

1 **Title Page**

2 **Title:** The association between displacement of sedentary time and chronic musculoskeletal  
3 pain: An isotemporal substitution analysis.

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16 Tel: 0044 (0)1642 384125

17 **Word Count:** 2,990

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25 **ABSTRACT**

26 **Objectives:** Physical activity is an effective intervention for the prevention and management of  
27 chronic musculoskeletal pain (CMP). However, there is a lack of research to inform the intensity  
28 of physical activity that should be recommended. The aim of this study was to investigate the  
29 association between substituting 10 minutes of sedentary time with either 10 minutes of light  
30 physical activity (LPA) or moderate-to-vigorous physical activity (MVPA) and the CMP  
31 prevalence ratio.

32 **Design:** Secondary Analysis (November 2015) of data from the Health Survey for England  
33 (2008).

34 **Setting:** n/a

35 **Participants:** 2313 adults ( $\geq 16$  years).

36 **Interventions:** n/a

37 **Main Outcome Measures:** Sedentary time, LPA and MVPA were measured using  
38 accelerometry. We used isotemporal models to quantify the prevalence ratio for CMP of  
39 replacing 10 minutes of sedentary time with 10 minutes of LPA or MVPA.

40 **Results:** The prevalence of CMP in this sample was 17%. The unadjusted prevalence ratio was  
41 0.99 (95% CI: 0.97 to 1.01) for LPA and 0.76 (0.70 to 0.84) for MVPA. The fully adjusted  
42 prevalence ratio was 1.01 (95% CI: 0.99 to 1.02) for LPA and 0.89 (0.82 to 0.96) for MVPA.

43 **Conclusions:** Substituting 10 minutes of sedentary time with an equivalent period of LPA was  
44 not associated with a reduction in the prevalence ratio for CMP, whereas the equivalent  
45 replacement with MVPA showed a small protective relationship. Regarding CMP prevalence,  
46 physical activity intensity appears to be important, with MVPA rather than LPA showing a  
47 protective relationship. Prospective studies are needed to investigate causality.

48

49 **Key words:** Isotemporal substitution; chronic pain; prevalence ratio

50

51 **Contribution of the paper**

52 • The replacement of 10 minutes of sedentary time with 10 minutes of light physical  
53 activity was not substantially associated with chronic musculoskeletal pain  
54 prevalence.

55 • Substituting 10 minutes of sedentary time with 10 minutes of moderate-to-  
56 vigorous physical activity resulted in an 11% relative reduction in chronic  
57 musculoskeletal pain prevalence.

58 • Substituting 30 minutes of sedentary time with 30 minutes of moderate-to-  
59 vigorous physical activity resulted in a 29% relative reduction in chronic  
60 musculoskeletal pain prevalence.

61

62 **INTRODUCTION**

63 Chronic musculoskeletal pain (CMP) affects 13 – 47% of the general population and is  
64 associated with a range of health conditions, disability, and work loss [1,2]. The relationship  
65 between physical activity and CMP is complex and only partially understood. However, a  
66 number of systematic reviews have consistently identified a small but positive protective effect  
67 of physical activity for the prevention and management of CMP [3-11].

68

69 Currently there is little evidence regarding what specific type of physical activity should be  
70 undertaken with respect to the principles of frequency, intensity, time and type (FITT) [4-10].  
71 Often, reporting of the FITT components within exercise studies for CMP is incomplete,  
72 especially with respect to intensity [12,11]. To date, only one study has specifically investigated

73 the association between different intensities of physical activity and CMP [13]. Heneweer et al.  
74 [13] quantified the relationship between chronic low back pain (CLBP) prevalence and the  
75 intensity of self-reported daily physical activity. Activity intensity was quantified using  
76 Ainsworth's Compendium [14]. There was no substantial relationship between physical activity  
77 intensity and CLBP. However, those with a sedentary lifestyle, and those reporting the highest  
78 strenuous activity levels (defined as a high frequency of high intensity activity), had a greater  
79 risk of CLBP than those undertaking moderate levels of activity, thus implying a potential U-  
80 shaped relationship between physical activity and CMP. A key limitation of this work was the  
81 use of subjectively measured physical activity, which is open to bias and should be supplemented  
82 with objective methods [15].

83  
84 The effects of reducing a potentially negative behavior, like sedentary behavior, may be  
85 dependent on the behavior replacing it [16,17]. *Isotemporal substitution* is an important  
86 advancement in this field [17]. With this method, the relative health effects of displacing a period  
87 of sedentary behavior by an equivalent period of light physical activity (LPA) or moderate-to-  
88 vigorous physical activity (MVPA) can be identified [17]. This method is becoming increasingly  
89 used in public health with conditions such as cardiovascular disease, **mental health**, diabetes and  
90 obesity [17-25]. Early findings indicate that varying intensities of activity have different health  
91 effects, with MVPA substitution producing greater benefits than LPA **for cardiovascular risk**  
92 **factors such as waist circumference, lipid profile and insulin sensitivity** [20]. **However, LPA**  
93 **might be more beneficial with regards to psychosocial wellbeing** [19]. Thus, the benefits of  
94 replacing sedentary behavior with physical activity, with respect to CMP prevalence, may be  
95 dependent upon the intensity of the substituted activity.

96

97 Within the CMP literature, isotemporal substitution has not previously been used to investigate  
98 the association between replacing sedentary behavior with different intensities of physical  
99 activity. The aim of this study was to investigate the association between substituting 10 minutes  
100 of sedentary behavior with either 10 minutes of LPA or MVPA and the CMP prevalence ratio.

101

## 102 **METHODS**

### 103 **Sample and design**

104 This study is a secondary analysis [undertaken in November 2015] of data from the 2008 Health  
105 Survey for England (HSE) [26]. In the HSE, 16,056 addresses were selected using multistage  
106 stratified random sampling with postcode sector the primary sampling unit. Interviews were held  
107 with 15,102 adults. A subset of adults (n=4,507) was randomly selected to have their physical  
108 activity measured using accelerometry. The specific details of the collection procedures have  
109 been described previously [26]. Participants who were confined to a bed/wheelchair, had a latex  
110 allergy, were pregnant, had recent abdominal surgery or had a health problem that would make  
111 wearing the accelerometer uncomfortable were excluded from selection for the accelerometer-  
112 wearing subset. Furthermore, for the purpose of our analysis, individuals were excluded if they  
113 were <16 years of age or if their level of mobility [categorized as either: I have no problems in  
114 walking about; I have some problems in walking about; or I am confined to bed] was categorized  
115 as either confined to bed or not recorded.

116

### 117 **Measurements**

118 In the HSE 2008, there was no specific question asking individuals if they had CMP. Thus, for  
119 the purposes of our analysis we created a new, dichotomous CMP variable – *Presence of CMP*  
120 [*Yes/No*]. We created the new variable from three existing questions within the original HSE. In

121 the first question, participants were asked if they had a long-standing illness. If they answered  
122 yes, then in the second question they were asked to select, from a preordained list of conditions,  
123 up to six that they considered applicable to them. One of the options was a *musculoskeletal*  
124 *system condition*, which was aligned with the definition of the International Classification of  
125 Diseases (ICD) for diseases of the musculoskeletal system. It included the following sub-  
126 conditions: arthropathies, systemic connective tissue disorders, dorsopathies, soft tissue  
127 disorders, osteopathies and chondropathies, and other disorders of the musculoskeletal system  
128 and connective tissue [27]. In the third question, participants were asked if, on the day of  
129 completing the questionnaire, they were experiencing no pain, moderate pain or severe pain. If  
130 the individual had a long-standing illness, and one of the selected conditions was  
131 musculoskeletal, and if they had either moderate or severe pain that day, we categorized the  
132 individual as having CMP. Those who did not meet each of these criteria were categorized as not  
133 having CMP.

134  
135 Physical activity was measured using the Actigraph™ (model GT1M), **which is a valid and**  
136 **reliability measurement tool [28,29]. The Actigraph™ is a waist worn accelerometer, which**  
137 **converts body movement into counts, with higher counts indicating more vigorous activity.** In  
138 this study Sedentary behavior was classified as 0-199 counts-per-minute (cpm), LPA as 200-  
139 2019 cpm, and MVPA as  $\geq 2020$  cpm [26]. Within the HSE 2008, data were only processed for  
140 participants who wore the monitor for  $\geq 10$  hours in the day (accelerometers were not worn while  
141 the participant was asleep) for a minimum of four days.

142  
143 The following factors were entered as covariates within our analysis: age [years]; sex [male,  
144 female]; Body Mass Index (BMI); socioeconomic status [quintiles of the Index of Multiple

145 Deprivation: a measure of area deprivation based on income, employment, health deprivation &  
146 disability, education, skills and training, barriers to housing and services, and crime and living  
147 environment]; diet [ $<2$  portions of fruit and vegetables per day, 2-4 portions of fruit and  
148 vegetables per day,  $\geq 5$  portions of fruit and vegetables per day]; smoking history [never smoked,  
149 used to smoke, current smoker]; alcohol intake [none,  $\leq 4$  (men)/ $\leq 3$  (women) units/day,  $>4$  and  
150  $\leq 8$  (men)/ $>3$  and  $\leq 6$  (women) units/day,  $>8$  (men)/ $>6$  (women) units/day]; anxiety/depression [I  
151 am not anxious or depressed, I am moderately anxious or depressed, I am extremely anxious or  
152 depressed]; and presence of a non-musculoskeletal long-standing illness [CVD, endocrine and  
153 metabolic conditions, respiratory conditions and neurological conditions (yes/no)].

154

### 155 **Statistical analysis**

156 To account for the complex survey design of the HSE, we used a design-based approach. **In this**  
157 **method** survey weights, strata, and the primary sampling unit (postcode sector) were set prior to  
158 the main analyses using the STATA software ‘svyset’ commands (v. 13.1; Stata Corp. College  
159 Station, Texas, USA). We implemented an ‘ultimate cluster’ approach, negating the need to  
160 specify the secondary sampling unit (household) [30]. The analyses were carried out using the  
161 statistical software package Stata® (StataCorp. 2013. *Stata Statistical Software: Release 13*.  
162 College Station, TX: StataCorp LP). In all analyses, our “presence of chronic musculoskeletal  
163 pain [yes/no]” variable was entered as the binary dependent variable.

164

165 In keeping with work by Hamer et al. [22] we used 10-minute time units for sedentary and  
166 physical activity time. Ten-minute periods were used as it is recommended that the 30 minutes of  
167 MVPA, which individuals are encouraged to achieve everyday should be accumulated in bouts  
168 of ten minutes or more [31,32]. We performed an isotemporal substitution analysis to examine

169 the association between replacing a 10-minute unit of sedentary behavior with an equivalent unit  
170 of LPA or MVPA and CMP prevalence. We analyzed three models: Model 1 was unadjusted,  
171 Model 2 was adjusted for age and sex, and Model 3 was adjusted for all covariates. Our analysis  
172 involved the inclusion of total wear time, LPA and MVPA in the model, with sedentary time  
173 excluded. The resulting coefficients for LPA and MVPA are estimates of the association  
174 between replacing 10 minutes of sedentary time with the equivalent amount of LPA or MVPA  
175 and the prevalence of CMP, expressed as a risk ratio.

176

177 In a secondary analysis, we substituted 30 minutes of sedentary behavior with MVPA to  
178 determine the association with the prevalence of CMP. This is consistent with current activity  
179 guidelines [31,32]. For all analyses, we report the **prevalence ratios** along with 95% confidence  
180 intervals (CI). A generalized linear model with a binomial distribution and log-link failed to  
181 converge; therefore, we derived the risk ratios using Cox regression with a constant time at risk  
182 and robust variance estimator [33]. A priori, the threshold for the minimum clinically important  
183 association was set at a **prevalence ratio** of 0.9 (a small association) and smaller risk ratios than  
184 these were regarded as trivial. **This threshold implies that for every 10 cases with CMP, one is**  
185 **prevented due to the exposure in question (displacement of sedentary time with physical**  
186 **activity).**

187

188 Of the participants with complete data for the outcome and primary exposure (physical activity/  
189 sedentary time), 232 had missing covariate data comprising n=16 for anxiety/ depression, 14 for  
190 alcohol intake, 5 for smoking status, and 202 for BMI (5 participants with missing data for  
191 multiple variables). For the primary analysis, we used multiple imputation (MI) as a principled  
192 method of dealing with these missing data [34]. Under a missing at random assumption, we



193 imputed the 237 missing values using chained equations via the Stata MI module [34]. We used  
194 20 imputations, to ensure that the number of imputed data sets was greater than the frequency of  
195 missing information to ensure reproducibility of results [35]. Missing values were predicted  
196 using all variables in the analysis model, plus the chronic musculoskeletal pain outcome variable  
197 [36]. We applied ordinal logistic regression models (ologit) to impute missing values for the  
198 anxiety/depression, alcohol intake, and smoking status variables, and linear regression for the  
199 BMI variable. We conducted subsequent analysis for the fully-adjusted model using all 20  
200 imputed data sets with results combined using Rubin's rules [37]. As recommended [34], we also  
201 conducted an analysis of complete cases only (n=2081). Figure 1 shows that there were 8 cases  
202 with missing outcome data (CMP); these were removed from the analysis, as under a missing at  
203 random assumption imputing missing outcome data provides no additional information.

204

## 205 **RESULTS**

206 Of the subset (n = 4,507) who were randomly chosen to have their physical activity monitored,  
207 1,207 were removed from the sample as they had incomplete objective physical activity data.  
208 Nine hundred and seventy nine participants were removed as they were confined to bed or  
209 provided insufficient mobility data to determine their mobility status. A further 8 participants  
210 were removed from the sample as they did not have outcome variable data. Thus, 2313 were  
211 included in our analysis (See supplementary Figure S1).

212

213 The descriptive characteristics of the included and excluded participants are shown in Table 1.  
214 The summary data for those participants with complete data, along with those with missing data,  
215 are shown in supplementary Table S1. Of the individuals eligible for this study, 17% were  
216 classified as having CMP. There were no substantial differences between those with complete

217 data and those with missing covariate data, apart from a higher prevalence in the missing data  
218 group of the CMP outcome variable and the original variable of presence of a long-standing  
219 illness.

220

221 *Insert table 1 here (supplementary table S1 and supplementary figure S1 are online)*

222

223 In all models, replacing 10 minutes of sedentary behavior with 10 minutes of LPA was not  
224 associated with a substantial reduction in the risk ratio for CMP (Table 2). Replacing 10 minutes  
225 of sedentary behavior with 10 minutes of MVPA resulted in a small reduction in the prevalence  
226 ratio for CMP (11% relative risk reduction for the fully-adjusted model), achieving the  
227 minimally clinical important threshold set a priori. In a secondary analysis, we estimated that  
228 replacing 30 minutes of sedentary behavior with 30 minutes of MVPA time would result in a  
229 fully-adjusted relative risk reduction of 29% (prevalence ratio for CMP of 0.71).

230 Table 3 shows the risk ratios from the analysis of complete cases. Point estimates and confidence  
231 intervals are not materially different from those derived from the multiple imputation analysis.

232

233 *Insert table 2 and 3 here*

234

## 235 **DISCUSSION**

236 Substituting 10 minutes of sedentary time with an equivalent amount of MVPA resulted in a  
237 small reduction in the prevalence ratio for CMP. The replacement of 10 minutes of sedentary  
238 time with 10 minutes of LPA was not substantially associated with CMP prevalence. These  
239 results show that the beneficial associations of reducing sedentary behavior with regards to CMP  
240 prevalence are largely dependent on the intensity of physical activity that displaces it.

241 Furthermore, the magnitude of the reduction in prevalence ratio (PR = 0.89) for substituting 10  
242 minutes of sedentary time with the equivalent amount of time in MVPA was a small but  
243 clinically important association. The risk reduced further (PR = 0.71) when 30 minutes of  
244 sedentary time was replaced with current guideline recommendations of 30 minutes of MVPA  
245 [31].

246  
247 Only one previous study has specifically investigated the relationship between physical activity  
248 intensity and CMP [13]. The authors reported that whilst intensity was not related to CLBP  
249 prevalence, those who were most inactive and those who were most active had a higher  
250 prevalence of CLBP than those who were moderately active, indicating a U-shaped curve. In  
251 contrast, we observed that intensity of physical activity was associated with CMP prevalence.  
252 We found that substituting LPA for sedentary time was not substantially associated with CMP  
253 prevalence but substituting MVPA had a small protective effect. The study methods used likely  
254 explain the differences in findings. A key difference was that our study used objectively  
255 measured physical activity while Heneweer et al. [13] used subjectively measured physical  
256 activity, which can be inaccurate/imprecise and should be supplemented with objective methods  
257 [15].

258  
259 Given the cross-sectional nature of this study, it is not possible to investigate causality, and  
260 longitudinal studies are needed to explore this further. However, the presence of the association  
261 has important clinical implications independent of the direction of the relationship. If  
262 undertaking greater amounts of MVPA rather than LPA can lead to a reduction in CMP  
263 prevalence, then guidelines should encourage individuals to undertake more MVPA, both for  
264 prevention and management of pain. Alternatively, if the association seen in this study reflects

265 the case that those individuals with CMP simply do less MVPA than those without CMP then  
266 this has serious implications for the cardiovascular and metabolic health of individuals with  
267 CMP. This latter interpretation would still reinforce the need for MVPA to be emphasized in  
268 guidelines for management of CMP but the rationale would then be the prevention of secondary  
269 co-morbidities.

270  
271 There are a number of reasons why MVPA may be more beneficial than LPA with respect to  
272 CMP prevalence. First, MVPA may result in better conditioning of the musculoskeletal system.  
273 Second, the effects may be related to psychological wellbeing. There is a strong link between  
274 psychological factors, such as depression, and pain [38] and MVPA may have greater effects on  
275 mild-to-moderate depression than LPA [39]. Third, in animal models the natural analgesic  
276 system is enhanced by regular physical activity and this has been shown to attenuate the  
277 development of CMP [40]. In addition, in humans the body's natural analgesic system is more  
278 strongly activated by MVPA rather than LPA [41,42]. Finally, based upon the fear avoidance  
279 model [43] we can speculate that enhancing exposure to more physically stressful activity by  
280 way of undertaking MVPA may help to reduce pain-related fear and reduce fear avoidant  
281 behavior in comparison to LPA.

282  
283 **Limitations**

284  
285 A key strength of this study was the use of a large nationally representative sample, adjusted for  
286 a range of known covariates, and an objective measure of physical activity. A number of  
287 limitations should also be considered. First, cross-sectional studies are prone to bias including  
288 temporal/ reverse causation bias, restricting inferences to association only. Second, the

289 reallocation of time in our analysis is not true isotemporal substitution (an experimental design  
290 would be required for this). Third, whilst physical activity was measured objectively using the  
291 Actigraph™, such count-based accelerometers can have difficulty distinguishing between the  
292 postures of lying/sitting and quiet standing [44] and thus it may not be ideal for distinguishing  
293 between sedentary behavior and LPA. **In addition, the Actigraph™ is unable to measure certain**  
294 **activities such as swimming or cycling [45].** Finally, our classification of CMP is a combination  
295 of three separate questions in the HSE rather than a single direct measure of CMP. We have used  
296 this variable previously [46]. The limitation is that we cannot be sure that the pain indicated by  
297 respondents is related to their musculoskeletal condition. While this misclassification of pain is  
298 possible, the logic underpinning our CMP variable is sound - that for the vast  
299 majority reporting a musculoskeletal condition, their moderate/severe pain is linked with that  
300 condition; and that the sample size is sufficiently large to minimize any confounding effects of  
301 the minority of respondents whose pain would be unrelated.

302

303 It is worth highlighting that the HSE used a cut-off of 0-199 cpm to classify sedentary behavior,  
304 though evidence suggests 150 cpm is optimal [47]. This study was constrained to the HSE cut-  
305 off points. It is possible that more activity was classified as sedentary, compared to if the  
306 empirically based lower cut-off point had been used. Future work assessing sedentary behavior  
307 using both cut-off points may be warranted to investigate the potential impact of this data-  
308 processing decision. Additionally, it could also be argued that due to the physiological decline  
309 associated with ageing, a lower cpm threshold for MVPA would have been more appropriate to  
310 categorize relative LPA and MVPA intensity in older adults with cut-offs as low as 1040 cpm  
311 proposed to equate to the threshold for MVPA in older adults [48,49]. Thus, the amount of  
312 MVPA undertaken in this study by older adults may have been underestimated.

313  
314 Current physical activity guidelines recommend 30 minutes of moderate intensity activity on five  
315 or more days per week to be accumulated in bouts of 10 minutes or more [31, 32]. Our findings  
316 highlight the potential clinical benefit of current guidelines for patients with CMP, reinforcing  
317 the case for recommending these guidelines to patients. Our findings have two main implications  
318 for future research. First, given the current limited evidence base, more randomized controlled  
319 trials of interventions specifically aimed at investigating the effectiveness of different intensities  
320 of physical activity in the management of CMP are warranted. Such trials should consider the  
321 specific needs of certain sub-groups such as those with high levels of pain-related fear. Second,  
322 more research is required to corroborate the findings of this study, using prospective study  
323 designs (observational and randomized controlled trials) to evaluate causal pathways.

324

## 325 **Conclusions**

326 In conclusion, substituting 10 minutes of sedentary time with the equivalent amount of MVPA,  
327 but not LPA, has a small but clinically relevant protective association with CMP prevalence  
328 ratio. Prospective studies are needed to further investigate these findings.

329

## 330 **Acknowledgements**

331 The authors would like to thank the Economic and Social Data Service (ESDS) for providing  
332 access to the Health Survey for England (2008). The authors would like to acknowledge the  
333 original Health Survey for England data creators, depositors or copyright holders, the funders of  
334 the Data Collection and the UK Data Archive, and to acknowledge Crown Copyright. The  
335 original Health Survey for England data creators, depositors or copyright holders, the funders of  
336 the Data Collection and the UK Data Archive bear no responsibility for the analysis and

337 interpretation of the analysis presented in this study. All authors contributed substantially to the  
338 work in keeping with ICJME authorship guidelines.

339

#### 340 **Ethical Approval**

341 The study was approved by Teesside University's School of Health and Social Care Research  
342 Governance and Ethics Board.

343

#### 344 **Funding**

345 This study was unfunded.

346

#### 347 **Conflict of Interest**

348 The authors have no conflicts of interest and no financial disclosures were reported by the  
349 authors of this paper.

350

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474 Table 1. Key Characteristics for Included and excluded cases.  
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	Included n = 2313 <sup>s</sup>	Excluded n = 2194 <sup>*</sup>	476 477 478 479 480 481 482 483 484 485 486 487 488 489 490 491 492 493 494 495 496 497 498 499 500 501 502 503 504 505 506 507 508 509 510 511 512
Age (years)	52 (18)	52 (20)	
Sex			
Men	45%	44%	
Women	55%	57%	
BMI (kg/m <sup>2</sup> )	28 (5)	27 (5)	
Socio-economic status			
1 (least deprived)	24%	22%	
2	21%	20%	
3	19%	19%	
4	19%	19%	
5 (most deprived)	17%	20%	
Diet			
<2 portions of fruit and vegetables	20%	24%	
2-4 portions of fruit and vegetables	50%	48%	
≥5 portions of fruit and vegetables	29%	28%	
Anxiety/Depression			
Not anxious/ depressed	81%	79%	
Moderately anxious/ depressed	18%	19%	
Extremely anxious/ depressed	1%	2%	
Alcohol intake			
No units/day	33%	40%	
≤4 (men), ≤3 (women) units/day	30%	28%	
≥4 and ≤8 (men), >3 and ≤6 (women) units/day	18%	15%	
>8 (men), >6 (women) units/day	18%	17%	
Smoking history			
Never smoked	47%	46%	
Used to smoke	33%	32%	
Current smoker	20%	21%	
Long standing illness	30%	32%	
CMP condition present	17%	17%	
Objective light activity (min)	227 (79)	205 (101)	
Objective MVPA/day (min)	29 (25)	22 (25)	
Objective sedentary time/day (min)	577 (94)	574 (103)	

513 BMI - body mass index, CMP – chronic musculoskeletal pain, MVPA – moderate-to-vigorous physical activity  
 514 <sup>s</sup>n=2313 for all variables except: BMI n=2111, Anxiety/depression n=2297, Alcohol intake n=2299, Smoking history n=2308.  
 515 <sup>\*</sup>n=2194 for all variables except: BMI n=1698, Diet n=2193, Anxiety/depression n=1992, Alcohol intake n=2170, smoking history  
 516 n=2171, CMP condition n=1989, Objective light activity/MVPA/sedentary time n=43. Data presented in brackets are standard  
 517 deviations.

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**Table 2.** The prevalence ratio for CMP: substituting 10-minutes of sedentary time with LPA or MVPA.

Model	LPA		MVPA	
	Prevalence ratio	95% CI	Prevalence ratio	95% CI
Unadjusted	0.99	0.97, 1.01	0.76	0.70, 0.84
Age/sex	1.00	0.98, 1.02	0.86	0.79, 0.94
All covariates	1.01	0.99, 1.02	0.89	0.82, 0.96

530 All covariates model adjusted for: Age, sex, smoking status, socio-economic status, diet, alcohol intake, anxiety/depression,  
531 Body Mass Index, presence of a long-standing illness.

532 LPA = Light physical activity; MVPA = Moderate-to-vigorous physical activity; CI = Confidence Interval.

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534 Total sample included in the analysis = 2313. Of these, 388 cases reported chronic musculoskeletal pain. Mean (SD) duration of  
535 MVPA for these cases was 17.5 (19.5). Substitution of this amount of sedentary time with MVPA (all covariates model) gives a  
536 prevalence ratio of 0.82. The prevalence ratio associated replacing sedentary time with the recommended amount of MVPA (30  
537 min per day) is 0.71 (95%CI 0.55, 0.88).

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**Table 3.** Isotemporal substitution of a 10-minute unit of sedentary time with LPA or MVPA: Complete cases analysis.

Model	LPA		MVPA	
	Prevalence ratio	95% CI	Prevalence ratio	95% CI
Unadjusted	0.99	0.98, 1.01	0.78	0.71, 0.86
Age/sex	1.00	0.98, 1.02	0.87	0.80, 0.96
All covariates	1.01	0.99, 1.02	0.90	0.82, 0.98

544 All covariates model adjusted for: Age, sex, smoking status, socio-economic status, diet, alcohol intake, anxiety/depression, BMI,  
545 presence of a long-standing illness.

546 LPA = Light physical activity; MVPA = Moderate-to-vigorous physical activity; CI = Confidence Interval.

547 Complete cases analysis. Total sample included = 2081.

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Table S1. Key Characteristics for Complete Case and Missing Data Groups.

	Complete n = 2081	Missing n = 232*	563 564
Age (years)	51 (18)	54 (21)	565
Sex			566
Men	46%	39%	567
Women	54%	61%	568
BMI (kg/m <sup>2</sup> )	28 (5)	27 (6)	569
Socio-economic status			570
1 (least deprived)	25%	21%	571
2	21%	21%	572
3	19%	18%	573
4	19%	18%	574
5 (most deprived)	16%	23%	575
Diet			576
<2 portions of fruit and vegetables	20%	23%	577
2-4 portions of fruit and vegetables	50%	50%	578
≥5 portions of fruit and vegetables	30%	26%	579
Anxiety/Depression			580
Not anxious/ depressed	82%	76%	581
Moderately anxious/ depressed	17%	22%	582
Extremely anxious/ depressed	1%	2%	583
Alcohol intake			584
No units/day	32%	38%	585
≤4 (men), ≤3 (women) units/day	30%	36%	586
≥4 and ≤8 (men), >3 and ≤6 (women) units/day	19%	16%	587
>8 (men), >6 (women) units/day	19%	11%	588
Smoking history			589
Never smoked	48%	45%	590
Used to smoke	32%	35%	591
Current smoker	20%	20%	592
Long standing illness	29%	41%	593
CMP condition present	16%	28%	594
Objective light activity (min)	227 (79)	201 (85)	595
Objective MVPA/day (min)	29 (25)	24 (26)	596
Objective sedentary time/day (min)	577 (94)	591 (95)	597
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BMI - body mass index, CMP – chronic musculoskeletal pain, MVPA – moderate to vigorous physical activity  
\*n=232 for all variables except: BMI n=30, Anxiety/depression n=216, Alcohol intake n=218, smoking history n=227. Data presented in brackets are standard deviations.

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615 **Figure legends:**

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617 **Supplementary Figure S1.** Sampling process - flow chart.

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