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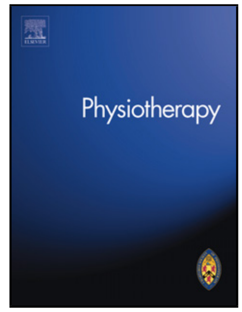

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The association between displacement of sedentary time and chronic musculoskeletal pain: An isotemporal substitution analysis

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ABSTRACT

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

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

Setting: n/a

Participants: 2313 adults (≥ 16 years).

Interventions: n/a

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

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

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

Keywords: Isotemporal substitution; chronic pain; prevalence ratio

INTRODUCTION

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

Currently there is little evidence regarding what specific type of physical activity should be undertaken with respect to the principles of frequency, intensity, time and type (FITT) [4-10]. Often, reporting of the FITT components within exercise studies for CMP is incomplete, especially with respect to intensity [12,11]. To date, only one study has specifically investigated the association between different intensities of physical activity and CMP [13]. Heneweer et al. [13] quantified the relationship between chronic low back pain (CLBP) prevalence and the intensity of self-reported daily physical activity. Activity intensity was quantified using Ainsworth’s Compendium [14]. There was no substantial relationship between physical activity intensity and CLBP. However, those with a sedentary lifestyle, and those reporting the highest strenuous activity levels (defined as a high frequency of high intensity activity), had a greater risk of CLBP than those undertaking moderate levels of activity, thus implying a potential U-shaped relationship between physical activity and CMP. A key limitation of this work was the use of subjectively measured physical activity, which is open to bias and should be supplemented with objective methods [15].

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

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

METHODS

Sample and design

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

Measurements

In the HSE 2008, there was no specific question asking individuals if they had CMP. Thus, for the purposes of our analysis we created a new, dichotomous CMP variable – *Presence of CMP [Yes/No]*. We created the new variable from three existing questions within the original HSE. In the first question, participants were asked if they had a long-standing illness. If they answered yes, then in the second question they were asked to select, from a preordained list of conditions, up to six that they considered applicable to them. One of the options was a *musculoskeletal system condition*, which was aligned with the definition of the International Classification of Diseases (ICD) for diseases of the musculoskeletal system. It included the following sub-conditions: arthropathies, systemic connective tissue disorders, dorsopathies, soft tissue disorders, osteopathies and chondropathies, and other disorders of the musculoskeletal system and connective tissue [27]. In the third question, participants were asked if, on the day of completing the questionnaire, they were experiencing no pain, moderate pain or severe pain. If the individual had a long-standing illness, and one of the selected conditions was musculoskeletal, and if they had either moderate or severe pain that day, we categorized the individual as having CMP. Those who did not meet each of these criteria were categorized as not having CMP.

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

The following factors were entered as covariates within our analysis: age [years]; sex [male, female]; Body Mass Index (BMI); socioeconomic status [quintiles of the Index of Multiple Deprivation: a measure of area deprivation based on income, employment, health deprivation & disability, education, skills and training, barriers to housing and services, and crime and living environment]; diet [<2 portions of fruit and vegetables per day, 2-4 portions of fruit and vegetables per day, ≥5 portions of fruit and vegetables per day]; smoking history [never smoked, used to smoke, current smoker]; alcohol intake [none, ≤4 (men)/≤3 (women) units/day, >4 and ≤8 (men)/>3 and ≤6 (women) units/day, >8 (men)/>6 (women) units/day]; anxiety/depression [I am not anxious or depressed, I am moderately anxious or depressed, I am extremely anxious or depressed]; and presence of a non-musculoskeletal long-standing illness [CVD, endocrine and metabolic conditions, respiratory conditions and neurological conditions (yes/no)].

Statistical analysis

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

In keeping with work by Hamer et al. [22] we used 10-minute time units for sedentary and physical activity time. Ten-minute periods were used as it is recommended that the 30 minutes of MVPA, which individuals are encouraged to achieve everyday should be accumulated in bouts of ten minutes or more [31,32]. We performed an isotemporal substitution analysis to examine the association between replacing a 10-minute unit of sedentary behavior with an equivalent unit of LPA or MVPA and CMP prevalence. We analyzed three models: Model 1 was unadjusted, Model 2 was adjusted for age and sex, and Model 3 was adjusted for all covariates. Our analysis involved the inclusion of total wear time, LPA and MVPA in the model, with sedentary time excluded. The resulting coefficients for LPA and MVPA are estimates of the association between replacing 10 minutes of sedentary time with the equivalent amount of LPA or MVPA and the prevalence of CMP, expressed as a risk ratio.

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

Of the participants with complete data for the outcome and primary exposure (physical activity/ sedentary time), 232 had missing covariate data comprising n=16 for anxiety/ depression, 14 for alcohol intake, 5 for smoking status, and 202 for BMI (5 participants with missing data for multiple variables). For the primary analysis, we used multiple imputation (MI) as a principled method of dealing with these missing data [34]. Under a missing at random assumption, we imputed the 237 missing values using chained equations via the Stata MI module [34]. We used 20 imputations, to ensure that the number of imputed data sets was greater than the frequency of missing information to ensure reproducibility of results [35]. Missing values were predicted using all variables in the analysis model, plus the chronic musculoskeletal pain outcome variable [36]. We applied ordinal logistic regression models (ologit) to impute missing values for the anxiety/depression, alcohol intake, and smoking status variables, and linear regression for the BMI variable. We conducted subsequent analysis for the fully-adjusted model using all 20 imputed data sets with results combined using Rubin’s rules [37]. As recommended [34], we also conducted an analysis of complete cases only (n=2081). Figure 1 shows that there were 8 cases with missing outcome data (CMP); these were removed from the analysis, as under a missing at random assumption imputing missing outcome data provides no additional information.

RESULTS

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

The descriptive characteristics of the included and excluded participants are shown in Table 1. The summary data for those participants with complete data, along with those with missing data, are shown in supplementary Table S1. Of the individuals eligible for this study, 17% were classified as having CMP. There were no substantial differences between those with complete data and those with missing covariate data, apart from a higher prevalence in the missing data group of the CMP outcome variable and the original variable of presence of a long-standing illness.

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

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

DISCUSSION

Substituting 10 minutes of sedentary time with an equivalent amount of MVPA resulted in a small reduction in the prevalence ratio for CMP. The replacement of 10 minutes of sedentary time with 10 minutes of LPA was not substantially associated with CMP prevalence. These results show that the beneficial associations of reducing sedentary behavior with regards to CMP prevalence are largely dependent on the intensity of physical activity that displaces it. Furthermore, the magnitude of the reduction in prevalence ratio (PR = 0.89) for substituting 10 minutes of sedentary time with the equivalent amount of time in MVPA was a small but clinically important association. The risk reduced further (PR = 0.71) when 30 minutes of sedentary time was replaced with current guideline recommendations of 30 minutes of MVPA [31].

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

Given the cross-sectional nature of this study, it is not possible to investigate causality, and longitudinal studies are needed to explore this further. However, the presence of the association has important clinical implications independent of the direction of the relationship. If undertaking greater amounts of MVPA rather than LPA can lead to a reduction in CMP prevalence, then guidelines should encourage individuals to undertake more MVPA, both for prevention and management of pain. Alternatively, if the association seen in this study reflects the case that those individuals with CMP simply do less MVPA than those without CMP then this has serious implications for the cardiovascular and metabolic health of individuals with CMP. This latter interpretation would still reinforce the need for MVPA to be emphasized in guidelines for management of CMP but the rationale would then be the prevention of secondary co-morbidities.

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

Limitations

A key strength of this study was the use of a large nationally representative sample, adjusted for a range of known covariates, and an objective measure of physical activity. A number of limitations should also be considered. First, cross-sectional studies are prone to bias including temporal/ reverse causation bias, restricting inferences to association only. Second, the reallocation of time in our analysis is not true isotemporal substitution (an experimental design would be required for this). Third, whilst physical activity was measured objectively using the Actigraph™, such count-based accelerometers can have difficulty distinguishing between the postures of lying/sitting and quiet standing [44] and thus it may not be ideal for distinguishing between sedentary behavior and LPA. In addition, the Actigraph™ is unable to measure certain activities such as swimming or cycling [45]. Finally, our classification of CMP is a combination of three separate questions in the HSE rather than a single direct measure of CMP. We have used this variable previously [46]. The limitation is that we cannot be sure that the pain indicated by respondents is related to their musculoskeletal condition. While this misclassification of pain is possible, the logic underpinning our CMP variable is sound - that for the vast majority reporting a musculoskeletal condition, their moderate/severe pain is linked with that condition; and that the sample size is sufficiently large to minimize any confounding effects of the minority of respondents whose pain would be unrelated.

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

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

Conclusions

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

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Contribution of the paper

- The replacement of 10 minutes of sedentary time with 10 minutes of light physical activity was not substantially associated with chronic musculoskeletal pain prevalence.
- Substituting 10 minutes of sedentary time with 10 minutes of moderate-to-vigorous physical activity resulted in an 11% relative reduction in chronic musculoskeletal pain prevalence.
- Substituting 30 minutes of sedentary time with 30 minutes of moderate-to-vigorous physical activity resulted in a 29% relative reduction in chronic musculoskeletal pain prevalence.

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Ethical Approval

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

Conflict of Interest

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

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Table 1. Key Characteristics for Included and excluded cases.

	Included		Excluded
	n = 2313$		n = 2194*
Age (years)	52 (18)		52 (20)
Sex			
Men	45%		44%
Women	55%		57%
BMI (kg/m^2)	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)

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

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

	LPA		MVPA	
Model	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

All covariates model adjusted for: Age, sex, smoking status, socio-economic status, diet, alcohol intake, anxiety/depression, Body Mass Index, presence of a long-standing illness.
LPA = Light physical activity; MVPA = Moderate-to-vigorous physical activity; CI = Confidence Interval.

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

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

	LPA		MVPA	
Model	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

All covariates model adjusted for: Age, sex, smoking status, socio-economic status, diet, alcohol intake, anxiety/depression, BMI, presence of a long-standing illness.
LPA = Light physical activity; MVPA = Moderate-to-vigorous physical activity; CI = Confidence Interval.
Complete cases analysis. Total sample included = 2081.