The Extent to Which Adiposity Markers Explain the Association Between Sedentary Behavior and Cardiometabolic Risk Factors

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An emerging body of evidence suggests that sedentary behavior (SB) is an independent risk factor for cardiometabolic disease. Recent data suggest that multi-domain SB has detrimental associations with BMI, waist circumference (WC), and nonadiposity-related (total cholesterol, high density lipoprotein cholesterol (HDL-C), systolic (SBP) and diastolic (DBP) blood pressure) cardiometabolic risk markers. The aim of this cross-sectional study was to examine the extent to which the associations between SB and nonadiposity-related cardiometabolic risk markers are explained by adiposity markers. Subjects were 5,067 Health Survey for England (HSE) 2008 respondents (2,552 men) aged 16–65 years. The measurements protocol involved self-reports of television time, other recreational sitting, occupational sitting/standing, physical activity and objective measures of weight, height, WC, total cholesterol, HDL cholesterol, SBP, and DBP. BMI or WC adjustments of the multivariable models looking at the associations between SB and nonadiposity markers attenuated all associations towards the null. Using established logistic regression-based algorithms we calculated that a large percentage of the associations between SB time and nonadiposity risk factors is explained by BMI or WC (range: 27.3–95.9%). Future longitudinal studies should further examine the mediatory role of adiposity in explaining the associations between SB and cardiometabolic risk.

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INTRODUCTION

An emerging body of evidence consistently suggests that sedentary behavior (SB), as characterized by activities that involve sitting, is linked to increased risk for obesity (1), dyslipedimia (2), impaired glucose metabolism (3), all-cause mortality (4,5), and cardiovascular events (5) independently of self-reported (1,2,4,5) or objectively-assessed (3) volumes of moderate-to-vigorous physical activity (MVPA), defined as those activities with an intensity of ≥3 metabolic equivalents. We have shown that a key indicator of SB, screen-based entertainment time, is associated with both BMI, waist circumference (WC) (1) and that total SB and TV viewing time are associated with systolic (SBP) and diastolic (DBP) blood pressure, total cholesterol, and high density lipoprotein cholesterol (HDL-C), independently of MVPA and occupational physical activity and other potential confounders (E. Stamatakis, M. Hamer, K. Tiling and DA. Lawlor, unpublished data, under review). Although adiposity has been shown to predict overall SB (6) no studies have examined to what extent it explains the associations with other cardiometabolic risk factors. Hence, the aim of this study was to examine to what extent the above two established adiposity markers (BMI and WC) explain the associations between multi-domain SB and the cardiometabolic risk markers we have previously observed (E. Stamatakis, M. Hamer, K. Tiling and DA. Lawlor, unpublished data, under review).

METHODS AND PROCEDURE

The Health Survey for England (HSE) is a continuous survey that draws annually a nationally-representative general population sample of adults living in households. The sample is drawn using multi-stage stratified probability sampling with postcode sectors as the primary sampling unit and the Postcode Address File as the sampling frame for households. In the present analysis we used data from HSE 2008, which had a special focus on physical activity and fitness (7). In HSE 2008 the household response rate for the core sample was 64%. Ethical approval for the 2008 survey was obtained from the Oxford Research Ethics Committee (reference number 07/H0604/102). These analyses considered participants aged between 16 and 65 years and over with valid data on all demographic, behavioral, and biological variables of interest.

Trained interviewers assessed respondents' demographics, and eating, alcohol drinking, and smoking habits using Computer Assisted Personal Interviewing and took height

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and weight measurements using standard protocols (8). SB was assessed using sets of questions on: (i) the usual weekday and weekend day time spent on a TV watching (including DVDs and videos) (ii) any other sitting during leisure time, (iii) the average daily times spent sitting/standing while at work. Physical activity questions included weekly frequency and duration (minutes per day) of participation in walking for any purpose, and any recreational exercise, (e.g., cycling, swimming, aerobics, callisthenics, gym exercises, dancing, team sports, racket sports) (8). The walking section of the questionnaire also enquired about perceived walking pace (slow; average; brisk; fast). In consistency with previous work of ours (1,5,9) and other analysts (7,8), only walking of brisk or fast pace was classified as MVPA. Occupational activity was measured using a set of questions on average daily (per day at work) times spent on walking, climbing stairs or ladders, and lifting, carrying or moving heavy loads (8). In a separate visit, qualified nurses collected nonfasting blood samples that were used to measure total and HDL-C, and measured blood pressure using an Omron 907 digital monitor (Omron Electronics, London, UK).

We originally examined the relationships between self-reported SB and BMI, WC, SBP, DBP, total cholesterol, HDL, and hemoglobin A_{1c} using multiple linear regression adjusted for age, sex, social class, employment status, alcohol consumption, fruit and vegetable consumption, frequency of unhealthy foods consumption, psychological distress, antihypertensive medication, and MVPA (E. Stamatakis, M. Hamer, K. Tiling and DA. Lawlor, unpublished data, under review). Total SB showed multivariable-adjusted (including for MVPA) associations with SBP (mean difference per 10 min per day greater SB: 0.025 mm Hg, 95% confidence interval: 0.002 to 0.047), DPB (0.023 mm Hg, 0.007 to 0.040), total cholesterol (0.004 mmol/l, 0.002 to 0.005) and HDL-C (−0.0006 mmol/l, −0.00119 to −0.0001). TV time was associated with SBP (0.075 mm Hg, 0.036, 0.113), DBP (0.052 mm Hg, 0.024, 0.081), total cholesterol (0.005 mmol/l, 0.002 to 0.008), and HDL-C (−0.0013 mmol/l, −0.0023 to −0.0002). Neither total SB nor TV time were associated to hemoglobin A_{1c} (E. Stamatakis, M. Hamer, K. Tiling and DA. Lawlor, unpublished data, under review). We examined whether the observed associations between SB and nonadiposity risk factors are explained by the two adiposity proxies by examining them against the criteria used for prospective mediation (10). We then sought to quantify the extent to which (%) the adiposity proxies mediated the associations using a method used previously by us (5,9) and others (11). This method involved separately adding BMI or WC into a basic (sex and age-adjusted) logistic regression model. Outcomes in these models were dichotomised risk factor using standard cutoffs (HDL < 1.5 mmol/l; cholesterol > 5 mmol/l (13); SBP > 140 mm Hg; DBP > 90 mm Hg (13)). We calculated the extent to which the adiposity markers explained raised levels for each nonadiposity risk factor using this formula: $(OR_{\text{basic model}} - OR_{\text{adjusted}})/OR_{\text{basic model}} - 1) \times 100$ (4,9,11). In an alternative analysis we used the Sobel mediation bootstrapping technique (14) to test the explanatory power of the adiposity indexes entered as continuous variables. BMI, WC and all outcomes were entered as z scores for this analysis. Analyses were performed using SPSS version 17 (SPSS, Chicago, IL).

RESULTS

The present analysis included 5,067 participants with valid blood biomarkers and exposures/covariables data who reported no cardiovascular disease (stroke, ischemic heart disease). **Supplementary Table S1** online presents the descriptive characteristics of the sample. Men reported a mean of 435 ± 163 and women 378 ± 153 min per day of sedentary time (sex difference $P < 0.001$). Both BMI and WC fulfilled the basic criteria (10) to be considered as explanatory variables of the relationship between SB and the examined cardiometabolic risk factors: (i) the exposure (sedentary time) were associated with both BMI and WC. (ii) In fully-adjusted (including for MVPA) linear regression models where BMI or WC was the exposure and each nonadiposity risk factor was the outcome, both potential mediators were associated to the outcomes: BMI was associated with SBP (unstandardised β coefficient corresponding to mean difference per 0.1 unit increase in BMI: 0.542 mm Hg, 95% confidence interval: 0.468 to 0.617), DBP (0.538, 0.485 to 0.592), HDL (−0.022, −0.024 to −0.020), total cholesterol (0.026, 0.020 to 0.032). WC was associated with SBP (0.211, 0.181 to 0.242), DBP (0.221, 0.199 to 0.243), HDL (−0.009, −0.010 to −0.008), total cholesterol (0.011, 0.009 to 0.013). TV time exhibited similar associations (data not shown). (iii) When the potential mediators are entered in (mutually exclusive) regression models assessing the association between SB and each outcome, the associations were no longer significant or were considerably weakened. Entering BMI in the SBP models changed the β coefficient (corresponding to mean difference per 10 min greater SB) from 0.0287 (0.0049 to 0.0525) to 0.0090 (−0.0146 to 0.0325), in the DBP models from 0.0279 (0.0106 to 0.0451) to 0.0083 (−0.0086 to 0.0251), in the HDL models from −0.0008 (−0.0014 to

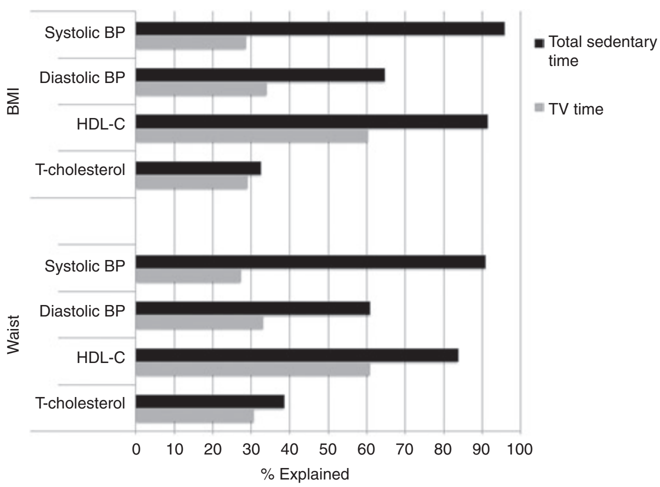

Figure 1 The extent to which adiposity markers explain the association between total self-reported and television viewing sedentary time with raised cardiovascular risk factors. BP, blood pressure; HDL-C, high density lipoprotein cholesterol; T-Cholesterol, total cholesterol.

−0.0002) to −0.0002 (−0.0008 to 0.0004), in the total cholesterol models from 0.0036 (0.0017 to 0.0055) to 0.0028 (0.0009 to 0.0047). Entering WC in the SBP models changed the SB β coefficient to 0.0111 (−0.0124 to 0.0347), in the DBP models to 0.0095 (−0.0073 to 0.0263), in the HDL models to −0.0003 (−0.0008 to 0.0003), and in the total cholesterol models to 0.0027 (0.0009 to 0.0045). TV time alone met all above criteria in a similar fashion (data not shown). **Figure 1** shows that BMI explained a large proportion of the observed associations of total sedentary time, particularly with SBP (95.9%), HDL-C (91.4%), and DBP (64.7%). Compared to BMI, WC explained a slightly lower, but still large, proportion of the associations with each risk factor. A lower, but still considerable, proportion of the associations between TV time and risk factors were explained by BMI (range 28.6–60.3%) and WC (27.3–60.7%) (**Figure 1**). Repeating the explanatory analyses with BMI and WC entered as continuous variables using the Sobel method (14) also showed that both adiposity indicators were significant mediators of the associations between SB and the outcomes (data not shown).

DISCUSSION

In this study of a representative sample of the English adult population we observed that the associations between SB and cardiometabolic risk factors are largely explained by markers of adiposity. Previous evidence suggests that the association between sedentary time and adiposity might be bidirectional (6). Some evidence shows that obesity might increase SB, whilst other data from the 1958 British birth cohort has shown that more frequent television viewing in adolescence and early adulthood is associated with greater BMI gains through to mid-adulthood (15). Given that our study was cross-sectional we were unable to explore the direction of the association, nor the extent to which the association between sedentary time and adiposity is causal. For associations with other cardiometabolic risk factors adjustment for BMI or WC attenuated these towards the null. Given the possibility that greater BMI/WC may result in increased SB or TV viewing or vice versa and that our study is cross-sectional we are unable to determine whether this attenuation represents confounding by these measures or possibly mediation. To further address this, large prospective studies with measures of SB and with repeat measurements of BMI/WC would be required. The finding that adiposity markers explain the associations between SB and other cardiometabolic risk markers partly confirms our earlier work that showed BMI explained ~12% of the relationship between screen-based entertainment and risk of future cardiovascular disease events (5).

The key strengths of our study were the large sample size and our SB questions enquired about multiple domains including both leisure time and occupational sitting/standing. The main limitation of this study is the cross-sectional design, which precludes us from making strong statements about mediation as this would require prospective design. Another limitation is that the occupational SB variable also include sitting. Nevertheless, we would expect that it is by far more likely that the large majority of office-based occupations involve much more sitting than standing and very few occupations involve standing quietly for more than a few seconds. Finally, the SB measurements were self-reported and therefore may contain biases. Although objective data were available to us, accelerometry-measured SB was not associated with any of the biomarkers or blood pressure and as such it would be inappropriate to examine if the adiposity markers explain nonexistent associations.

In conclusion, adiposity seems to largely explain these associations between SB and the examined cardiometabolic risk markers. Future prospective studies with capacity to test for mediation should replicate these results.

SUPPLEMENTARY MATERIAL

Supplementary material is linked to the online version of the paper at http://www.nature.com/oby

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DISCLOSURE

The authors declared no conflict of interest.

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