made previously[11] but not in the context of depressive symptoms or disorders. Given the nature of depression, which is

associated with cognitive deficits, behavioural inactivation, and higher than average durations of physical inactivity,[12] it is plausible that some sedentary behaviours – particularly those that are passive – may increase the risk of depression more than others. In a 2-year prospective study examining associations of TV-viewing, internet use and reading with mental health, TV-viewing time at baseline (≥ 6 vs. <2 h) was associated with more depressive symptoms and worse global cognitive functioning, while internet use and reading were associated with less depressive symptoms.[13] Using the same data reported here, we previously examined longitudinal relationships of passive and mentally-active sedentary behaviours with incident major depressive disorder in 37,504 adults.[14] After adjustment for relevant co-variates including physical activity, engaging in mentally-active sedentary behaviours for ≥3 hours/day (compared to < 3 hours/day) was associated with significantly reduced hazards of developing a depressive illness over 13-years. Conversely, a non-significant inverse (i.e., detrimental) association was found for time spent in passive sedentary behaviours, suggesting possible differential effects on depression. Although our previous findings on associations of sedentary behaviours with depression are informative, they do not identify specifically the benefits that might arise if other activities are substituted. While several studies have independently shown the harms associated with too much sitting.[5, 6] in the context of depression, none have examined the effects of replacing passive with mentally-active sedentary behaviours. Revealing the intricacy of these relationships could have public health and clinical relevance.

Additional prospective studies utilizing clinician-diagnoses of depression are needed to reduce the misclassification bias that arises when depression is self-rated. Equally, however, self-report questionnaires are relevant as they may capture sub-threshold symptoms which are perceived as distressing and could precede the onset of major depression. Thus, comparing self-reported symptoms of depression with clinician-diagnoses may provide a more complete

and clinically-relevant picture of these relationships. Our aim was to model the potential impact on depression of substituting short (30 minute) durations of passive sedentary behaviour with equivalent durations of mentally-active sedentary behaviour; light physical activity, and moderate-to-vigorous activity. The primary outcomes were self-reported frequent symptoms of depression (cross-sectional analyses) and clinician-diagnosed incident major depressive disorder (MDD; prospective analyses). Associations were examined using both cross-sectional and longitudinal data.

2. METHOD

2.1 Participants

Data originate from the Swedish National March Cohort (http://ki.se/en/meb/the-swedish-national-march-cohort-nmc),[15] a four-day national fundraising event arranged by the Swedish Cancer Society in some 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 findings for the activity questionnaire has been published previously, and the survey has been used extensively.[16] Exclusion criteria included: participants who were younger than 18 years at the beginning of the follow-up (n=1,741), those who emigrated (n=465) or died (n=8), or that had a primary diagnosis of any mental disorder (ICD-8: 290-315; ICD-9 290-319; ICD-10; F00-F99) (n=1,089) before the beginning of the follow-up. After removing these cases, the sample eligible for follow-up was 40,569 participants. For the current analyses, only complete cases were included, where participants provided data for all exposures and co-variates (n=24,060). In prospective analyses, to examine only incident cases, we further excluded 1,526 participants based on the presence of self-reported frequent symptoms of depression at baseline (n=22,534). The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant

national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. All procedures involving human subjects/patients were approved by The Research Ethics Vetting Board in Stockholm. Verbal informed consent was obtained from all participants (witnessed and formally recorded).

2.2 Study outcomes: Self-reported frequent symptoms of depression and clinician-diagnosed major depressive disorder (MDD).

Depression was assessed in two ways: in cross-sectional analyses, baseline depression was assessed using the self-rated question, *"How often do you feel sad, low-spirited, depressed?'* where the last two response alternatives (never, sometimes, *often, always*) were categorized as having frequent symptoms of depression (for brevity, also referred to as 'symptoms of depression'). For prospective analyses, 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. All 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. Currently, there is no nationwide primary healthcare register in Sweden.

2.3 Exposures: sedentary behaviours and physical activity

Four categories were assessed: (1) passive sedentary behaviours, (2) mentally-active sedentary behaviours, (3) light physical activity, and (4) moderate-to-vigorous physical activity. The last two activity categories were obtained from separate questions within the baseline questionnaire, as described below. For prospective analyses, total activity was calculated by summing time spent in these four activities, as described below. To facilitate

interpretation of the results, and in line with previous studies,[10, 17] we examined the associations with depression of replacing 30-minutes of passive sedentary behaviour with equivalent durations of mentally-active sedentary behaviour, light physical activity, and moderate-to-vigorous physical activity (defined below). This duration (30 minutes) was also chosen for practical reasons; longer duration changes in activity could have stronger effects, but may not be feasible for most people.

Two questions assessed participation in passive and mentally-active sedentary behaviours. Both were prefaced with the following: *How physically active are you on an ordinary weekday? Specifically, how much time per day/night do you devote to activities that require effort similar to: (a) Watching TV, listening to music, sitting in the bathtub?* (passive sedentary behaviours); and *(b) Office work, sitting in a meeting, knitting/sewing?* (mentally-active sedentary behaviours). Each activity category was illustrated with a relevant visual image. For each question, eight response alternatives were provided to estimate the amount of time typically spent in each activity (in minutes): 0-4, 5-9, 10-19, 20-39, 40-89, 90-179, 180-359, and 360-720. The mid-point of each response was calculated and added to determine a continuous sedentary behaviour score for each activity.

The average weekly duration of moderate-to-vigorous 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; each rated separately. The question implied that these activities were undertaken in a purposeful or structured manner; thus, walking was included in the definition of moderate-to-vigorous physical activity, as previously recommended.[18] For each question, there were six response alternatives: 0, 0-1, 2, 3, 4, and ≥5 hours 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 minutes, respectively. After adding the total number of moderate-to-vigorous physical activity minutes, participants were categorized as 'below' (0-149 minutes), 'achieving' (150-299 minutes) or 'exceeding' (≥300 minutes) the World Health Organization (WHO) recommended durations. The last category is recommended for attaining additional health benefits from physical activity,[18] but has rarely been assessed in previous studies. The method used to calculate moderate-to-vigorous physical activity is comparable to recent studies using METs-minutes.[19] Both the physical activity and the sedentary behaviour questions have been validated and used extensively in previous studies.[16, 20, 21]

2.4 Covariates

Based on previous evidence of association with sedentary behaviour and/or depression,[8] the following variables were included in the statistical models:

Body mass index (BMI): was calculated from self-reported weight and height (kg/m^2) then categorised according to the WHO's BMI classification for adults; not overweight (<25), overweight (25-<30), and obese (≥30). Due to the small number of observation for underweight (1.3%), this group was collapsed with the first category.

Education: was assessed by a question about the kind of education/school attended, Participants were grouped into 4 categorises: Compulsory school (year 9); Upper-secondary (years 10-12), Tertiary; Vocational and other.

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

Comorbidities: were assessed based on whether or not the following twelve self-reported conditions had been treated by a medical doctor; asthma, heart attack, high blood pressure, angina pectoris, angina pectoris in legs (claudication), lipid disturbance, stroke, rheumatoid

arthritis, tuberculosis (TB), cancer, diabetes, multiple sclerosis. A total score was determined by adding each condition.

Age and Sex: Age was categorized into three groups based on the distribution of data; <45, 45-59 and ≥60 years. Sex was considered a confounder due to the reported gender differences in depression.

2.5 Statistical analyses

Baseline characteristics were calculated using descriptive statistics (mean, median, SD). Isotemporal substitution modelling (ISM)[22] has been used previously to estimate the effects of replacing different durations of physical activity on body weight and the risk of chronic disease.[22-24] Compared with conventional regression modelling, ISM can provide a more accurate estimation of the potential effects of different activities. Within total waking hours, time spent in one type of activity usually occurs at the expense of time engaged in related activities; ISM uniquely enables examination of the potential impact on depression of substituting one type of activity with another. Given these advantages, ISM was used to assess the associations with depression of replacing 30-minutes of passive sedentary behaviour with 30-minutes of (a) mentally-active sedentary behaviour, (b) light physical activity, and (c) moderate-to-vigorous physical activity. Associations were examined cross-sectionally using self-reported frequent symptoms of depression at baseline, and longitudinally using clinician-diagnosed major depressive disorder (MDD) as outcome. For cross-sectional analyses, logistic regression was used to calculate odds ratios (ORs), 95% confidence intervals (CIs) and p-values. For longitudinal analyses, Cox proportional hazards regression analyses were used to calculate hazard ratios (HRs) and associated CIs. Survival time was censored at the date of death from all causes or at the end of the follow-up for those who did not have MDD. For both sets of analyses, three models are reported; single, partition, and substitution models. The three models are briefly explained below using logistic regression as an example. The

same principles were applied for Cox regression models. For brevity, we use PA for physical activity and SB for sedentary behaviour in these equations.

Single models assessed the association of each type of activity with depression (as defined previously), adjusting for confounders: $Log\ (odds\ depression) = B_0 + B_1*Passive\ SB + B_2*Covariates.$

Partition models assessed the association between each type of activity and depression adjusting for confounders, while keeping other activities constant: $Log\ (odds\ depression) = B_0 + B_1*Passive\ SB + B_2*Mentally\text{-}active\ SB + B_3*Light\ PA + B_4*\ Moderate\text{-}to\text{-}vigorous\ PA + B_6*Covariates.$ As total activity is not controlled in the partition model, the beta-coefficient of each activity represents the additive effect of these activities on depression, not the substitutive effects.

Substitution models assessed the effect of replacing 30-minutes of passive sedentary behaviour with 30-minutes of mentally-active sedentary behaviour, light physical activity, and moderate-to-vigorous physical activity: $Log\ (odds\ depression) = B_0 + B_2*Mentally\ active\ SB + B_3*Light\ PA + B_4*\ Moderate\text{-}to\text{-}vigorous\ PA + B_5*Total\ activity + B_6*Covariates.$ In the substitution models, passive sedentary behaviour is dropped, but total activity (that is, all sedentary behaviour and physical activity) is retained. Because total activity is held constant, a 30 minute increase in mentally-active sedentary behaviour results in an equivalent decrease in activities not included in the model (i.e. passive sedentary behaviours), Thus, the beta coefficients B_2, B_3, and B_4 can be interpreted as the effect on depression of replacing 30-minutes of passive sedentary behaviour with the equivalent duration of mentally-active sedentary behaviour, light physical activity, and moderate-to-vigorous physical activity, respectively. Before running the prospective models (Cox regression), 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.

3. RESULTS

3.1 Participant characteristics

Participant characteristics are shown in Table 1. Sixty-six percent were female (mean age = 49.2 years; SD = 15.8) and 30% had a tertiary education. Thirty-nine percent of participants were overweight or obese; 39% reported having ever smoked cigarettes (≥ 6 months) and 30% had ≥1 co-morbidity. Participants reported approximately 5.5 hours/day in total sedentary behaviours, and 37 minutes/day in light physical activity and moderate-to-vigorous activity combined. Of the total sample, 6.3% reported having frequent symptoms of depression at baseline, and 1.7% was diagnosed with MDD over the 13-year follow-up. Among the 22,534 participants who did not report symptoms of depression at baseline, 320 (1.4%) developed MDD during the course of follow-up. There was a significant inverse association between the passive and mentally-active sedentary behaviours (Spearman's *rho* = -0.071, $p<0.01$). There were some differences between the analytic and excluded sample (i.e. those with missing data on covariates). Specifically, the excluded sample included more participants that were: male, elderly, obese, smoked, had ≥ 1 co-morbidity, less formal education, and spent more time in passive sedentary behaviours. A detailed comparison is available in Supplementary Table 1.

Insert Table 1 here

3.2 Cross-sectional associations with self-reported frequent symptoms of depression

Table 2 shows associations between self-reported symptoms of depression, with sedentary behaviours, light physical activity and moderate-to-vigorous physical activity. The single models indicate the association between each type of activity and symptoms of depression adjusting for confounders (listed above). Passive sedentary behaviours significantly increased the odds of reporting depressive symptoms. A 30-minute increase in light physical activity

and moderate-to-vigorous activity reduced the odds of having symptoms of depression by 23% (OR=0.87, 95% CI=0.77-0.99), and 28% (OR=0.82, 95% CI=0.74-0.91), respectively. In the partition model, a 30-minute increase in passive sedentary behaviour increased the odds of depressive symptoms by 6% (OR=1.06, 95% CI=1.04-1.07); conversely, and a 30-minute increase in mentally-active sedentary behaviour reduced the odds of depressive symptoms by 14% (OR=0.86, 95% CI=0.77-0.95). In the substitution model, replacing 30 minutes of passive sedentary behaviour with 30 minutes of mentally-active sedentary behaviour, light physical activity, and moderate-to-vigorous activity significantly reduced the odds of depressive symptoms by 5% (OR=0.95, 95% CI=0.94-0.97), 13% (OR=0.87, 95% CI=0.76-1.00), and 19% (OR=0.81, 95% CI=0.93-0.90) respectively. Thus, there was a dose-response relationship where substituting passive sedentary behaviours with higher-intensity activities had a greater benefit on depressive symptoms.

3.3 Prospective associations with clinician-diagnosed MDD

In prospective analyses (Table 3) using substitution models, replacing 30-minutes of passive sedentary behaviour with 30 minutes of mentally-active sedentary behaviour reduced the risk of clinician-diagnosed MDD by 5% (HR=0.95, 95% CI=0.91-0.99). No other prospective associations were statistically significant.

Insert Tables 2 and 3 here

4. DISCUSSION

In the context of emerging research demonstrating links between sedentary behaviour and mood disorders,[25-27] this is the first study to examine the potential impact on depression of replacing passive with mentally-active sedentary behaviours. In both cross-sectional and prospective analyses, substituting 30-minutes of passive sedentary behaviour with 30-minutes

of mentally-active sedentary behaviour reduced the odds of depressive symptoms and clinician-diagnosed MDD by 5%, respectively. Cross-sectionally, compared to replacement with mentally active sedentary behaviours (5%), larger magnitude effects on depressive symptoms were observed when replacing passive sedentary behaviours with light physical activity (23% lower odds), and moderate-to-vigorous activity (28% lower odds). Consistent with our previous work,[14] these findings suggest that passive sedentary behaviours may heighten the risk of depression in adults. The current study adds the observation that substituting common passive sedentary behaviours with mentally-active sedentary behaviours, or (preferably) with light physical activity or moderate-to-vigorous activity, may reduce depressive symptoms in adults.

Previous longitudinal studies have consistently shown beneficial relationships of moderate-to-vigorous physical activity with lower risk of depression.[1] Unlike the cross-sectional results, no significant associations were found with moderate-to-vigorous activity in the prospective substitution models. Differences between the cross-sectional and prospective models may be attributable to several factors, including the relatively low incidence rate of MDD in the current study. Diagnoses were obtained from specialist inpatient and outpatient healthcare registers, not from primary care, where some individuals with mildly severe depression (yet still meeting the criteria for MDD) could initially seek treatment. Thus, the incidence rate of MDD may have been underestimated slightly, making it less likely to observe an association where one may exist. An alternative interpretation could be that the beneficial substitution effects seen here do not occur at higher 'thresholds' of depression; in this case MDD diagnosed by a specialist clinician. Despite these inconsistencies, the cross-sectional self-report data offers a relevant perspective by taking into account self-rated symptoms of depression, which are prevalent in the general population and frequently precede the onset of major depression.[28] Thus, the cross-sectional findings could be particularly relevant from a

prevention perspective. Although the associations of replacing passive sedentary behaviours with moderate-to-vigorous physical activity were not statistically significant in longitudinal analyses, the direction of these relationships was as predicted (i.e. beneficial). Moreover, there is evidence from previous prospective studies and controlled trials indicating the benefits of moderate-intensity physical activity on both depression and somatic health generally.[2, 29] Taken together, and seen in the context of existing research, these findings suggest potential mental health benefits of replacing passive sedentary behaviours with moderate-to-vigorous physical activity.

Our findings are consistent with recent studies demonstrating beneficial associations of light physical activity and lower levels of sedentary behaviour with depression.[8, 30] Two previous studies have used ISM to explore relationships of sedentary behaviour with depression. In a recent cross-sectional study involving 276 older adults, and using objective measures of activity, Yasunaga et al. (2018) found that replacing 30-minutes/day of sedentary behaviour with 30-minutes/day of light physical activity was negatively associated with self-rated depression (β= -0.131, 95%CI -0.260 to -0.002)[17]. Mekary et al. (2013) prospectively examined the associations of different activities with various activity displacements and depression risk among 32,900 US women over ten years[27]. An isotemporal substitution gradient was found for TV-viewing, such that replacing 60-minutes/day of this activity with 60-minutes/day of brisk walking was associated with lower depression risk. However, a similar 'protective' association was not seen when TV-viewing was replaced with slow walking, which could indicate that a minimum physical activity 'dose' is required to elicit these effects.[27] In the current study, similar beneficial associations with self-reported symptoms of depression were seen for replacing passive sedentary behaviours with walking.

There are several plausible explanations for the differential effects of passive and mentally-active sedentary behaviours on depression. One explanation relates to the context of these activities. Office work and 'sitting in a meeting' (both assessed here) usually occur in work environments. Employment is linked to better mental health, even when it involves sedentary behaviour, as it can promote a sense of autonomy, belonging, and achievement. Work can also foster supportive social relationships. Thus, the negative mood states associated with passive sedentary behaviours could potentially heighten the risk of depression more than mentally-active sedentary behaviours, despite equivalent energy expenditure. We also speculate that substituting passive with mentally-active sedentary behaviours might reduce negative rumination which, in turn, may counteract the vicious cycle of maladaptive cognitions often seen in depressed individuals. Other physiological mechanisms could also underlie these relationships; sedentary behaviours impact adversely on glycemic control, and evidence suggests that glycemic variability may influence brain health and cognition.[31] However, it remains to be seen whether or not this variability is linked to different types of sedentary behaviour.

Substituting passive sedentary behaviour with light or moderate physical activity could reduce depression through several related mechanisms. Physical activity has been shown to upregulate monoamine neurotransmission in the animal brain; changes which may be linked to mood disorders in humans.[32] Exercise also appears to regulate the hypothalamo-pituitary-adrenal (HPA) axis, leading to reductions in glucocorticoid stress hormones.[33] Research supports the role of inflammation, oxidative and nitrogen stress, and neurotrophins as key mediators in the pathogenesis of mood disorders.[34] Some studies suggest that higher doses of physical activity are needed to elicit these biological mechanisms. However, in a recent 12-week community-based randomized controlled trial of exercise for mild-to-moderate depression in adults, we observed equivalent magnitude effects of light, moderate, and

vigorous exercise on self-rated depression severity.[35] The largest absolute improvement in depressive symptoms was seen in the light exercise group,[36] suggesting that low-intensity exercise can also have beneficial effects on depressive symptoms. Psychosocial factors are also relevant; exercise can act as a distraction from stressful life events, improve self-esteem, and may reduce negative attentional biases.

Our distinction between passive and mentally-active sedentary behaviours is relatively new, though its importance has been recognized in at least one previous study.[11] Kikuchi *et al.* (2014) examined cross-sectional relationships of passive (TV-time, listening or talking while sitting, and sitting around) and mentally-active (computer-use and reading books or newspapers) leisure-time activities in older Japanese adults. Higher passive sedentary time was associated with greater odds of being overweight and engaging in lower levels of physical activity. Conversely, higher mentally-active sedentary time was associated with lower odds of low physical activity.[11] Psychological outcomes were also examined. Higher passive sedentary time increased the odds of psychological distress (Kessler K6 scale), but not after adjustment for MVPA. Other categories of sedentary behaviour have been explored. A meta-analysis examined possible differential effects of TV-viewing and Computer or internet use on depression. Both outcomes were associated with a similar increased risk of depression. Unlike these previous investigations, the current study did not assess computer or mobile phone use which - although certainly relevant - could involve both passive and mentally-active behaviours.

This study has notable strengths. The analyses are based on a large participant sample, and the comprehensive baseline survey enabled relevant covariates to be included in the fully-adjusted models. The physical activity questionnaire has been validated in previous studies,[16, 20] and importantly, included separate items assessing passive and mentally-active sedentary

behaviours. The analytic approach (ISM) might also be considered an advantage, as it enables substitution effects to be examined. Some potential limitations are also acknowledged. The exposure was self-reported which may overestimate physical activity levels generally. One of the study outcomes (frequent symptoms of depression) was self-rated, based on a single item that has not been validated for this purpose, and cannot be regarded as equivalent to a clinician diagnosis of major depression. The cohort displayed some characteristics which may not reflect the general Swedish adult population; for example, participants were more overweight than adults surveyed in national health surveys.[37] Our reliance on clinician diagnoses of depression is a potential strength as it reduces misclassification bias, but as noted, the true incidence of MDD may have been underestimated slightly in prospective analyses. However, the specialist registers are widely used in Sweden for longitudinal research, including studies within psychiatry. To address the issue of reverse-causality, those with indications of frequent depressive symptoms at baseline were removed from the prospective analyses. Mental ill-health exists on a continuum and major depression is an episodic disorder; thus, our analytic approach could limit the generalizability of our findings to some degree. Finally, due to the age of the baseline data (1997), some relevant sedentary behaviours were not assessed (e.g. internet and smart phone use).

In sum, these findings suggest that substituting passive with mentally-active sedentary behaviours, light physical activity or moderate-to-vigorous activity may reduce feelings of depression in adults, which in turn could lower the risk of developing major depression. In the context of research showing that depressed adults are more sedentary than age-gender matched controls,[12] and studies indicating detrimental links between sedentary behaviour and depression,[8] these results are also clinically relevant. They reinforce the notion that clinical interventions for adults reporting symptoms of depression may be enhanced by screening physical activity habits and promoting increased activity when levels fall below recommended

guidelines.[38] Such interventions should aim to increase total daily physical activity while also reducing sedentary behaviours, particularly those which are passive.[3, 14] Currently, there is active discussion in the scientific literature regarding the optimal format of physical activity interventions and their structure within psychiatric settings.[39, 40]

There is an opportunity for future research to further elucidate the relationships that we have identified. Detrimental effects of sedentary behaviours on cardiovascular disease and mortality have been established, and emerging evidence of negative mental health consequences points to the need for further research in this context. Epidemiological investigations combining objective measurements of total sedentary time with self-report methods to identify which components are passive and mentally-active would be informative. Intervention trials comparing the effects on depression of reducing passive sedentary behaviours, versus increasing structured exercise would also be informative, as would trials in which physical activity is increased specifically by reducing both types of sedentary behaviour.

Table 1: Characteristics of participants

Characteristic (n=24,060)	n	%*
Female	15,773	65.6
Age; mean (SD), median	49.2 (15.8), 50.5	-
Age group		
18 - 44	9,096	37.8
45 - 64	8,116	33.7
>65	6,848	28.5
Educational level		
Compulsory (9 years)	11,194	46.5
Upper-secondary (10-12 years)	5,442	22.6
Vocational and other	201	0.8
Tertiary	7,223	30.0
BMI (kg/m^2)		
Not overweight (<25)	14,593	60.7
Overweight	7,706	32.0
Obese (≥30)	1,761	7.3
Ever smoked		
No	14,698	61.1
Yes	9,362	38.9
≥1 co-morbidity	7,102	29.5
Passive SB minutes/day; mean (SD), median	133 (85.6), 135	
Mentally active SB minutes/day; mean (SD), median	204 (206.8), 135	
Light PA minutes/day; mean (SD), median	21.9 (12.9) 21.4	
Moderate-to-vigorous PA minutes/day; mean (SD), median	15.0 (16.7), 8.6	
Total PA minutes/day; mean (SD), median	374.2 (217.0), 319.1	
Frequent symptoms of depression at baseline	1,526	6.3
Cumulative incidence MDD	416	1.7

*Total could be over/below 100% due to rounding. SB - sedentary behaviour; PA - physical activity; MDD - major depressive disorder.

Table 2: **Odds ratios (ORs) for self-reported depression when substituting 30 minutes of passive sedentary behaviour (SB) with other types of activity (n= 24,060; cases=1,526)**

Method	Passive SB		Mentally active SB		Light activity		Moderate-to-vigorous PA		Total activity	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Substitution models (A)	-	-	0.95***	0.94-0.97	0.87*	0.76-1.00	0.81***	0.73-0.90	1.06***	1.04-1.07
Partition models (B)	1.06***	1.04-1.07	1.01	1.00-1.01	0.92	0.81-1.05	0.86**	0.77-0.95	-	-
Single models	Model C[3]		Model D[4]		Model E[5]		Model F[6]		Model G[7]	
	1.06***	1.04-1.07	1.01	1.00-1.01	0.87*	0.77-0.99	0.82***	0.74-0.91	1.01***	1.01-1.02

(A) Substituting Passive SB with other activities: [1]Log (odds depression symptom) = B0 + B2*Mentally active SB + B3*Light activity + B4*Moderate-to-vigorous activity + B5*Total activity + B6*Covariates
(B) Additive effect of each activity on depression holding other activities constant:
[2]Log (odds depression symptom) = B0 + B1*Passive SB + B2*Mentally active SB + B3*Light activity + B4*Moderate-to-vigorous activity + B6*Covariates
(C-G): Single effect of each activity on depression
[3]Log (odds depression symptom) = B0 + B1*Passive SB + B6*Covariates
[4]Log (odds depression symptom) = B0 + B2*Mentally active SB + B6*Covariates
[5]Log (odds depression symptom) = B0 + B3*Light activity + B6*Covariates
[6]Log (odds depression symptom) = B0 + B4*Moderate-to-vigorous activity + B6*Covariates
[7]Log (odds depression symptom) = B0 + B5*Total activity + B6*Covariates)

*p<0.05, **p<0.01, ***p<0.001

Table 3: Hazard ratios (HRs) for incident major depressive disorder when substituting 30 minutes of passive sedentary behaviour (SB) with other types of activity (n= 22,534; cases=320)

Method	Passive SB		Mentally active SB		Light activity		Moderate-to-vigorous PA		Total activity	
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
Substitution models (A)	-	-	0.95*	0.91-0.99	1.04	0.79-1.37	0.83	0.66-1.04	1.03	0.99-1.07
Partition models (B)	1.03	0.99-1.07	0.98	0.97-1.00	1.07	0.82-1.40	0.86	0.69-1.08	-	-
Single models	**Model C[3]**		**Model D[4]**		**Model E[5]**		**Model F[6]**		**Model G[7]**	
	1.03	1.00-1.07	0.98	0.97-1.00	1.05	0.81-1.37	0.87	0.70-1.08	0.99	0.97-1.01

(A) Substituting Passive SB with other activities: [1]$h(t) = h_0(t)$ exp (B2*Mentally active SB + B3*Light activity + B4*Moderate-to-vigorous activity + B5*Total activity + B6*Covariates)
(B) Additive effect of each activity on depression holding other activities constant:
[2]$h(t) = h_0(t)$ exp (B1*Passive SB + B2*Mentally active SB + B3*Light activity + B4*Moderate-to-vigorous activity + B6*Covariates)
(C-G): Single effect of each activity on depression
[3]$h(t) = h_0(t)$ exp (B1*Passive SB + B6*Covariates)
[4]$h(t) = h_0(t)$ exp (B2*Mentally active SB + B6*Covariates)
[5]$h(t) = h_0(t)$ exp (B3*Light activity + B6*Covariates)
[6]$h(t) = h_0(t)$ exp (B4*Moderate-to-vigorous activity + B6*Covariates)
[7]$h(t) = h_0(t)$ exp (B5*Total activity + B6*Covariates)
*$p<0.05$

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