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- 1 Title
- 2 JOINT EFFECT OF PHYSICAL ACTIVITY AND SEDENTARY BEHAVIOUR ON CARDIOVASCULAR RISK
- 3 FACTORS IN CHILEAN ADULTS

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5 **Short title -** Physical activity, sedentary behaviour and cardiometabolic health

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39	ABSTRACT
40	Background - To investigate the associations between combined categories of moderate-to-vigorous physical
41	activity (MVPA) and sedentary behaviour (SB) and markers of adiposity and cardiovascular risk in adults.
42	Methods - 5,040 participants (mean age 46.4 years and 59.3% women) from the cross sectional Chilean National
43	Health Survey 2009-2010 were included in this study. MVPA and SB were measured using the Global Physical
44	Activity questionnaire. Four categories were computed using MVPA- and SB-specific cut-offs ("High-SB &
45	Active", "Low-SB & Active", "High-SB & Inactive" and "Low-SB & Inactive").
46	Results - Compared to the reference group ("High-SB & Inactive"), those in "High-SB & Active" and "Low-SB &
47	Active" were less likely to have an obese BMI (OR: 0.67 [0.54; 0.85], p=0.0001 and 0.74 [0.59; 0.92] p=0.0007,
48	respectively) and less likely to have metabolic syndrome (OR: 0.63 [0.49; 0.82], p<0.0001 and 0.72 [0.57; 0.91],
49	p=0.007), central obesity (OR: 0.79 [0.65; 0.96], p=0.016 and 0.71 [0.59; 0.84], p<0.0001), diabetes (OR: 0.45
50	[0.35; 0.59], p<0.0001 and 0.44 [0.34; 0.56], p<0.0001) and hypertension (OR: 0.52 [0.43; 0.63], p<0.0001 and 0.60
51	[0.50; 0.72], p<0.0001), respectively.
52	Conclusions - Being physically active and spending less time in sedentary behaviours was associated with lower
53	adiposity and improvements in cardiovascular risk factors.
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55	Keywords: physical activity, sedentary behaviour, cardiovascular, obesity

INTRODUCTION

There is strong evidence linking physical inactivity and sedentary behaviour (SB) to increased risk of adverse health outcomes, including type 2 diabetes (T2D), cardiovascular disease (CVD) and all- and specific-cause mortality(1, 2). Increases in physical activity (PA), particularly moderate-to-vigorous physical activity (MVPA), are associated with improved health outcomes, with strong evidence of a dose response relationship(1-3). SB and MVPA share a weak inverse relationship, and it is possible for an individual to be highly physically active but also highly sedentary(2).

Most previous research has focused on the independent associations of PA, MVPA or SB with markers of adiposity and cardiometabolic risk(4, 5). Research into the associations between combined PA / SB behaviours and morbidity and mortality outcomes is therefore limited. Some studies have explored techniques for quantifying the relationships and patterns of MVPA and SB(6-8), however few studies have investigated the associations between combined categories of PA and sedentary time and cardiometabolic markers(9, 10). These studies reported that participants who engaged in ≥150 min/week of MVPA had favourable cardiometabolic health profiles compared to adults who engaged in <150 min/week of MVPA, regardless of their sedentary status(9, 10). While this may have important clinical implications, as those with highly sedentary lifestyles may be able to attenuate the deleterious effects of SB by increasing their MVPA, further population level research is required to validate these findings.

Using data from the Chilean National Health Survey (CHNS) 2009-2010, a sexennial assessment of population health, the following research questions were investigated: 1) What are the associations between combined PA and sedentary time and obesity and metabolic markers? 2) What is the relationship between combined PA / SB categories and cardiometabolic risk?

METHODS

Study Population

Participants from the 2009-2010 Chilean National Health Survey (aged >18 years) were used as the cohort for this cross-sectional analysis. The CNHS is a large, nationally representative population-based study of biological and lifestyle risk factors, dietary status and health conducted every six years in Chile(11). Complex random stratified

sampling was used to cover a nationally representative sample based on statistics from the 2002 Chilean National Census, which included strata from administrative regions (county) and urban/rural locations, as described in detail elsewhere(11). Participants who were pregnant at the time of the assessment, those who were unable to attend an assessment centre and individuals aged <18 years were excluded from the National Health Survey sampling(11). The CNHS was funded by the Chilean Ministry of Health and led by the Department of Public Health, The Pontificia Universidad Católica de Chile. The CNHS was approved by the Ethics Research Committee of the Faculty of Medicine at the Pontificia Universidad Católica de Chile. All participants who participated in the CNHS provided written informed consent. Data collection took place in two stages: the first stage (n=5,434) comprised face-to-face interviews to collect information on self-reported health, household characteristics and living conditions. Response rate from the eligible population to the CNHS was 85%. In total, 5,276 participants (97%) provided data on PA behaviours collected with the Global Physical Activity Questionnaire (GPAQ), version 2(12). Complete data was available for 5,040 participants for the present analysis. Measurements To ensure quality of data collection, standardised protocols were followed by trained nurses and technicians. Sociodemographic data was collected for all participants, including age, sex, place of residency (urban/rural), education level (primary, secondary or beyond secondary) and monthly gross household income (≤US \$247.00 (lowest), US \$248.00-1180.00 (middle) and >US \$1180.00 (highest). Height was measured to the nearest 0.1 cm using a portable stadiometer and weight was measured to the nearest 0.1 kg using a digital scale (Tanita HD313) with participants removing their shoes and wearing light clothing. Body mass index (BMI) was calculated as weight/height² and classified using the World Health Organization (WHO) criteria ($<18.5 \text{ kg.m}^{-2}$ – underweight, 18.5 to 24.9 kg.m⁻² – normal, 25.0 to 29.9 kg.m⁻² – overweight and \ge 30 kg.m⁻²

- obese)(13). Central obesity was defined as waist circumference >88 cm for women and >102 cm for men(14).

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Venous blood samples were drawn after an overnight fast. Glucose, HbA1c (%), triglycerides, total cholesterol and HDL cholesterol concentrations were determined by enzymatic colorimetric methods using standardised commercially available kits as described elsewhere(11). Blood pressure was measured by trained staff and the mean of three readings recorded. Hypertension was defined as systolic blood pressure ≥ 140 mmHg and diastolic blood pressure ≥ 90 mmHg or current treatment for hypertension(15). Type 2 diabetes was defined as fasting glucose ≥ 7.0 mmol. 1^{-1} or current treatment for diabetes(16). High total cholesterol was defined as \geq 5.2 mmol. 1^{-1} , high triglycerides >1.7 mmol.l⁻¹ and low HDL cholesterol ≤1 mmol.l⁻¹ for women and ≤1.3 mmol.l⁻¹ for men, or current treatment for dyslipidaemia. The presence of metabolic syndrome was defined using the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria (17): Waist circumference >102 for men and > 88 cm for women; serum triglycerides >1.7 mmol.l⁻¹; HDL cholesterol: <1.0 mmol.l⁻¹; systolic blood pressure ≥130 mm Hg or diastolic blood pressure >85 mmHg; fasting serum glucose >5.6 mmol.l⁻¹ or current treatment for diabetes. Each metabolic syndrome component was classified as either present or absent per the above criteria. The number of metabolic syndrome components present for each participant were calculated to provide an ordinal measure of cardiometabolic health. The presence of ≥ 3 components were used to indicate the presence of metabolic syndrome. The GPAQ (version 2) was used to measure PA and SB in the CNHS. Developed by the WHO to measure population-level PA behaviours, the GPAO uses standardised protocols shown to be valid and reliable and adaptable to incorporate cultural and other differences(18-20). The GPAQ assesses sedentary behaviour (total time spent sitting) and three domains of PA: occupational (PA at work), active-commuting (PA from travel) and recreational (PA at leisure). Occupational, active-commuting and recreational PA were assigned a metabolic-equivalent value (MET; where 1 MET = \sim 3.5 ml.kg⁻¹.min⁻¹) using recommendations made by the GPAQ protocol (4-METs was used for moderate and transport-related activities and 8-METs for Vigorous activities)(12). PA was then categorised into: inactive individuals (<600 MET.min.week⁻¹) and active individuals (≥600 MET.min.week⁻¹)(12). Sedentary behaviour was derived using the following question: 'How much time do you usually spend sitting or reclining on a typical day?' The GPAQ specified that this question is about sitting or reclining. It includes time spent sitting at a desk, sitting with friends, travelling in a car, bus or train, reading, playing cards or watching television, but does not include time spent sleeping(12, 20).

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For each individual, the average number of minutes spent in MVPA, light-intensity physical activity and SB were calculated. Based on other studies(10), the SB to light-intensity PA ratio (average sedentary time / average light-intensity PA time) was used for the classification of sedentary status. Participants were then split into quartiles based on this ratio. Given that the levels of SB in the general population are predominantly high(10), a conservative, data-driven approach was undertaken and individuals were classified as 'low sedentary' if they resided in quartile 1 or 2 and 'high sedentary' if they resided in quartiles 3 or 4. MVPA was classified as 'physically active' or 'physically inactive' on the basis of whether or not participants accumulated at least 600 MET.min.week-1 of MVPA. This allowed the formation of four mutually exclusive behavioural categories.

Smoking was collected with self-reported questionnaires and classified as non-smoker, ex-smoker or smoker. A Healthy Diet Score using food intake information was collected using a self-reported food frequency questionnaire, as described elsewhere (21, 22). The intakes of four food groups (whole grain, fish, fruit and vegetables) were translated into a point-based score (low=0, moderate=0.5 and high=1 point). As four foods items were considered the total diet score for each individual could range from 0 (unhealthy diet) to 4 points (healthy diet) (Table S1).

Statistical Analysis

Survey-weighted descriptive characteristics are presented as adjusted means with standard deviation (SD) for quantitative variables or as a proportion for categorical variables. To account for the differential probability of selection, all percentages and means were weighted using the sample weights provided by CNHS (11). Quantitative data were checked for normality using skewness and kurtosis normality tests.

To investigate associations between combined SB/PA categories and health outcomes, all continuous outcomes were standardised and then analysed using multiple linear regression analyses, with adjustment for potential confounders. The results therefore were presented as standardised beta coefficients with their respective 95% confidence intervals (95% CI). The "High-SB & inactive" group was used as the reference for all analyses. Associations between SB/PA categories and binary health outcomes were investigated using logistic regression. All models were adjusted for age,

sex, place of residency (urban/rural), education, income, smoking and Healthy Diet Score. Metabolic outcomes were additionally adjusted for BMI categories. Statistical significance was accepted at p <0.05, and all statistical analyses were conducted using STATA 14 (StataCorp; College Station, TX).

RESULTS

Overall, 5,040 participants with available data were included in the study, mean age 46.4 years (SD=18.6, range 18 to 100 years), mean BMI 27.9 kg.m⁻² (SD=5.4) and 59.3% of the cohort were women. Compared to physically active individuals, irrespective of SB category, those who were classified as physically inactive were older, more likely to be female, had higher BMI and WC and therefore a higher prevalence of obesity and central obesity. They also had a lower proportion of current smokers and had a lower Healthy Diet Score. Those classified as highly sedentary, independent of physical activity levels, were predominately from the highest education group, were the most affluent and were more likely to be city-dwellers compared to the low SB group. The highest Healthy Diet Score was observed for those who were physically active with higher time spent sitting.

The associations of combined PA and SB categories with standardised adiposity and cardiovascular risk markers are reported in Table 2. Overall there were significant negative associations between adiposity and metabolic markers and behaviour categories "High-SB & Active" and "Low-SB & Active". For adiposity, when compared to participants categorised as "High-SB & Inactive", those categorised as "High-SB & Active" or "Low-SB & Active" showed significant negative associations with both waist circumference (WC) (standardised β : -0.258 and β = -0.233, respectively) and BMI (standardised β : -0.182 and -0.156, respectively).

In terms of cardiometabolic risk factors, participants categorised as "High-SB & Active" or "Low-SB & Active" showed significant negative associations with systolic blood pressure (standardised β : -0.290 and -0.184, respectively), HbA1c (standardised β : -0.286 and β = -0.183, respectively) and fasting glycaemia (standardised β : -0.238 and β = -0.174, respectively). Compared to participants categorised as "High-SB & Inactive" participants classified as "Low-SB & Inactive" had a lower HbA1c concentration but no significant differences were observed for other metabolic markers (Table 2).

Compared to the reference group, those in "Low-SB & Active" and "High-SB & Active" were less likely to have a BMI ≥30 kg.m⁻² (overall obesity) (OR: 0.74 [95% CI: 0.59; 0.92] and OR: 0.67 [95% CI: 0.54; 0.85], respectively) or be centrally obese (OR: 0.71 [0.59; 0.84] and OR: 0.79 [0.65; 0.96], respectively) (Table 3). These groups were also less likely to have hypertension (OR: 0.60 [0.50; 0.72] and OR: 0.52 [0.43; 0.63]), or have metabolic syndrome (OR: 0.72 [0.57; 0.91] and OR: 0.63 [0.49; 0.82]). "Low-SB & Active", "High-SB & Active" and "Low-SB & Inactive" groups were 56%, 55% and 31% less likely, respectively, to have T2D than those classified as "High-SB & Inactive" (Table 3).

DISCUSSION

Main finding of this study

The main finding of this study is that a combination of being physically active and spending low time in sitting-related behaviours is beneficial for markers of adiposity and cardiometabolic health. Our data also suggest that people who are categorised as 'highly sedentary' may be able to attenuate the deleterious effects of this by increasing their physical activity. These results suggest the promoting increased MVPA should be priority to reduce cardiometabolic risk in adults.

What is already known on this topic

Although some studies have started to explore different techniques for quantifying combined connections and patterns of MVPA and SB, to our knowledge, only two studies have investigated the associations between combined categories of physical activity and sedentary behaviour with metabolic markers (9, 10). Loprinzi et al. found that in comparison to adults who engaged in <150 min.week⁻¹ of MVPA with high sedentary time (sedentary time > light-intensity physical activity time), participants engaging in ≥150 min/week of MVPA had a more favourable metabolic profile regardless of their sedentary status(9), suggesting that regular MVPA may offset some of the harmful consequences of a habitually sedentary lifestyle. Similar results have been published by Bakrania and colleagues on a subset of the 2008 Health Survey for England dataset where the effects of combined categories of PA and SB, measured objectively with accelerometer, on metabolic markers were investigated. The study reported

that in comparison to the "High-SB & inactive" group, the "Low-SB & Active" group had a significantly lower BMI (-1.67 kg.m⁻²), waist circumference (-1.17 cm), HbA1c (-0.12 %) and higher HDL-cholesterol (+0.09 mmol.l⁻¹). Those classified as "High-SB & Active" also had a more favourable BMI (-1.64 kg.m⁻²), HbA1c (-0.11 %) and HDL-cholesterol (+0.07 mmol.l⁻¹) compared to "High-SB & inactive" individuals. Our findings are in agreement with those reported by Bakrania and colleagues(10) with respect to obesity and HbA1c but not for lipids profile. These discrepancies may be explained by differences in measurement techniques. Bakrania *et al.* used accelerometry-measured PA and SB, while the CNHS used self-reported measures. Using self-reported measures may attenuate any true associations between behaviours and outcomes, as these data are prone to recall bias(23).

What this study adds

Each incremental improvement in the SB/PA profile was associated with a further reduction in the likelihood of T2D ("Low-SB & Inactive", "High-SB & Active", and "Low-SB & Active" show a 30%, 55% and 56% reduction, respectively). However, increasing physical activity may be more effective than reducing sedentary behaviours for adiposity and some cardiometabolic risk factors because having low SB while still being physically inactive was not associated with significantly reduced odds of obesity, high blood pressure, abnormal lipids profile or metabolic syndrome. Those who were in the physically active groups had reduced odds for all of these risk factors except abnormal lipids profile. The greatest health benefits, however, were seen in physically active people with High-SB. This group was associated with 7%, 8% and 9% reduced odds of obesity, hypertension and metabolic syndrome, respectively, compared to the "Low-SB & Active" group. Moreover, bigger magnitudes of association were observed for obesity and metabolic markers in the "High-SB & Active" compare to "Low-SB & Active" group. These greater benefits found for individuals who were active but spent more time sitting behaviours could be explained by the socio-demographic characteristics of this group. A higher proportion of people were from more affluent and highly educated groups more representative of office-related occupations.

The importance of physical activity is more pronounced than sedentary behaviour for markers of cardiometabolic health in South American adults. Those who were physically active showed significant improvements in more risk factors than those who simply reduced their sedentary time, compared to the inactive and highly sedentary reference

group. Reducing SB appears to have a beneficial impact on T2D risk, but positively modifies the odds of other cardiometabolic risk markers only in conjunction with a physically active lifestyle. This suggests that health promotion guidelines should focus primarily on increasing population levels of MVPA and secondarily on reducing sedentary time.

Limitations of this study

The advantages of this study are that it used a representative sample of a national population and is the first of its kind to investigate the combined effects of PA and SB on adiposity and cardiometabolic outcomes in a sample of South American adults. However, there are also important limitations that need to be considered. The self-reported information used to determine PA and SB may limit data accuracy and subsequently moderate the results, as shown in previous studies(23). The use of cross-sectional data does not permit assessment of any cause and effect of the associations described, and there is possibility of reverse causality and residual confounding. Since the reference group of highly sedentary physically inactive adults is substantially and significantly older than the physically active groups, the former may have had a longer exposure to the detrimental behaviour of physical inactivity and prolonged sitting time. Although our models were adjusted for age we cannot rule out that differences within groups may be due to longer exposure time to unhealthy behaviours (24). Another important limitation of our study was the lack of data on specific types of sedentary behaviour undertaken, such as TV-viewing or PC screen time at leisure or during working hours. Previous studies have shown that not all sedentary behaviours have the same detrimental effect on health (25, 26). Discretionary behaviours such as TV-viewing has been associated with larger adverse effects than PC screen or sitting time during working hours (26, 27).

In conclusion, being physically active and spending low time in sitting-related behaviours was associated with a healthier metabolic and adiposity profile. Individuals who are categorised as 'highly sedentary' may be able to attenuate the deleterious effects of this by increasing their physical activity. Therefore, promoting increased population PA levels alongside recommendations to reduce sitting time, or break prolonged periods of sitting time, should be treated as a priority to reduce cardiometabolic risk in adults. However, given the observational nature of

this study, the interaction and relative magnitude of effects of physical activity and sedentary behaviours on health needs further elucidation through intervention trials to better inform public health policy and guidance.

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Competing interests

None

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