

## Title page

**Title:** Displacing sedentary time: Association with cardiovascular disease prevalence

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## **ABSTRACT**

**Purpose:** Isotemporal substitution analysis offers new insights for public health, but has only recently been applied to sedentary behavior research. We aimed to quantify associations between the substitution of 10 minutes of sedentary behavior with 10 minutes of light physical activity (LPA) or moderate-to-vigorous physical activity (MVPA) and the prevalence of cardiovascular disease (CVD). Age was also explored as a potential effect modifier.

**Methods:** We completed a secondary analysis of data from 1477 adults from the Health Survey for England (2008). Sedentary time, LPA and MVPA were measured using accelerometry. We applied isotemporal models to quantify the relationship with CVD prevalence of replacing 10 minutes of sedentary time with equivalent amounts of LPA or MVPA. Prevalence risk ratios (RR) with 95% confidence intervals (CI) are presented, adjusted for covariates. The role of age as an effect modifier was explored via age  $\times$  MVPA and age  $\times$  LPA interactions. CVD was defined as per the International Classification of Diseases.

**Results:** The prevalence of CVD was 24%. The RR was 0.97 (95% CI: 0.96 to 0.99) for LPA and 0.88 (0.81 to 0.96) for MVPA. Substitution of approximately 50 minutes of LPA would be required for an association equivalent to 10 minutes of MVPA. The beneficial association of MVPA was attenuated with age, with a decrease in the relative risk reduction of  $\sim 7\%$  per decade.

**Conclusions:** Isotemporal substitution of sedentary time with LPA was associated with a trivial relative risk reduction for CVD, whereas the equivalent replacement with MVPA had a small beneficial relationship. With respect to CVD prevalence, MVPA might become decreasingly important in older individuals. Prospective studies are needed to investigate causality.

**Key words:** Isotemporal substitution; public health; prevalence risk ratio; physical activity

1 **INTRODUCTION**

2 In 2008 17.3 million deaths were attributable to cardiovascular disease (CVD) and this is  
3 expected to increase to 23.3 million by 2030 (24, 39). There is a growing body of literature  
4 suggesting that sedentary behavior is an important risk factor for CVD (11, 20, 21, 25, 28, 30,  
5 31, 36). Such findings have resulted in recommendations (35) that individuals of all ages  
6 should minimize their sedentary time (sitting) and an increasing number of controlled trials of  
7 interventions explicitly attempting to reduce sedentary behavior (6, 9, 33).

8

9 The amount of time in the day is fixed. Reducing one form of behavior for a period of time  
10 will result in another form of behavior taking its place for an equivalent period. The  
11 beneficial health effects of reducing a potentially negative behavior, like sedentary time,  
12 might be dependent on the behavior with which it is replaced (14, 26). It has been argued that  
13 the positive effects of reducing sedentary behavior might be largely attributed to the resultant  
14 increase in time spent being active (17). A relatively new method of analysis known as  
15 *isotemporal substitution* has recently been identified as an important advancement in this  
16 field (26). With this method the relative health effects of displacing a period of sedentary  
17 behavior for an equivalent period of light physical activity (LPA) or moderate-to-vigorous  
18 physical activity (MVPA) can be identified, providing useful insights for public health  
19 recommendations (26).

20

21 Two recent studies have used isotemporal substitution to investigate the associations between  
22 replacing sedentary behavior with different intensities of activity and CVD risk factors (4,  
23 17). Both studies, using objective measures of behavior, identified that displacing sedentary  
24 behavior with MVPA was associated with a reduction in CVD risk factors such as body mass  
25 index and glucose homeostasis (4, 17). However, one study found no substantial association

26 of displacing the sedentary behavior with LPA (17) while the other did (though a smaller  
27 association than was seen with MVPA) (4). Thus it is unclear if replacing sedentary behavior  
28 with LPA has beneficial associations in relation to CVD risk factors. Furthermore, these  
29 studies focused on CVD risk factors rather than CVD itself.

30

31 Likewise, the role of age as a moderator (effect modifier) of the relationship between  
32 sedentary behavior and CVD has not been explored using isothermal substitution. An  
33 isothermal substitution study replacing sedentary behaviors in older adults (mean age 75  
34 years) with different levels of physical activity found that replacing sedentary behavior with  
35 LPA was associated with better subjectively-rated wellbeing while replacement with MVPA  
36 was not (3). Thus, it is possible that the benefits associated with reduced sedentary behavior  
37 are dependent on both the activity substituted and the age of the individual.

38

39 The aims of the current study were 1) to investigate the association between substituting 10  
40 minutes of sedentary behavior with either LPA or MVPA and the CVD prevalence risk ratio,  
41 and 2) to explore the extent to which the association is moderated by age.

42

## 43 **METHODS**

44 *Sample and design.* This study involved a secondary analysis of data from the 2008 Health  
45 Survey for England, a population-based survey of individuals in England (8). In the survey,  
46 16,056 addresses were selected using multistage stratified random sampling to ensure a  
47 proportionate sampling across the nine Government regions of England. Postcode sector was  
48 the primary sampling unit. Face-to-face interviews were held in 9,191 of these households  
49 with 15,102 adults. A subset of adults (n=4,507) was randomly selected to have their  
50 sedentary behavior/physical activity levels measured objectively using an accelerometer for

51 one week. The specific details of the collection procedures have previously been described in  
52 detail (8). Participants who were confined to a bed/wheelchair, pregnant, had a latex allergy,  
53 had recent abdominal surgery or a health problem which would make wearing the  
54 accelerometer uncomfortable were excluded from selection. Furthermore, for the purpose of  
55 our analysis individuals were excluded if any of the following applied: they were <45 years  
56 of age (as younger individuals would be less likely to have CVD); their level of mobility  
57 [categorized as either: I have no problems in walking about; I have some problems in walking  
58 about; I am confined to bed] was categorized as either confined to bed or data for mobility  
59 were missing.

60

## 61 **Measurements**

62 *Cardiovascular disease (CVD)*: Participants were categorized as having CVD or not  
63 according to the original 2008 Health Survey for England variable (*D*) *VII Heart and*  
64 *Circulatory condition*, which followed the definition of the International Classification of  
65 Diseases for diseases of the circulatory system. It includes the following sub-conditions:  
66 acute rheumatic fever; chronic rheumatic heart disease; hypertensive diseases; ischaemic  
67 heart disease; pulmonary heart disease and diseases of pulmonary circulation; other forms of  
68 heart disease; cerebrovascular disease; diseases of arteries, arterioles and capillaries; diseases  
69 of veins, lymphatic vessels and lymph nodes; and unspecified disorders of the circulatory  
70 system (40). This variable was calculated from a question asking individuals if they had a  
71 long-standing illness. If they replied yes, then in the second question they were asked to  
72 select, from a preordained list of conditions, up to six that they considered applicable to them.

73

74 *Sedentary behavior and physical activity*: Sedentary behavior and physical activity were  
75 measured using the Actigraph™ (Actigraph™ model GT1M). From the Actigraph™ counts

76 per minute output, sedentary behavior was classified as 0-199 counts-per-minute (cpm), LPA  
77 was classified as 200-2019 cpm, and MVPA was classified as  $\geq 2020$  cpm (8). Data were only  
78 processed for participants who wore the monitor for  $\geq 10$  hours in the day (accelerometers  
79 were not worn while sleeping) for a minimum of four days.

80

81 *CVD risk factors:* To attempt to derive an unbiased association between sedentary time/  
82 physical activity and CVD, the following CVD risk factors were entered as covariates within  
83 our statistical analysis: age [years], sex [male, female], socioeconomic status [quintiles of the  
84 Index of Multiple Deprivation: a measure of area deprivation based on income, employment,  
85 health deprivation and disability, education, skills and training, barriers to housing and  
86 services, and crime and living environment], diet [ $< 2$  portions of fruit and vegetables per day;  
87 2-4 portions of fruit and vegetables per day;  $\geq 5$  portions of fruit and vegetables per day],  
88 smoking history [never smoked; used to smoke; current smoker], alcohol intake [none,  $\leq 4$   
89 (men),  $\leq 3$  (women) units/day;  $> 4$  and  $\leq 8$  (men),  $> 3$  and  $\leq 6$  (women) units/day;  $> 8$  (men),  $> 6$   
90 (women ) units/day], anxiety/depression [I am not anxious or depressed; I am moderately  
91 anxious or depressed; I am extremely anxious or depressed] and musculoskeletal medication  
92 use [yes/no].

93

94 *Statistical analysis:* The design of the Health Survey for England is a multi-stage stratified  
95 random sample. We accounted for the complex survey design using a design-based approach.  
96 Survey weights, strata, and the primary sampling unit, which was postcode sector, were  
97 entered prior to the main analyses using the Stata software 'svyset' commands (v. 13.1; Stata  
98 Corp. College Station, Texas, USA). We adopted an 'ultimate cluster' approach, assuming  
99 that the variance between primary sampling units addresses any later stages of clustering,  
100 negating the need to specify the secondary sampling unit (household) (38). All analyses were

101 carried out using the statistical package STATA (v. 13.1; Stata Corp. College Station, Texas,  
102 USA). In all analyses “(D) *VII Heart and Circulatory condition*” was entered as the binary  
103 dependent variable.

104

105 Similar to previous work by Hamer et al. we chose to use 10-minute time units for sedentary  
106 and physical activity behaviors (17). This bout duration is the minimum recommended time  
107 period for accumulation of activity to meet current physical activity guidelines (18, 35). An  
108 isothermal substitution analysis (26) was performed to examine the association between  
109 replacing a 10-minute unit of sedentary activity with an equivalent unit of LPA or MVPA and  
110 CVD prevalence. Three models were analyzed. Model 1 was adjusted for age alone, Model 2  
111 was adjusted for age and sex, and Model 3 was adjusted for all covariates. This analysis  
112 involves the inclusion of total wear time, LPA, and MVPA in the model, with sedentary time  
113 omitted. The resulting coefficients for LPA and MVPA are estimates of the association  
114 between replacing 10 minutes of sedentary time with the equivalent amount of LPA or  
115 MVPA and CVD (expressed as a prevalence risk ratio). Finally, via age  $\times$  MVPA and age  $\times$   
116 LPA interaction terms, we explored the extent to which these associations were moderated by  
117 age.

118

119 In a secondary analysis, we examined the association between substituting 20 minutes of  
120 sedentary activity with 20 minutes of LPA and CVD prevalence. Our rationale here is that it  
121 is easier for people to replace sedentary time with light as opposed to moderate-vigorous  
122 activity, so a larger epoch might be more appropriate for LPA with respect to public health  
123 recommendations. For a pragmatic comparison, we also estimated the average amount of  
124 time required for substitution of sedentary behavior with LPA to observe an association with  
125 the prevalence risk ratio of CVD equivalent to that of substitution with MVPA. For all



126 analyses we report prevalence risk ratios together with 95% confidence intervals (CI). As a  
127 generalized linear model with a binomial distribution and log link failed to converge, we  
128 derived the risk ratios using Cox regression with a constant time at risk and robust variance  
129 estimator (2). A priori, we defined the threshold for the minimum clinically important  
130 association as a prevalence risk ratio of 0.9 (a small association). This threshold implies that  
131 for every ten cases of CVD, one case is prevented due to the exposure in question. Smaller  
132 associations than this are regarded as trivial.

133

134 Of the participants with complete outcome and accelerometry data, 150 had missing covariate  
135 data comprising n=19 for anxiety/ depression and n=134 for use of musculoskeletal  
136 medications (3 participants with missing data for both variables). For the primary analysis,  
137 we used multiple imputation (MI) as a principled method of dealing with these missing data  
138 (34). Under a missing at random assumption (missing data dependent on the observed data),  
139 we imputed the 153 missing values using chained equations via the Stata MI module (37).  
140 We used 20 imputations, as the number of imputed data sets should be greater than the  
141 frequency of missing information to ensure reproducibility of results (37). Missing values  
142 were predicted using all variables in the analysis model including the interaction terms, plus  
143 the CVD outcome variable (27). We applied an ordinal logistic regression model (ologit) to  
144 impute missing values for the 3-level anxiety/depression variable, and a logistic regression  
145 model (logit) for the binary musculoskeletal medication variable. We conducted subsequent  
146 analysis for Model 3, above, using all 20 imputed data sets with results combined using  
147 Rubin's rules (32). As recommended (34), we also conducted an analysis of complete cases  
148 only (n=1327).

149

150 **RESULTS**

151 Of the subset (n = 4,507) who were randomly chosen to have their physical activity  
152 monitored, 1477 were included in our analysis (See Figure 1). The descriptive characteristics  
153 of the included and excluded participants are shown in Table 1. The descriptive  
154 characteristics of the participants with complete data, along with those with missing data, are  
155 shown in Table 2. Of the individuals eligible for this study, 24% were classified as having a  
156 CVD condition. There were no substantial differences for outcome or exposure variables  
157 between those with complete and incomplete data apart from the proportion using  
158 musculoskeletal medicines - the variable with the most missing data, imputed for the primary  
159 analysis as detailed above.

160

161 *Insert figure 1 here*

162 *Insert tables 1 & 2 here*

163

164 Prevalence risk ratios for adjusted and unadjusted models are shown in Table 3. In all  
165 models, replacing 10 minutes of sedentary behavior with 10 minutes of LPA was associated  
166 with a trivial risk ratio for CVD (3% relative risk reduction). Replacing 10 minutes of  
167 sedentary behavior with 10 minutes of MVPA resulted in a small beneficial effect (12%  
168 relative risk reduction).

169

170 The secondary analyses revealed a prevalence risk ratio of 0.95 (95% CI: 0.92, 0.98) for  
171 replacing 20 minutes of sedentary time with the equivalent amount of LPA. We estimated  
172 that approximately 50 minutes of sedentary time would have to be replaced with LPA to  
173 observe an association with CVD equivalent to substitution with 10 minutes of MVPA. In  
174 Table 4 we report the exploratory analysis of the observed age by MVPA interaction. The  
175 protective association on CVD prevalence of replacing sedentary behavior with MVPA

176 decreased with age. Back-transformation of the coefficient for the interaction effect revealed  
177 that the risk ratio is attenuated by a factor of 1.083 per decade (95% CI, 1.025 to 1.146); for  
178 example, risk ratio=0.80 (age 50) multiplied by 1.083 = 0.87 (age 60). There was no  
179 substantial interaction of age with LPA, with the trivial risk ratio essentially unchanged  
180 across the age range (risk ratio changes by a factor of 0.9996 per decade: 95% CI, 0.9985 to  
181 1.0008).

182

183 Table 5 shows the risk ratios from the analysis of complete cases. Point estimates and  
184 confidence intervals are not materially different from those derived from the multiple  
185 imputation analysis.

186

187 *Insert table 3 here*

188 *Insert table 4 here*

189 *Insert table 5 here*

190

191

## 192 **DISCUSSION**

193 Substituting 10 minutes of sedentary behavior with an equivalent amount of MVPA resulted  
194 in a small relative risk reduction for CVD. This relationship was affected by age with the  
195 protective association of substituting sedentary behavior with MVPA decreasing with age.  
196 The replacement of 10 minutes of sedentary time with 10 minutes of LPA had a trivial  
197 association with CVD prevalence. A longer duration of LPA (~50 minutes) would be needed  
198 to achieve the same effect as 10 minutes of MVPA.

199

200 These results show that the beneficial associations of reducing sedentary behavior are largely  
201 dependent on the intensity of physical activity that displaces it. These findings support recent  
202 moves to make recommendations regarding the reduction of sedentary behavior in public  
203 health guidelines (35). Furthermore, this study provides preliminary data on the associations  
204 with CVD prevalence of displacing different durations of sedentary behavior with physical  
205 activity of different intensities for different age groups. Such data might help to develop more  
206 specific guidelines that can be tailored to enhance adherence. For example, if an individual  
207 wanted to gain the apparent CVD-reducing benefits of replacing sedentary behavior with  
208 MVPA but was unwilling or unable to undertake MVPA, the duration of LPA required to  
209 produce the equivalent health-enhancing association is identified. Our data suggest that it  
210 requires a replacement of sedentary time with approximately 5 times as much LPA versus  
211 MVPA to derive the equivalent association.

212

213 We found that substituting sedentary behavior with both LPA and MVPA reduced the risk for  
214 CVD, although the association was trivial for LPA and small for MVPA. This finding is in  
215 keeping with the work by Buman et al. (4) who found that replacement of sedentary behavior  
216 with both LPA and MVPA activity reduced risk factors for CVD. Our findings are also  
217 consistent with those of Hamer et al. (17) who reported a protective association on  
218 cardiometabolic risk factors of replacing sedentary time with MVPA, with no substantial  
219 association of LPA.

220

221 There was a decreasing protective association of substituting sedentary behavior with MVPA  
222 with increasing age. The reason for this apparent moderation cannot be elucidated given the  
223 cross-sectional design and the data at hand. It might be that as individuals age the importance  
224 of MVPA diminishes relative to other risk factors for CVD. It could also relate to the

225 negative association between age and MVPA (8). Further research is required to confirm and  
226 explain this finding.

227

228 The findings of this study, that substituting sedentary behavior with physical activity has a  
229 beneficial association with the CVD prevalence, support the recent increase in trials  
230 conducted of interventions which attempt to reduce sedentary behavior (6, 9, 33). However,  
231 for older adults only a small number of either non-randomized controlled trials or feasibility  
232 studies exist (5, 10, 12, 13, 22). Such work is particularly needed given that healthy older  
233 adults spend, on average (including sleep), 18 hours per day sedentary with values as high as  
234 22 hours per day reported in care settings (15).

235

236 A key strength of this study was the use of a large nationally representative sample, with the  
237 ability to adjust for known covariates, and objective measures of sedentary time, LPA and  
238 MVPA. Furthermore, we used a principled method – multiple imputation - for addressing  
239 missing covariate data, resulting in the inclusion of an additional 150 participants versus a  
240 complete case analysis. We believe that the imputation of missing covariate values using all  
241 variables in the analysis (Model 3) together with the outcome variable (CVD) makes the  
242 missing at random assumption plausible. We note that the results from the complete case  
243 analysis (Table 5) are essentially equivalent to those from the multiple imputation analysis  
244 (Table 4). In the current study, where data were missing only in the predictors, a complete  
245 case analysis is unbiased if the missingness mechanism is unrelated to the outcome (CVD  
246 status) (34). For the covariate with the most missing data (use of musculoskeletal medications  
247 with 134/1477 missing), 9.7% of those with no CVD had missing data versus 7.2% of those  
248 with CVD. The similarity of these proportions suggests that the missingness is unrelated to  
249 the outcome, and a complete case analysis is unbiased. The only benefit of using multiple

250 imputation in the current study, therefore, was to avoid any unnecessary loss of power and  
251 precision. However, with our relatively large sample size, there is no discernible gain in  
252 precision by including an additional 150 participants in the analysis, as indicated by the  
253 similar width of the confidence intervals for the risk ratios for complete case versus multiple  
254 imputation analyses.

255

256 It is important to acknowledge a number of limitations. First, a cross-sectional study is prone  
257 to a number of sources of bias. These include reverse causation/temporal bias, which  
258 constrains inferences to association only, and incidence-prevalence bias. Secondly, the  
259 reallocation of time in our analysis is, of course, not true isotemporal substitution (for which  
260 an experimental design would be required). Thirdly, whilst physical activity was measured  
261 objectively using the Actigraph<sup>TM</sup>, distinguishing between the postures of lying/sitting and  
262 quiet standing is difficult using count-based accelerometry data (1). Therefore, posture-based  
263 objective measures (16) may provide a more sensitive measure of sedentary behavior.

264

265 It is also noteworthy that the Health Survey for England used a cut-off of 0-199 cpm to  
266 classify sedentary behavior, while evidence suggests 150 cpm to be optimal (23). As this  
267 study was constrained to the Health Survey for England cut-off points, it is possible that more  
268 activity was classified as sedentary, compared to if the empirically-based lower cut-off point  
269 had been used. Future research would benefit from assessing sedentary behavior using both  
270 cut-off points to investigate the potential impact of this data-processing decision. In addition,  
271 it could be argued that due to the physiological decline associated with ageing, a lower  
272 absolute cpm threshold for MVPA would have been more appropriate to categorize relative  
273 MVPA intensity in older adults. It has been proposed that a cut-off point as low as 1040 cpm  
274 equates to the threshold for moderate intensity activity in older adults (7, 19), which is around

275 half the cut-off point (2020 cpm) used in the Health Survey for England for all adults. Thus,  
276 the amount of MVPA undertaken by older adults in this study might have been  
277 underestimated.

278

279 The findings from this study have a number of potential implications for future research.  
280 First, given the current limited evidence base (6) there should be a focus on the development  
281 and implementation of more randomized controlled trials of interventions specifically aimed  
282 at reducing sedentary activity and replacing it with different levels of physical activity. This  
283 research should include the continued exploration of new technology (22), and the  
284 investigation of multilevel determinants of different sedentary behaviors, tailored to the needs  
285 of specific groups (29). This issue is particularly important for older adults who are more  
286 likely to have functional limitations and a range of residential/hospital care settings, all of  
287 which may impact upon their sedentary behavior (15). Second, more research is required to  
288 further validate the findings presented in this study, using prospective study designs  
289 (observational and randomized controlled trials) to evaluate proposed causal pathways,  
290 including the potential modifying effect of age. Third, obtaining more robust answers to  
291 research questions in this field likely requires the use of new, more sensitive, objective  
292 technology for measuring sedentary behavior such as posture-based accelerometers (16).

293

294 Substituting sedentary time with MVPA has a small protective association with CVD  
295 prevalence. However, the relationship is influenced by age with MVPA becoming  
296 decreasingly important in older individuals. Prospective studies are needed to confirm and  
297 further investigate these relationships.

298

299 **ACKNOWLEDGMENTS**

300 The authors would like to thank the Economic and Social Data Service (ESDS) for providing  
301 access to the Health Survey for England (2008). The authors would like to acknowledge the  
302 original Health Survey for England data creators, depositors or copyright holders, the funders  
303 of the Data Collection and the UK Data Archive, and to acknowledge Crown Copyright. The  
304 original Health Survey for England data creators, depositors or copyright holders, the funders  
305 of the Data Collection and the UK Data Archive bear no responsibility for the analysis and  
306 interpretation of the analysis presented in this study. This was a piece of unfunded research.

307

### 308 **CONFLICT OF INTEREST**

309 The authors have no conflicts of interest to declare. The results of the present study do not  
310 constitute endorsement by ACSM.

311

312

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Table 1. Key Characteristics for Included and Excluded Cases.

	Included n = 1477 <sup>^</sup>	Excluded n=3030*
Age (years)	62.8 (11.0)	46.1 (19.4)
Sex		
Men	45.8%	43.6%
Women	54.2%	56.4%
Socio-economic status		
1 (least deprived)	25.4%	22.4%
2	23.5%	19.1%
3	19.1%	19.1%
4	16.7%	19.7%
5 (most deprived)	15.3%	19.6%
Diet		
<2 portions of fruit and vegetables	17.3%	24.5%
2-4 portions of fruit and vegetables	50.8%	48.5%
≥5 portions of fruit and vegetables	31.9%	27.0%
Anxiety/Depression		
Not anxious/ depressed	70.2%	79.8%
Moderately anxious/ depressed	18.5%	19.2%
Extremely anxious/ depressed	1.3%	2.0%
Using musculoskeletal medicine	11.5%	6.1%
Alcohol intake		
No units/day	31.2%	38.5%
≤4 (men), ≤3 (women) units/day	36.6%	25.8%
≥4 and ≤8 (men), >3 and ≤6 (women) units/day	18.8%	16.0%
>8 (men), >6 (women) units/day	13.5%	19.7%
Smoking history		
Never smoked	44.3%	48.1%
Used to smoke	40.2%	28.5%
Current smoker	15.5%	23.4%
Endocrine and metabolic condition present	13.5%	7.8%
CVD condition present	23.6%	12.5%
Sedentary time/day (min)	592.7 (88.8)	553.6 (98.1)
Light physical activity/ day (min)	218.0 (81.5)	233.1 (77.5)
MVPA/day (min)	23.7 (23.6)	35.6 (26.1)
MVPA/day (min) [median (IQR)]	16.8 (6.7 - 34.1)	30.0 (17.0 - 47.3)

Data are mean (SD) unless stated.

CVD - cardiovascular disease, MVPA – moderate to vigorous physical activity

Median and interquartile range (IQR) is presented for MVPA as this variable was severely skewed.

<sup>^</sup>n=1477 for all variables except: Anxiety/depression n=1458, musculoskeletal medication use n=1343.

\*n=3030 for all variables except: Anxiety/depression n=2831, diet n=3029, musculoskeletal medication use n=2044, alcohol intake n=2992, smoking history n=3002.

Table 2. Key Characteristics for Complete Case and Missing Data Groups.

	Complete n = 1327	Missing n = 150*
Age (years)	63.0 (11.0)	61.9 (10.7)
Sex		
Men	46.1%	42.7%
Women	53.9%	57.3%
Socio-economic status		
1 (least deprived)	25.9%	20.7%
2	23.6%	22.7%
3	18.7%	22.7%
4	17.1%	13.3%
5 (most deprived)	14.7%	20.7%
Diet		
<2 portions of fruit and vegetables	17.2%	18.0%
2-4 portions of fruit and vegetables	51.1%	48.0%
≥5 portions of fruit and vegetables	31.7%	34.0%
Anxiety/Depression		
Not anxious/ depressed	79.8%	84.0%
Moderately anxious/ depressed	18.8%	16.0%
Extremely anxious/ depressed	1.4%	0.0%
Using musculoskeletal medicine	11.6%	6.3%
Alcohol intake		
No units/day	32.1%	23.3%
≤4 (men), ≤3 (women) units/day	35.8%	43.3%
≥4 and ≤8 (men), >3 and ≤6 (women) units/day	18.5%	20.7%
>8 (men), >6 (women) units/day	13.6%	12.7%
Smoking history		
Never smoked	44.4%	43.3%
Used to smoke	40.2%	40.6%
Current smoker	15.4%	16.7%
Endocrine and metabolic condition present	13.8%	10.7%
CVD condition present	24.0%	20.0%
Sedentary time/day (min)	593.2 (88.3)	588.9 (93.7)
Light physical activity/day (min)	218.4 (81.9)	214.4 (77.9)
MVPA/day (min)	23.9 (24.0)	21.5 (19.8)
MVPA/day (min) [median (IQR)]	16.8 (6.9 – 34.3)	16.8 (6.1 – 31.8)

CVD - cardiovascular disease, MVPA – moderate to vigorous physical activity.

Data are mean (SD) unless stated.

Median and interquartile range (IQR) is presented for MVPA as this variable was severely skewed.

\*n=150 for all variables except: Anxiety/depression n=131, musculoskeletal medication use n=16

Table 3. Isotemporal Substitution of a 10-Minute Unit of Sedentary Time With LPA or MVPA.

Model	LPA		MVPA	
	Risk Ratio	95% CI	Risk Ratio	95% CI
Age	0.97	0.95, 0.98	0.89	0.82, 0.96
Age/sex	0.97	0.96, 0.99	0.87	0.81, 0.94
All covariates	0.97	0.96, 0.99	0.88	0.81, 0.96

LPA - Light physical activity; MVPA - Moderate-to-vigorous physical activity, CI - confidence interval.

All covariates model adjusted for: Age, sex, smoking status, socio-economic status, diet, alcohol intake, anxiety/depression, musculoskeletal medication.

Table 4: The effect of substituting a 10-minute unit of sedentary time with Moderate-to-vigorous physical activity by age.

Age	Risk Ratio	95% CI
50	0.80	0.71, 0.91
55	0.84	0.76, 0.93
60	0.87	0.80, 0.95
65	0.91	0.84, 0.98
70	0.94	0.87, 1.02
75	0.98	0.90, 1.07
80	1.02	0.92, 1.14
85	1.06	0.94, 1.21

CI - confidence interval.

All covariates model adjusted for: Age, sex, smoking status, socio-economic status, diet, alcohol intake, anxiety/depression, musculoskeletal medication.



Table 5. Isotemporal Substitution of a 10-Minute Unit of Sedentary Time With LPA or MVPA from analysis of complete cases only (n=1327)

Model	LPA		MVPA	
	Risk Ratio	95% CI	Risk Ratio	95% CI
Age	0.97	0.95, 0.98	0.90	0.83, 0.98
Age/sex	0.97	0.95, 0.99	0.89	0.82, 0.96
All covariates	0.97	0.96, 0.99	0.89	0.82, 0.97

LPA - Light physical activity; MVPA - Moderate-to-vigorous physical activity, CI - confidence interval.

All covariates model adjusted for: Age, sex, smoking status, socio-economic status, diet, alcohol intake, anxiety/depression, musculoskeletal medication.

Figure 1: Sampling Process Flow chart

