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7 **Cross-sectional and prospective relationships of passive and mentally-active sedentary**
8 **behaviours and physical activity with depression**
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13
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30

31 **ABSTRACT**

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

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

47 **Results:** Of 24,060 participants with complete data (mean age=49.2 years, SD=15.8, 66%
48 female), 1,526 (6.3%) reported having frequent symptoms of depression at baseline. There
49 were 416 (1.7%) incident cases of MDD during the 13-year follow-up. Modelled cross-
50 sectionally, replacing 30-minutes/day of passive sedentary behaviour with 30-minutes/day of
51 mentally-active sedentary behaviour, light physical activity, and moderate-to-vigorous
52 activity reduced the odds of having frequent symptoms of depression by 5% (OR=0.95, 95%
53 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),
54 respectively. Modelled prospectively, substituting 30-minutes/day of passive with 30-
55 minutes/day of mentally-active sedentary behaviour reduced the risk of MDD by 5%
56 (HR=0.95, 95% CI=0.91-0.99); no other prospective associations were statistically
57 significant.

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

60 **Declaration of interest:** None.

61 **Keywords:** Sedentary behaviour, physical activity, depression, isotemporal substitution
62 modelling. **Relevance statement** (93/100 words):

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

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90 **1. INTRODUCTION**

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

111
112 However, it remains unclear whether all types of sedentary behaviour can have equivalent
113 detrimental effects on mental health. Some sedentary behaviours are characterized by
114 cognitive effort (e.g., desk-based office work), whereas others primarily involve more-passive
115 mental activity (e.g., TV-viewing). This distinction has been made previously¹¹ but not in the
116 context of depressive symptoms or disorders. Given the nature of depression, which is

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

137
138 Additional prospective studies utilizing clinician-diagnoses of depression are needed to
139 reduce the misclassification bias that arises when depression is self-rated. Equally, however,
140 self-report questionnaires are relevant as they may capture sub-threshold symptoms which are
141 perceived as distressing and could precede the onset of major depression. Thus, comparing
142 self-reported symptoms of depression with clinician-diagnoses may provide a more complete

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

150

151 **2. METHOD**

152 **2.1 Participants**

153 Data originate from the Swedish National March Cohort ([http://ki.se/en/meb/the-swedish-](http://ki.se/en/meb/the-swedish-national-march-cohort-nmc)
154 [national-march-cohort-nmc](http://ki.se/en/meb/the-swedish-national-march-cohort-nmc)),¹⁵ a four-day national fundraising event arranged by the Swedish
155 Cancer Society in some 3600 Swedish cities and villages in September 1997. In total, 43,863
156 participants completed a 36-page survey with detailed questions about health behaviours and
157 lifestyle, including specific questions on physical activity habits (type, frequency and
158 duration). Reliability and validity findings for the activity questionnaire has been published
159 previously, and the survey has been used extensively.¹⁶ Exclusion criteria included:
160 participants who were younger than 18 years at the beginning of the follow-up (n=1,741),
161 those who emigrated (n=465) or died (n=8), or that had a primary diagnosis of any mental
162 disorder (ICD-8: 290-315; ICD-9 290-319; ICD-10; F00-F99) (n=1,089) before the beginning
163 of the follow-up. After removing these cases, the sample eligible for follow-up was 40,569
164 participants. For the current analyses, only complete cases were included, where participants
165 provided data for all exposures and co-variates (n=24,060). In prospective analyses, to
166 examine only incident cases, we further excluded 1,526 participants based on the presence of
167 self-reported frequent symptoms of depression at baseline (n=22,534). The authors assert that
168 all procedures contributing to this work comply with the ethical standards of the relevant

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

173

174 **2.2 Study outcomes: Self-reported frequent symptoms of depression and clinician-** 175 **diagnosed major depressive disorder (MDD).**

176 Depression was assessed in two ways: in cross-sectional analyses, baseline depression was
177 assessed using the self-rated question, “*How often do you feel sad, low-spirited, depressed?*”
178 where the last two response alternatives (never, sometimes, *often, always*) were categorized as
179 having frequent symptoms of depression (for brevity, also referred to as ‘symptoms of
180 depression’). For prospective analyses, the occurrences of incident MDD (ICD codes: F32.0,
181 F32.1, F32.2, F32.8, F32.9, F33.0, F33.1, F33.2, F33.4, F33.8, F33.9) during the 13-year
182 follow-up to 31st December 2010 were ascertained through linkages to existing nationwide,
183 complete and continuously updated specialist medical registers, including inpatient and
184 outpatient records. All diagnoses were made by a specialist clinician, often a psychiatrist or
185 clinical psychologist. Accurate linkages - and thus essentially complete follow-up were
186 attained using the individually unique National Registration Numbers (NRNs), assigned to all
187 Swedish residents as identifiers both in the baseline questionnaire and in all registers.
188 Currently, there is no nationwide primary healthcare register in Sweden.

189 **2.3 Exposures: sedentary behaviours and physical activity**

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

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

201
202 Two questions assessed participation in passive and mentally-active sedentary behaviours.
203 Both were prefaced with the following: *How physically active are you on an ordinary*
204 *weekday? Specifically, how much time per day/night do you devote to activities that require*
205 *effort similar to: (a) Watching TV, listening to music, sitting in the bathtub?* (passive
206 sedentary behaviours); and *(b) Office work, sitting in a meeting, knitting/sewing?* (mentally-
207 active sedentary behaviours). Each activity category was illustrated with a relevant visual
208 image. For each question, eight response alternatives were provided to estimate the amount of
209 time typically spent in each activity (in minutes): 0-4, 5-9, 10-19, 20-39, 40-89, 90-179, 180-
210 359, and 360-720. The mid-point of each response was calculated and added to determine a
211 continuous sedentary behaviour score for each activity.

212
213 The average weekly duration of moderate-to-vigorous physical activity was estimated by
214 asking participants how much time per week they usually spent in ‘exercise, athletics, and
215 sports’, including: (1) walking; (2) strenuous exercise (e.g. jogging, swimming); and (3) hard
216 training/competition; each rated separately. The question implied that these activities were
217 undertaken in a purposeful or structured manner; thus, walking was included in the definition
218 of moderate-to-vigorous physical activity, as previously recommended.¹⁸ For each question,
219 there were six response alternatives: 0, 0-1, 2, 3, 4, and ≥ 5 hours per week. Ratings were
220 made separately for summer and winter and then averaged. Hours per week were converted

221 into minutes: 0, 30, 120, 180, 240, and 300 minutes, respectively. After adding the total
222 number of moderate-to-vigorous physical activity minutes, participants were categorized as
223 'below' (0-149 minutes), 'achieving' (150-299 minutes) or 'exceeding' (≥ 300 minutes) the
224 World Health Organization (WHO) recommended durations. The last category is
225 recommended for attaining additional health benefits from physical activity,¹⁸ but has rarely
226 been assessed in previous studies. The method used to calculate moderate-to-vigorous
227 physical activity is comparable to recent studies using METs-minutes.¹⁹ Both the physical
228 activity and the sedentary behaviour questions have been validated and used extensively in
229 previous studies.^{16, 20, 21}

230

231 **2.4 Covariates**

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

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

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

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

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

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

248 Age and Sex: Age was categorized into three groups based on the distribution of data; <45,
249 45-59 and ≥ 60 years. Sex was considered a confounder due to the reported gender differences
250 in depression.

251

252 **2.5 Statistical analyses**

253 Baseline characteristics were calculated using descriptive statistics (mean, median, SD).
254 Isotemporal substitution modelling (ISM)²² has been used previously to estimate the effects of
255 replacing different durations of physical activity on body weight and the risk of chronic
256 disease.²²⁻²⁴ Compared with conventional regression modelling, ISM can provide a more
257 accurate estimation of the potential effects of different activities. Within total waking hours,
258 time spent in one type of activity usually occurs at the expense of time engaged in related
259 activities; ISM uniquely enables examination of the potential impact on depression of
260 substituting one type of activity with another. Given these advantages, ISM was used to assess
261 the associations with depression of replacing 30-minutes of passive sedentary behaviour with
262 30-minutes of (a) mentally-active sedentary behaviour, (b) light physical activity, and (c)
263 moderate-to-vigorous physical activity. Associations were examined cross-sectionally using
264 self-reported frequent symptoms of depression at baseline, and longitudinally using clinician-
265 diagnosed major depressive disorder (MDD) as outcome. For cross-sectional analyses,
266 logistic regression was used to calculate odds ratios (ORs), 95% confidence intervals (CIs)
267 and p-values. For longitudinal analyses, Cox proportional hazards regression analyses were
268 used to calculate hazard ratios (HRs) and associated CIs. Survival time was censored at the
269 date of death from all causes or at the end of the follow-up for those who did not have MDD.
270 For both sets of analyses, three models are reported; single, partition, and substitution models.
271 The three models are briefly explained below using logistic regression as an example. The

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

274 Single models assessed the association of each type of activity with depression (as defined
 275 previously), adjusting for confounders: $\text{Log}(\text{odds depression}) = B_0 + B_1 * \text{Passive SB} +$
 276 $B_2 * \text{Covariates}$.

277 Partition models assessed the association between each type of activity and depression
 278 adjusting for confounders, while keeping other activities constant: $\text{Log}(\text{odds depression}) = B_0$
 279 $+ B_1 * \text{Passive SB} + B_2 * \text{Mentally-active SB} + B_3 * \text{Light PA} + B_4 * \text{Moderate-to-vigorous PA} +$
 280 $B_6 * \text{Covariates}$. As total activity is not controlled in the partition model, the beta-coefficient of
 281 each activity represents the additive effect of these activities on depression, not the
 282 substitutive effects.

283 Substitution models assessed the effect of replacing 30-minutes of passive sedentary
 284 behaviour with 30-minutes of mentally-active sedentary behaviour, light physical activity, and
 285 moderate-to-vigorous physical activity: $\text{Log}(\text{odds depression}) = B_0 + B_2 * \text{Mentally active SB}$
 286 $+ B_3 * \text{Light PA} + B_4 * \text{Moderate-to-vigorous PA} + B_5 * \text{Total activity} + B_6 * \text{Covariates}$. In the
 287 substitution models, passive sedentary behaviour is dropped, but total activity (that is, all
 288 sedentary behaviour and physical activity) is retained. Because total activity is held constant,
 289 a 30 minute increase in mentally-active sedentary behaviour results in an equivalent decrease
 290 in activities not included in the model (i.e. passive sedentary behaviours), Thus, the beta
 291 coefficients B_2 , B_3 , and B_4 can be interpreted as the effect on depression of replacing 30-
 292 minutes of passive sedentary behaviour with the equivalent duration of mentally-active
 293 sedentary behaviour, light physical activity, and moderate-to-vigorous physical activity,
 294 respectively. Before running the prospective models (Cox regression), we used Schoenfeld
 295 residuals to test the assumption of proportional hazards for each covariate adjusting for other
 296 covariates in the model. There was no evidence for a violation of the assumption.

297

298 **3. RESULTS**

299 **3.1 Participant characteristics**

300 Participant characteristics are shown in Table 1. Sixty-six percent were female (mean age =
301 49.2 years; SD = 15.8) and 30% had a tertiary education. Thirty-nine percent of participants
302 were overweight or obese; 39% reported having ever smoked cigarettes (≥ 6 months) and
303 30% had ≥ 1 co-morbidity. Participants reported approximately 5.5 hours/day in total
304 sedentary behaviours, and 37 minutes/day in light physical activity and moderate-to-vigorous
305 activity combined. Of the total sample, 6.3% reported having frequent symptoms of
306 depression at baseline, and 1.7% was diagnosed with MDD over the 13-year follow-up.
307 Among the 22,534 participants who did not report symptoms of depression at baseline, 320
308 (1.4%) developed MDD during the course of follow-up. There was a significant inverse
309 association between the passive and mentally-active sedentary behaviours (Spearman's $\rho =$
310 -0.071 , $p < 0.01$). There were some differences between the analytic and excluded sample (i.e.
311 those with missing data on covariates). Specifically, the excluded sample included more
312 participants that were: male, elderly, obese, smoked, had ≥ 1 co-morbidity, less formal
313 education, and spent more time in passive sedentary behaviours. A detailed comparison is
314 available in Supplementary Table 1.

315

316 **Insert Table 1 here**

317

318 **3.2 Cross-sectional associations with self-reported frequent symptoms of depression**

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

324 and moderate-to-vigorous activity reduced the odds of having symptoms of depression by
325 23% (OR=0.87, 95% CI=0.77-0.99), and 28% (OR=0.82, 95% CI=0.74-0.91), respectively. In
326 the partition model, a 30-minute increase in passive sedentary behaviour increased the odds of
327 depressive symptoms by 6% (OR=1.06, 95% CI=1.04-1.07); conversely, and a 30-minute
328 increase in mentally-active sedentary behaviour reduced the odds of depressive symptoms by
329 14% (OR=0.86, 95% CI=0.77-0.95). In the substitution model, replacing 30 minutes of
330 passive sedentary behaviour with 30 minutes of mentally-active sedentary behaviour, light
331 physical activity, and moderate-to-vigorous activity significantly reduced the odds of
332 depressive symptoms by 5% (OR=0.95, 95% CI=0.94-0.97), 13% (OR=0.87, 95% CI=0.76-
333 1.00), and 19% (OR=0.81, 95% CI=0.93-0.90) respectively. Thus, there was a dose-response
334 relationship where substituting passive sedentary behaviours with higher-intensity activities
335 had a greater benefit on depressive symptoms.

336

337 **3.3 Prospective associations with clinician-diagnosed MDD**

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

342

343 **Insert Tables 2 and 3 here**

344

345 **4. DISCUSSION**

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

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

360

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

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

384

385 Our findings are consistent with recent studies demonstrating beneficial associations of light
386 physical activity and lower levels of sedentary behaviour with depression.^{8, 30} Two previous
387 studies have used ISM to explore relationships of sedentary behaviour with depression. In a
388 recent cross-sectional study involving 276 older adults, and using objective measures of
389 activity, Yasunaga et al. (2018) found that replacing 30-minutes/day of sedentary behaviour
390 with 30-minutes/day of light physical activity was negatively associated with self-rated
391 depression ($\beta = -0.131$, 95% CI -0.260 to -0.002)¹⁷. Mekary et al. (2013) prospectively
392 examined the associations of different activities with various activity displacements and
393 depression risk among 32,900 US women over ten years²⁷. An isotemporal substitution
394 gradient was found for TV-viewing, such that replacing 60-minutes/day of this activity with
395 60-minutes/day of brisk walking was associated with lower depression risk. However, a
396 similar 'protective' association was not seen when TV-viewing was replaced with slow
397 walking, which could indicate that a minimum physical activity 'dose' is required to elicit
398 these effects.²⁷ In the current study, similar beneficial associations with self-reported
399 symptoms of depression were seen for replacing passive sedentary behaviours with walking.

400

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

416

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

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

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433 Our distinction between passive and mentally-active sedentary behaviours is relatively new,
434 though its importance has been recognized in at least one previous study.¹¹ Kikuchi *et al.*
435 (2014) examined cross-sectional relationships of passive (TV-time, listening or talking while
436 sitting, and sitting around) and mentally-active (computer-use and reading books or
437 newspapers) leisure-time activities in older Japanese adults. Higher passive sedentary time
438 was associated with greater odds of being overweight and engaging in lower levels of
439 physical activity. Conversely, higher mentally-active sedentary time was associated with
440 lower odds of low physical activity.¹¹ Psychological outcomes were also examined. Higher
441 passive sedentary time increased the odds of psychological distress (Kessler K6 scale), but not
442 after adjustment for MVPA. Other categories of sedentary behaviour have been explored. A
443 meta-analysis examined possible differential effects of TV-viewing and Computer or internet
444 use on depression. Both outcomes were associated with a similar increased risk of depression.
445 Unlike these previous investigations, the current study did not assess computer or mobile
446 phone use which - although certainly relevant - could involve both passive and mentally-
447 active behaviours.

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

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

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

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

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

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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/m²)		
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.

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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 C³		Model D⁴		Model E⁵		Model F⁶		Model G⁷	
	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: ¹Log (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:

²Log (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

³Log (odds depression symptom) = B0 + B1*Passive SB + B6*Covariates

⁴Log (odds depression symptom) = B0 + B2*Mentally active SB + B6*Covariates

⁵Log (odds depression symptom) = B0 + B3*Light activity + B6*Covariates

⁶Log (odds depression symptom) = B0 + B4*Moderate-to-vigorous activity + B6*Covariates

⁷Log (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: $^1h(t) = h_0(t) \exp (B2 * \text{Mentally active SB} + B3 * \text{Light activity} + B4 * \text{Moderate-to-vigorous activity} + B5 * \text{Total activity} + B6 * \text{Covariates})$

(B) Additive effect of each activity on depression holding other activities constant:

$^2h(t) = h_0(t) \exp (B1 * \text{Passive SB} + B2 * \text{Mentally active SB} + B3 * \text{Light activity} + B4 * \text{Moderate-to-vigorous activity} + B6 * \text{Covariates})$

(C-G): Single effect of each activity on depression

$^3h(t) = h_0(t) \exp (B1 * \text{Passive SB} + B6 * \text{Covariates})$

$^4h(t) = h_0(t) \exp (B2 * \text{Mentally active SB} + B6 * \text{Covariates})$

$^5h(t) = h_0(t) \exp (B3 * \text{Light activity} + B6 * \text{Covariates})$

$^6h(t) = h_0(t) \exp (B4 * \text{Moderate-to-vigorous activity} + B6 * \text{Covariates})$

$^7h(t) = h_0(t) \exp (B5 * \text{Total activity} + B6 * \text{Covariates})$

*p<0.05

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