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## 1 HIGHER LEVELS OF SELF-REPORTED SITTING TIME IS

# 2 ASSOCIATED WITH HIGHER RISK OF TYPE 2 DIABETES

# 3 INDEPENDENT OF PHYSICAL ACTIVITY IN CHILE

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5 Short title: Self-reported sitting time and Type 2 diabetes

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# 52 **Background** – Sitting behaviours have increased markedly during the last 2 decades in Chile. However, 53 their associations with health outcomes such as diabetes have not been reported. Therefore, the aim of this 54 study was to investigate the independent association of self-reported sitting time with diabetes-related markers and diabetes prevalence in Chile. 55 56 Methods – This cross-sectional study included participants (aged ≥18 years) from the Chilean National Health Survey 2009-2010 (n=4,457). Fasting glucose and haemoglobin A1c (HbA1c) were measured by 57 standardised protocols. The prevalence of type 2 diabetes (T2D) was determined using WHO criteria. 58 59 Physical activity and time spent sitting were determined using the Global Physical Activity Questionnaire 60 (GPAQ). 61 **Results:** The odds ratio for T2D was 1.10 [95% CI: 1.04 to 1.16, p=0.002] and 1.08 [1.02 to 1.14, 62 p=0.002] per one hour increase in sitting time in men and women, respectively, independent of age, 63 education, smoking, BMI and total physical activity. Overall, prevalence of T2D was 10.2% and 17.2% in 64 individuals classified in the lowest and highest categories of sitting time, respectively. No significant 65 associations were found between sitting time and glucose or HbA1c. 66 Conclusions: Sitting time is positively associated with diabetes risk, independent of socio-demographic, obesity and physical activity levels, in the Chilean population. 67 68

Abstract

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Keywords

Sitting time, type 2 diabetes, adiposity, glycaemia, HbA1c

# INTRODUCTION

Type 2 diabetes (T2D) is a major public health problem, accounting for 10% of healthcare expenditure
and almost 400 million cases globally (1). Although the prevalence of T2D is increasing worldwide, the
increase differs substantially by country, with 80% of people with diabetes living in low and middle
income countries (1). Compared to other Latin American countries, Chile has the second highest
prevalence of T2D (11.2%), which is below Guyana (15.8%) but above Brazil (8.7%) (1). Similarly, the
prevalence of risk factors for non-communicable diseases (NCDs) have been higher in Chile than the
average prevalence for the whole region (2). This could be explained by the rapid nutritional transition in
Chile(3), where the Chilean population's lifestyle, including diet and physical activity (PA), has become
progressively westernized. Concurrently, an increase in sedentary-related behaviours has been observed
due to urbanization and greater use of home appliances, cars and televisions (TVs) (3, 4). However, it is
unclear whether these changes have contributed to the increased prevalence of T2D and other NCDs (4-6).
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# **METHODS**

This analysis was based on participants aged ≥18 years from the 2009-2010 cross-sectional Chilean National Health Survey (CNHS). The CNHS is the largest, nationally representative population-based survey of risk factors, dietary status and health in Chile with a stratified multistage probability sample of 5,416 participants (6). 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. The response rate from the eligible population to the CNHS was 85%. In total, 5,276 participants (97%) provided data on sedentary behaviour and PA. In addition, 121 participants (2%) with PA data were excluded based on the Global Physical Activity Questionnaire (GPAQ) protocol for outlier detection (48% women and 83% urban). Complete data for self-reported sitting time and diabetes-related markers was available for 4,457 participants for the present analysis. Type 2 diabetes was used as the main outcome for the current study and sedentary behaviour (sitting time) was treated as the main exposure variable. Socio-demographics, smoking, BMI categories and total physical activity (which includes light, moderate and vigorous PA) were treated as covariates in this study. Analysis was performed for the overall cohort and also stratified by sex (See supplementary material). Sedentary behaviour was estimated using the following question: How much time do you usually spend sitting or reclining on a typical day? This was defined as sitting or reclining at work or at home, getting to and from places, or with friends and included time spent sitting at a desk, travelling by car, bus or train, reading, playing cards or watching television, but did not include time spent sleeping (13). Validation

studies have shown a weak correlation (range = 0.23-0.26) with objective measures (14) between self-

reported and objectively measured sedentary behaviour.

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The GPAQ (version 2) (13) was used to measure PA based on standardised protocols (13). Three domains of PA were assessed: occupational (PA at work), active-commuting (PA from travel) and recreational (PA at leisure). GPAQ has been previously validated against objective measures of PA showing a moderate correlation (15). Total physical activity was derived as the sum of work, leisure and transport physical activity, and presented as MET.hour.week⁻¹. Algorithms were used to categorize weekly PA into two categories: inactive individuals (<150 minutes of moderate to vigorous intensity PA per week or its equivalent, <600 MET.min.week⁻¹) and active individuals (≥600 MET.min.week⁻¹) (13).

Socio-demographic data was collected for all participants, including age, gender, education level (primary, secondary or beyond secondary), years of schooling, monthly household income and smoking status (non-smoker, ex-smoker or smoker). 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 (16) :<18.5 kg.m $^{-2}$  – underweight; 18.5 to 24.9 kg.m $^{-2}$  – normal; 25.0 to 29.9 kg.m $^{-2}$  – overweight and  $\geq$ 30 kg.m $^{-2}$  – obese. Waist circumference (WC), measured with standardised procedures and trained staff, was used to classify participants as centrally obese (>88 cm for women and >102 cm for men) (16).

Fasting glucose and haemoglobin A1c (HbA1c) were measured from whole blood collected by trained nurses after an eight hour overnight fast. Analysis of samples was conducted in a certified laboratory facility and have been described in detail elsewhere (6). T2D was determined via the WHO criteria (fasting plasma glucose  $\geq$  126mg.dl<sup>-1</sup>) (17) and/or by self-report of a pre-existing medical diagnosis and/or in those who reported using glucose lowering medication.

Statistical analyses were performed using survey-weighted values, including home area population density (urban or rural) and geographical regions. To account for the differential probability of selection, all

percentages and means were weighted using the sample weights provided by CNHS.(6) Statistical analyses were conducted using STATA 14 (StataCorp; College Station, TX). Descriptive characteristics are presented as adjusted means with 95% CI for quantitative variables or as a proportion for categorical variables. Quantitative data was checked for normality using skewness and kurtosis normality tests. To investigate the association between sitting time and socio-demographic, anthropometric and metabolic outcomes, four categories of sitting time were derived, where category 1 (Lowest) was <4 h.day<sup>-1</sup>, category 2 (Lower/Middle) was 4.0-5.9 h.day<sup>-1</sup>, category (Middle/Higher) was 6.0-7.9 h.day<sup>-1</sup> and category 4 (Highest) was ≥8.0 h.day<sup>-1</sup>. Associations between sitting time and continuous variables were investigated using regression analyses, adjusted for covariates as appropriate. Results are presented as means and 95% CI for the overall cohort and by sex. Associations between sitting time and categorical outcomes were investigated using Chi-Square analysis or logistic regression, as appropriate. The prevalence of T2D by sitting time was investigated using the Generalized Linear Model and trends were obtained from fitting sitting time as an ordinal exposure into the models. The association between sitting time and T2D risk was analysed using logistic regression. All models were adjusted for age, sex, home area population density (urban or rural), education level (primary, secondary, beyond secondary) and smoking (non-smoker, ex-smoker and smoker). Metabolic outcomes were additionally adjusted for BMI categories (underweight, normal, overweight and obese) and total physical activity expressed in METs.h.week<sup>-1</sup>. A p-value of <0.05 was considered significant in all analyses.

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#### **RESULTS**

From 5,416 participants included in the CNHS, 4,457 had both PA and metabolic data available. The mean age of the cohort was 41.6 years (SD: 18.6) and 60% were women. PA levels were higher in men (150.9 MET.h.week<sup>-1</sup>, SD: 170.4) than women (95.2 MET.h.week<sup>-1</sup>, SD: 117.5) (p<0.0001), but only 23.1% and 17.1% of men and women respectively met the WHO PA recommendation of ≥600 MET.min<sup>-1</sup>

<sup>1</sup>.week<sup>-1</sup>. No significant differences were found for total sitting time per day between men (3.72 h.day<sup>-1</sup>,

SD: 3.0) and women (3.38 h.day<sup>-1</sup>, SD: 2.9).

Both men and women showed a trend for increasing body weight as the time spent sitting/day increased (Table 1, S1, S2). However, waist circumference was significantly positively associated with sitting time in women (Table S2) but not men (Table S1), whereas BMI was significantly positively associated with sitting time in men but not women. No associations were found for blood glucose and HbA1c levels and time spent sitting/day (Table 1, S1, and S2). Participants in the highest category of sitting time (≥8h.day⁻¹) had a higher prevalence of physical inactivity compared to participants in the lowest category (<4h.day⁻¹). They were also more likely to be from an urban setting and have a higher education level (Tables 1, S1 and S2). Similarly, prevalence of T2D increased significantly by each category and by each hour increase in sitting time for both men and women (Fig. 1A, Tables 1, S1, S2). When a sensitivity analyses was conducted by adjusting the models for WC instead of BMI the results remain similar (Table S3)

The odds ratio for T2D was 1.10 (95%CI: 1.04 to 1.16) and 1.08 (1.02 to 1.14) per each extra hour increase in sitting time in men and women, respectively. For participants in the highest category of sitting time (≥8 h.day<sup>-1</sup>), the odds ratio for T2D was 1.82 and 1.81 for men and women, respectively, when compared to those in the lowest category of sitting time (Table 2). After adjustment for age, home area population density (rural/urban), education, BMI and total PA (Fig. 1B) the magnitude of the association remained similar.

#### DISCUSSION

#### Main finding of this study

The main finding of this study is that increasing sitting time correlates significantly with an increase in T2D risk independent of physical activity, obesity, smoking and main socio-demographic factors in both men and women. An additional hour of sitting per day increased the odds of T2D by 10% and 5% for

males and females, respectively. These finding provide evidence that may help to update the current Chilean physical activity guidelines by including recommendations aimed at reducing sitting time along with increasing PA levels.

#### What is already known on this topic

Sitting time is known to be a strong indicator of overall sedentary behaviour and our results are in agreement with previous cross-sectional and longitudinal studies which have reported a strong association between sitting time and T2D.(12, 18, 19) The odds for developing T2D reported in this study were 1.68 [95%CI: 1.03 to 2.74] for women and 2.10 [1.31 to 33.31] for men in the highest category of sitting time versus the lowest category of sitting time. These compare favourably with the results reported by Hu et al. in women (OR: 1.70 [1.19 to 2.42]) and men (OR: 2.87 [1.46 to 5.65]) from the United States.(20, 21) Our results are also comparable to findings from a recent meta-analysis conducted in 794,577 participants, where the greatest sedentary time compared with the lowest was associated with a 1.12 increase in the odds of T2D.(22) The dose-response relationship for T2D per hour increase in sedentary behaviours has been reported in a meta-analysis conducted by Grontved et al. in 175,938 individuals, where the odds of T2D increased by 20% per 2-hours increase in time spent in sedentary activities.(7) These results are similar to those found in our study, where the odds of T2D increased by 21% per 2 hours increase in sitting time (OR: 1.21 [1.09 to 1.33], p<0.0001).

## What this study adds

The current study has relevant public health implications. Rapid urbanization in Latin America has been accompanied by an increasing burden of NCDs.(3, 4, 23-25) It has led to important changes in modes of daily transportation; in particular, a major shift from public to individual motorised transport systems.(3, 26) This has played a role in reducing PA in the region(27, 28) but also in increasing sedentary behaviours.(3, 4, 27, 29) Surveillance data on sedentary behaviours in Chile will further increase understanding of the potential health burden the country may face in the future, as well as fill in the gaps

in our understanding of sedentary behaviour patterns in Latin American countries. In addition, the results described herein could support the national authorities in Chile to implement tailored PA and sedentary behaviour guidelines tackling prolonged sitting time in order to promote healthy and active lifestyles in atrisk population groups.

## **Limitations of this study**

There are strengths and limitations to be considered with respect to the interpretation of the current study. The CNHS provided an opportunity to test our research question in a large cohort and the main outcome used in this study was collected using trained staff and standard operating procedures.(17) The CNHS is representative of the general Chilean population with respect to age, sex and education but is not representative in other regards. Methodological issues related to the self-reported nature of the GPAQ are noted. Although sitting time and PA were measured by self-report using a validated questionnaire,(14, 15) misreporting of sedentary behaviours or PA may have attenuated the association between sitting time and T2D compared to objective measurement. Although our analyses excluded outliers and extreme values, potential bias arising from self-reported PA and sitting times cannot be fully disregarded. While the results presented in this study can be generalised to the Chilean population, as the survey was applied in a representative sample of the country, we cannot make any inferences or draw any causal associations from the results due to the cross-sectional nature of the survey.

Sitting time is associated with an increased risk of T2D in the Chilean population. This association was independent of main socio-demographic factors, obesity and PA levels, indicating that future public health messages should highlight the importance of reducing sitting time as well as increasing PA to help alleviate the effects of prolonged sitting time on health outcomes, such as T2D.

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#### **Competing interests**

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## FIGURE LEGEND

# Figure 1. Association of sitting time with type 2 diabetes in women and men.

Data is presented as prevalence per hour increase in sitting time (A) and as odds ratio (OR) per category of sitting time (B). Trend OR represents the odds ratio per category increase in sitting time. Model was adjusted for age, environment, education, smoking, BMI and total physical activity.

Table 1. Socio-demographic, adiposity, metabolic and physical activity characteristics by categories of sitting time.

	Categories of sitting time (h.day <sup>-1</sup> )				
	<4	4 - 5.9	6 - 7.9	≥8	P (trend)
Socio-demographic					
Age (y)	46.6 (45.9 to 47.2)	46.9 (45.6 to 48.2)	44.3 (42.4 to 46.1)	45.1 (43.5 to 46.7)	0.130
Women (%)	61.0 (59.3 to 62.6)	60.1 (56.9 to 63.3)	54.7 (49.7 to 59.6)	51.9 (47.7 to 56.1)	< 0.0001
Urban (%)	82.1 (80.7 to 83.4)	87.2 (85.1 to 89.4)	92.8 (90.2 to 95.3)	94.1 (92.1 to 96.1)	< 0.0001
Education (%)					< 0.0001
Up to Primary (≤8 y)	21.3 (16.3 to 27.4)	15.4 (11.3 to 20.6)	12.2 (8.3 to 17.5)	13.3 (8.2 to 20.7)	
Up to secondary (≤12 y)	57.8 (53.3 to 62.1)	56.3 (50.2 to 62.2)	56.2 (51.3 to 61.0)	49.4 (46.9 to 51.8)	
Beyond secondary (>12 y)	20.8 (16.7 to 25.6)	28.2 (24.3 to 32.4)	31.5 (26.7 to 36.9)	37.2 (29.7 to 45.4)	
Anthropometric					
Body weight (kg)	75.5 (72.3 to 78.6)	77.2 (71.3 to 83.1)	79.6 (70.1 to 88.5)	110.8 (103.4 to 118.2)	0.126
BMI (kg.m <sup>-2</sup> )	27.9 (27.7 to 28.1)	27.8 (27.4 to 28.2)	27.5 (26.9 to 28.1)	28.1 (27.6 to 28.5)	0.474
WC (cm)	95.7 (92.7 to 98.8)	101.1 (95.3 to 106.9)	98.2 (89.5 to 106.9)	118.2 (110.9 to 125.3)	0.024
Metabolic					
Glucose (mg.dl <sup>-1</sup> )	95.8 (94.6 to 96.9)	96.1 (93.8 to 98.2)	97.8 (94.6 to 101.3)	98.4 (95.6 to 101.2)	0.382
HbA1c (%)	6.40 (6.31 to 6.50)	6.31 (6.13 to 6.49)	6.61 (6.33 to 6.90)	6.51 (6.27 to 6.74)	0.334

T2D (%)	10.3 (9.2 to 11.4)	11.5 (9.3 to 13.7)	13.8 (10.2 to 17.4)	17.2 (13.8 to 20.5)	< 0.0001
Physical activity					
Total PA (MET.hr.wk <sup>-1</sup> )	146.4 (131.2 to 161.7)	130.9 (108.7 to 153.1)	63.4 (31.8 to 95.1)	60.0 (51.5 to 68.4)	<0.0001
Physical inactivity (%)	17.6 (16.2 to 18.9)	28.6 (25.6 to 31.5)	34.0 (29.3 to 38.7)	45.3 (41.2 to 49.5)	< 0.0001
Sitting time (hr.day <sup>-1</sup> )	1.87 (1.74 to 2.0)	4.44 (4.38 to 4.49)	6.38 (6.26 to 6.50)	9.51 (8.99 to 10.0)	< 0.0001

Data is presented as mean (95% CI) or as % for categorical variables. The p (trend) was estimated using General Linear Model for continuous variables and Chi-square test for categorical variables. Models were adjusted for age, education, home area population density (urban or rural) and smoking. Metabolic outcomes were further adjusted for BMI and total PA. Prevalence of T2D was estimated with Generalized Linear Models.

BMI, body mass index; HbA1c, haemoglobin A1c; MET, metabolic-equivalent value; PA, physical activity; T2D, type 2 diabetes; WC, waist circumference. Physical inactivity was defined as <600 MET.min<sup>-1</sup>.week<sup>-1</sup>.

**Table 2.** Odds ratio for type 2 diabetes by categories of sitting time

Categories of sitting time (h.day <sup>-1</sup> )					
<4	4 - 5.9	6 - 7.9	≥8	OR per category increase in sitting time	P (trend)
1.0 (ref)	0.94 (0.71 to 1.25)	1.51 (1.04 to 2.18)	1.73 (1.27 to 2.37)	1.20 (1.09 to 1.32)	<0.0001
1.0 (ref)	0.95 (0.71 to 1.26)	1.53 (1.05 to 2.21)	1.77 (1.29 to 2.42)	1.20 (1.09 to 1.33)	<0.0001
1.0 (ref)	0.88 (0.60 to 1.27)	1.48 (0.96 to 2.29)	1.62 (1.00 to 2.64)	1.15 (1.01 to 1.31)	0.037
1.0 (ref)	0.89 (0.62 to 1.30)	1.55 (1.00 to 2.40)	1.68 (1.03 to 2.74)	1.17 (1.02 to 1.33)	0.023
1.0 (ref)	1.04 (0.67 to 1.61)	1.38 (0.78 to 2.41)	2.09 (1.34 to 3.28)	1.26 (1.09 to 1.45)	0.002
1.0 (ref)	1.04 (0.66 to 1.62)	1.37 (0.77 to 2.42)	2.10 (1.31 to 3.31)	1.26 (1.08 to 1.46)	0.003
	1.0 (ref) 1.0 (ref) 1.0 (ref) 1.0 (ref) 1.0 (ref)	1.0 (ref) 0.94 (0.71 to 1.25) 1.0 (ref) 0.95 (0.71 to 1.26)  1.0 (ref) 0.88 (0.60 to 1.27) 1.0 (ref) 0.89 (0.62 to 1.30)  1.0 (ref) 1.04 (0.67 to 1.61)	1.0 (ref) 0.94 (0.71 to 1.25) 1.51 (1.04 to 2.18)  1.0 (ref) 0.95 (0.71 to 1.26) 1.53 (1.05 to 2.21)  1.0 (ref) 0.88 (0.60 to 1.27) 1.48 (0.96 to 2.29)  1.0 (ref) 0.89 (0.62 to 1.30) 1.55 (1.00 to 2.40)  1.0 (ref) 1.04 (0.67 to 1.61) 1.38 (0.78 to 2.41)	<4       4 - 5.9       6 - 7.9       ≥8         1.0 (ref)       0.94 (0.71 to 1.25)       1.51 (1.04 to 2.18)       1.73 (1.27 to 2.37)         1.0 (ref)       0.95 (0.71 to 1.26)       1.53 (1.05 to 2.21)       1.77 (1.29 to 2.42)         1.0 (ref)       0.88 (0.60 to 1.27)       1.48 (0.96 to 2.29)       1.62 (1.00 to 2.64)         1.0 (ref)       0.89 (0.62 to 1.30)       1.55 (1.00 to 2.40)       1.68 (1.03 to 2.74)         1.0 (ref)       1.04 (0.67 to 1.61)       1.38 (0.78 to 2.41)       2.09 (1.34 to 3.28)	<4       4 - 5.9       6 - 7.9       ≥8       OR per category increase in sitting time         1.0 (ref)       0.94 (0.71 to 1.25)       1.51 (1.04 to 2.18)       1.73 (1.27 to 2.37)       1.20 (1.09 to 1.32)         1.0 (ref)       0.95 (0.71 to 1.26)       1.53 (1.05 to 2.21)       1.77 (1.29 to 2.42)       1.20 (1.09 to 1.33)         1.0 (ref)       0.88 (0.60 to 1.27)       1.48 (0.96 to 2.29)       1.62 (1.00 to 2.64)       1.15 (1.01 to 1.31)         1.0 (ref)       0.89 (0.62 to 1.30)       1.55 (1.00 to 2.40)       1.68 (1.03 to 2.74)       1.17 (1.02 to 1.33)         1.0 (ref)       1.04 (0.67 to 1.61)       1.38 (0.78 to 2.41)       2.09 (1.34 to 3.28)       1.26 (1.09 to 1.45)

Data is presented as OR (95% CI) per categories of sitting time. The p (trend) was estimated by fitting sitting time categories as an ordinal variable into the Logistic regression models: Model 0 was adjusted for age, home area population density (urban or rural), education, smoking ad BMI; Model 1 was additionally adjusted for total physical activity and the analysis for the combined cohort (All) was additionally adjusted for sex. OR, odds ratio.