



## Revisión

### A systematic review of cross-sectional studies on the association of sedentary behavior with cardiometabolic diseases and related biomarkers in South American adults

#### *Revisión sistemática de estudios transversales sobre la asociación de la conducta sedentaria con las enfermedades cardiometabólicas y sus biomarcadores relacionados en adultos sudamericanos*

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### Abstract

**Introduction:** sedentary behavior (SB) has been independently associated with detrimental health outcomes in different regions worldwide. The aim of this systematic review was to examine whether domain-specific SB is associated with cardiometabolic diseases (CMD) and related biomarkers in South American adults.

**Methods:** nine electronic databases were searched to identify all studies that analyzed the association between SB and CMD –e.g. obesity, diabetes, hypertension, metabolic syndrome (MetS) and clustering of chronic diseases (CCD) – and related biomarkers in South American adults. Two independent reviewers performed the necessary Abstract/full-text screening, data abstraction, and quality assessments. The review protocol was registered in the PROSPERO database (CRD42018099319).

**Results:** from the 1,262 articles identified in the search 262 were reviewed in full and 20 were used in the analysis in accordance to the inclusion criteria. High SB (mainly sitting and TV time) was associated with an increased likelihood of obesity (n = 8), diabetes (n = 6), and CCD (n = 3), as well as high values of BMI (n = 8), WC (n = 7), % BF (n = 4), plasma lipids (n = 4), and glycemia (n = 5). Eleven out of 20 studies were of higher quality.

**Conclusion:** long time spent in SB, mainly sitting and TV time, was positively associated with the occurrence of CMD and related biomarkers in South American adults.

### Resumen

**Introducción:** el comportamiento sedentario (CS) se ha asociado de forma independiente con resultados perjudiciales para la salud en diferentes regiones del mundo. El objetivo de esta revisión sistemática fue examinar si el CS específico de cada dominio se asocia o no a enfermedades cardiometabólicas (ECM) y sus biomarcadores relacionados en adultos sudamericanos.

**Métodos:** se realizaron búsquedas en nueve bases de datos electrónicas para identificar todos los estudios que habían analizado la asociación entre CS y ECM –por ejemplo, obesidad, diabetes, hipertensión, síndrome metabólico y agrupación de enfermedades crónicas (AEC)– y sus biomarcadores relacionados en adultos sudamericanos. Dos revisores independientes realizaron evaluaciones de los resúmenes/textos completos, el resumen de los datos y evaluaciones de calidad. El protocolo de revisión está registrado en la base de datos PROSPERO (CRD42018099319).

**Resultados:** de los 1262 artículos identificados en la búsqueda, 262 se revisaron en su totalidad y 20 se utilizaron en el análisis de acuerdo con los criterios de inclusión. El gran CS (principalmente, tiempo sentado y de televisión) se asoció a una mayor probabilidad de obesidad (n = 8), diabetes (n = 6) y AEC (n = 3), así como a valores altos de IMC (n = 8), WC (n = 7), % BF (n = 4), lípidos plasmáticos (n = 4) y glucemia (n = 5). Once de los 20 estudios fueron de alta calidad.

**Conclusión:** la gran cantidad de tiempo invertido en el CS, principalmente el tiempo sentado y de televisión, se asoció positivamente con la aparición de ECM y sus biomarcadores relacionados en adultos de América del Sur.

#### Keywords:

Obesity. Diabetes mellitus. Hypertension. Body mass index. Metabolic syndrome.

#### Palabras clave:

Obesidad. Diabetes mellitus. Hipertensión. Índice de masa corporal. Síndrome metabólico.

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*Author's contribution:* KAM and AJN participated in the study design and methodology, developed the bibliographic search strategy, screened all abstracts and papers, performed the data abstraction and quality assessments, and drafted the manuscript. FACR, HHMH, MCGP and AJN conceived the study design and methodology, coordinated, and drafted and edited the manuscript. The authors read and approved the final manuscript.

*Conflict of interest:* the authors declare no conflict of interest.

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## INTRODUCTION

South America is comprised of nations and territories containing different environments and many complex and heterogeneous ethnicities, societies, and cultures in a population estimated at over 430 million. In South America upper-middle-income economies are predominant, and major demographic shifts like population growth, urbanization, technological advancements, and ageing are in course (1). Thus, behavior and environment factors, such as smoking, unhealthy diets (i.e., high energy-rich foods and low fruit and vegetables consumption), and physical inactivity are relevant modifiable risk factor for cardiometabolic diseases (CMD) (2-6).

Concerning physical inactivity, sedentarism is known to bring about serious health consequences and associations with all-cause mortality and other outcomes worldwide (2,7-10). Despite the fact that one in four adults worldwide does not meet the World Health Organization recommendations on physical activity to benefit from a reduced risk of common chronic diseases (11), failing to achieve the public health goals on physical activity is not the same as being sedentary. In this sense, sedentary behavior (SB) refers to activities that do not require significant energy expenditure – i.e., 1.5 METs or lower (12) – and is usually expressed as sitting time (ST) (13) such as in television (TV) viewing, computer use, transport, driving, reading or playing video games whilst in a sitting or reclining posture (14), in different everyday life domains (i.e., home, workplace, commuting, leisure time) (13,15). Sedentary behavior has been independently associated with detrimental health outcomes, including CMD, in adults from different regions worldwide (16-19). Moreover, SB presents high values in populations of different ethnic background worldwide (20) – among adults, the proportion of individuals spending 4 or more hours a day in a sitting position varies from 23.8 % in Southeast Asia, 37.8 % in Africa, 39.8 % in the western Pacific, 41.4 % in the eastern Mediterranean, and 55.2 % in the Americas to 64.1 % in Europe (21).

In South America's adult population physical inactivity reaches levels of over 40 % (21), and SB has been assessed as almost 6 h/day (22). In addition, the prevalence of CMD and its risk factors in South America is high (4,6,23,24). Nevertheless, the association between SB and CMD and its risk factors in South Americans is not well known. Identifying the association of SB in different domains with CMD is not only important for public health interventions, but also for occupational health, urban planning, and transport-related initiatives. Therefore, the aim of this study was to systematically review the literature to examine whether domain-specific SB is associated with CMD and related biomarkers in South American adults.

## METHODS

### SEARCH STRATEGY

A broad and specialized search was performed. Studies reporting on the possible association between SB and/or domain-specific SB – e.g., ST, TV viewing time or frequency and overall SB (sedentary activity, screen time, computer time, reading time, passive trans-

port, and sedentary work) – with CMD diseases (primary outcomes) and or related biomarkers (secondary outcomes) in South American adults were examined. The reporting guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement were followed, and the criteria outlined in A Measurement Tool to Assess Systematic Reviews (AMSTAR) checklist (25,26) were observed. The methodology of this systematic review was prospectively registered with PROSPERO (CRD42018099319; <http://www.crd.york.ac.uk/PROSPERO>) under the title "Is sedentary behavior associated with risk for cardiometabolic diseases in South American adults? A systematic review".

This review examined studies completed from January 2010 to December 2018, written in English, Spanish or Portuguese or with translations into these languages. Relevant studies were identified using the following electronic databases: Medline (Medical Literature Analysis and Retrieval System Online /PubMed); Embase (Elsevier); Cochrane Central (The Cochrane Central Register of Controlled Trials The Cochrane Library); Lilacs (Scientific and technical literature of Latin America and Caribe); Science Direct; Bireme (Latin American and Caribe center of information in health science); Scielo.org; Scopus (Elsevier); and SPORTDiscus.

The exposure descriptors used were: a) "sedentary behavior or time or lifestyle"; b) "sitting or reclining or leisure time"; and c) "television or TV view or watch or time". The outcome descriptors used were: a) "cardiometabolic or metabolic health or markers or risk or disease or syndrome"; and b) "cardiovascular or CVD markers or risk or disease or syndrome". The population descriptors used were: a) "South America or South American countries and territories". Appropriate combinations of these descriptors were used to ensure quality, transparency and maximum sensitivity during article retrieval. The search strategies adapted to the indexing systems are available from the authors upon request.

### STUDY SELECTION

This review included studies that addressed the amount of time spent in SB or domains of SB as risk factors for CMD, either self-reported or objectively measured, reported on a continuous scale (e.g., minutes/day) or divided into categories (e.g., > 3 h of TV time vs. ≤ 3 h), and time spent in specific domains of SB (i.e., ST, TV time or frequency and overall SB). The presence of CMD such as obesity, diabetes, hypertension, metabolic syndrome (MetS), and a clustering of chronic diseases (CCD - Heart attack, heart failure, angina, hypertension, DM, or arthritis) were the primary outcomes of interest in this review. Related biomarkers like total cholesterol (TC), high density lipoprotein (HDL) and low density lipoprotein (LDL) cholesterol, triglycerides (TG), blood glucose and insulin, glycated hemoglobin (HbA1c), insulin resistance (HOMA-IR), hypercholesterolemia, dyslipidemia and anthropomorphic measures such as body mass index (BMI), waist circumference (WC) and percentage of body fat (% BF) were the secondary outcomes of interest. Articles excluded were those on non-South American populations and/or non-adult populations (mean age < 18 years), those that did not report exposure to SB or the association between SB and health

outcomes, those that were duplicated, impossible to locate or obtain, and reviews or meta-analyses.

The screening of titles and abstracts for all studies was independently performed by two authors (KAM and AJN) in order to identify potential relevant articles. Likewise, these two authors (KAM and AJN) performed full-text screenings, and with mutual consensus confirmed that studies met the study's inclusion and exclusion criteria. The authors resolved discrepancies after discussion.

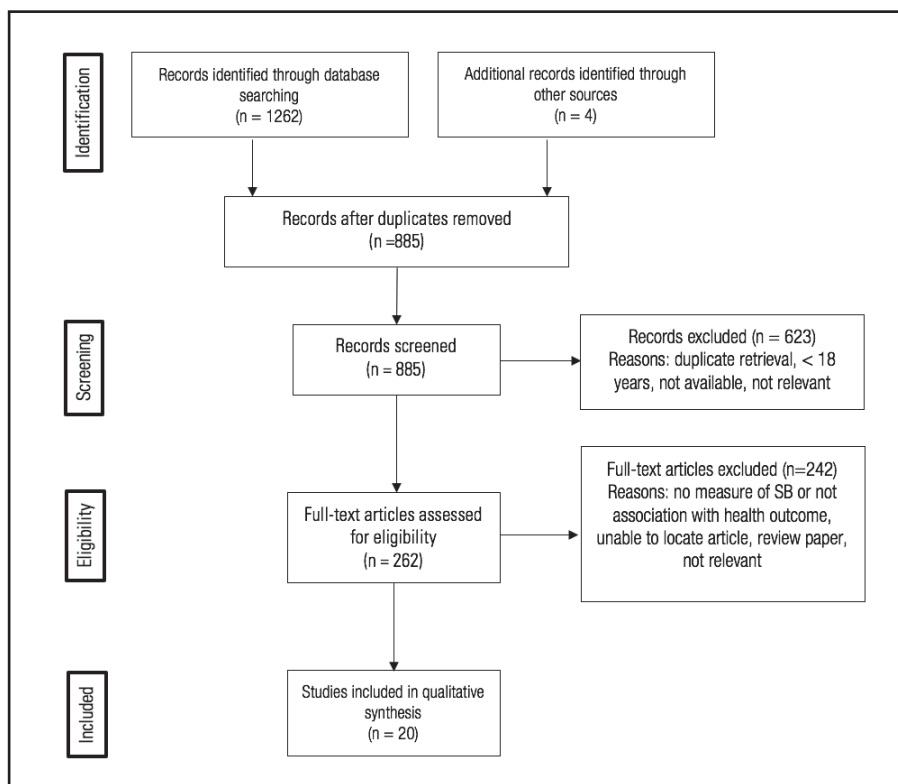
## DATA EXTRACTION AND ANALYSIS

Data and informations of interest were extracted by KAM or AJN. The main information obtained was on study characteristics, population characteristics, country of study, sample size analyzed, SB exposure and methods, outcome measurement, and measure of effect or correlation. Study quality was assessed using an adapted 20-item checklist (originally 27 items) of the Downs and Black checklist (27). Good quality was determined by using the overall numeric score of quality out of 20 possible points. Studies showing 16/20 median split or higher were considered of high quality. KAM independently assessed quality using the checklist, and AJN reviewed all scores. Disagreements were resolved upon consensus or were refereed by a third researcher.

The study-specific ORs for obesity or diabetes were combined as a generic inverse variance to estimate the pooled OR with 95 % CI by using the inverse variance statistical method with a random effects model. The pooled OR was calculated from a natural logarithm of OR [ $\ln(\text{OR})$ ] and the standard error of  $\ln(\text{OR})$  was obtained for the 95 % CI. A two-sided p-value lower than 0.05 was considered significant for all analyses. Studies were not included in the meta-analysis if the summary statistics of OR and 95 % CI were not available (31), or when the subjects evaluated were not sedentary (29). This meta-analysis was conducted using the RevMan 5.3 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, 2012), a free download at <http://tech.cochrane.org/revman/download>.

## RESULTS

The search identified 1,262 articles, and the screening of their primary titles and abstracts generated 262 articles. Then these 262 articles were reviewed in full and 20 articles met the inclusion and exclusion criteria. Figure 1 shows the flow diagram and the reasons for exclusion. In all, 55 % of the analyzed studies were considered to be high-quality. Five out of 20 studies scored 17 points; six scored 16 points, eight scored 15 points, and one scored 14 points.



**Figure 1.**

Flow diagram for literature search, January 2010 – December 2018. (SB: sedentary behaviour. Source: prepared by the authors from the study results).

In this review eleven out of the 20 analyzed studies were carried out on Brazilian, seven on Chilean, one on Colombian, and one on Peruvian adults, and were published prior to and including December 2018, specifically from 2010 to 2018. We observed that most studies were published from 2017 on ( $n = 11$ ). The selected studies analyzed adults (mean age: 30 to 70 years) from urban ( $n = 20/20$ ) and rural ( $n = 8/20$ ) areas.

The qualitative analysis revealed that 13 out of 20 studies reported on CMD (obesity, diabetes, hypertension, CCD, and MetS) (Table I), and 16 studies reported results related to CMD biomarkers. Overall, the results were consistent in showing that an increase in time spent in SB was associated with an increase in obesity ( $n = 8/8$ ), diabetes ( $n = 6/7$ ), CCD (3/4), hypertension ( $n = 3/4$ ), and MetS ( $n = 2/2$ ). Along with these diseases, SB was associated with high values of the following related biomarkers (Table II): BMI ( $n = 8/9$ ), waist circumference ( $n = 7/7$ ), % BF (4/4), HOMA-IR ( $n = 4/4$ ), glucose ( $n = 5/6$ ), insulin ( $n = 4/4$ ), and TG ( $n = 4/6$ ), and low levels of HDL-c ( $n = 4/6$ ). Dyslipidemia (1/1) and hypercholesterolemia (1/1) were also positively associated with SB. Despite that, TC ( $n = 3/6$ ), and LDL-c ( $n = 3/5$ ) were associated with SB in only three out of six and five studies, respectively. Regarding HbA1c (1/2), this glycemic control biomarker was associated with SB in only one study.

## CARDIOMETABOLIC DISEASES (PRIMARY OUTCOMES)

The association between SB and CMD as primary outcome was observed in different studies (Table I). For example, high SB ( $> 4$  h/day) was associated with central obesity in Chilean adults (28); and those categorized as either low SB (i.e., ST of  $1.56 \pm 0.7$  h/day) or high SB (i.e., ST of  $5.31 \pm 2.2$  h/day) and physically active were less likely to have obesity or central obesity when compared to those in the high SB (i.e., ST of  $6.14 \pm 2.6$  h/day) and inactive category (29). In addition, Chilean men exhibiting a higher ST were more likely obese (30). A ST of over 8 h/day during the week discriminated the presence of abdominal obesity, but not of obesity in Brazilian women (31); and obesity was associated with SB in Brazilian adults (32). Furthermore, a higher TV time was associated with greater abdominal obesity (33) and obesity (34) in Brazilian and Peruvian (35) women. The pooled odds ratio for obesity in association with sedentary behavior – 1.30 (1.14-1.49) – is presented in figure 2.

Regarding DM, an overall sedentary time and TV time  $\geq 3$  h/day (36) or  $\geq 4$  h/day (37) was positively associated with DM in Brazilian adults. Likewise, ST ( $> 4$  h/day) was positively associated with DM in Chilean adults (2,28). Furthermore, Chilean adults categorized as with either low or high SB and physically active were less likely to have DM, as compared to those in the high SB and inactive category (29). Finally, a ST of more than 5.5 h/day was positively associated with a high likelihood of having DM in Brazilian older adults (38). However, in Brazilian workers a high SB time (i.e., TV viewing, passive transport, sedentary work, and sedentary lifestyle) was not associated with DM (32).

The pooled odds ratio for diabetes in association with sedentary behavior – 1.16 (1.07-1.25) – is presented in figure 3.

Concerning CCD, Brazilian men who used a passive form of transport to go to work, and had a sedentary job and sedentary lifestyle were more likely to have  $> 2$  CDs, whereas women who reported  $\geq 3$  hours/day of TV time were more likely to have one CD versus no CD (32). TV time  $> 4$  h/day was positively associated with the presence of heart disease (i.e., heart failure, heart attack, and angina) among Brazilian adults (37). Moreover, Brazilian adults who spent  $> 4$  h/day sitting had a higher risk for the presence of  $> 2$  CDs (39). Nevertheless, Brazilian adults diagnosed with  $> 2$  CDs exhibited a similar amount of daily ST ( $\sim 4$  h) as compared to those diagnosed with zero or one CD (40).

As regards hypertension, it was positively associated with high TV time ( $> 4$  h/day) in Brazilian (32) but not in Chilean adults (28). Moreover, Chilean and Brazilian adults categorized in the high overall SB or high SB at work groups, respectively, had a high occurrence of hypertension (29,32).

With reference to MetS, Chilean adults in the low or high SB and physically active group were less likely to have MetS when compared to those in the high SB time and inactive category (29). In addition, high ST ( $> 4$  h/day) was positively associated with MetS among Chilean adults (28).

## RELATED BIOMARKERS (SECONDARY OUTCOMES)

The association between SB and CMD-related biomarkers was also reported in the reviewed studies (Table II). Regarding BMI, its positive association with SB was found in Chilean adults (29,41-43) and in Colombian men (44). Such association was also reported in Chilean men only (2), whereas a positive association of TV frequency with BMI was observed in Brazilian (34) and in Peruvian women only (35). However, SB ( $> 4$  h/day) was negatively associated with BMI in Chilean women, but positively in Chilean men (28). In addition, ST ( $> 4$  h/day) was not associated with BMI in Brazilian adults (45). Concerning % BF, it was positively associated with sedentary behavior and ST in Chilean adults (41-43) and in Colombian men (44).

With regard to WC, its positive association with SB was reported in Brazilian (33) and Chilean (2) women. Chilean adults categorized as 'high SB-active' or 'low SB-active' showed significant negative associations with WC when compared to those in the 'high SB-inactive' category (29). Moreover, in Chilean adults a high ST was positively associated with WC (41). Furthermore, per one-hour decrease in sedentary time, there was a significant decrease in WC among Chilean adults (42). SB was also positively associated with WC in Colombian men (44), whereas SB, but not ST, was positively associated with WC in Chilean adults (43).

With respect to blood glucose, a positive association between ST and fasting glycemia was found in Chilean adults (29,41-43), whereas such association was not observed by others among Chilean adults (2) and in Colombian men (44).

**Table I.** Cardiometabolic diseases (primary outcomes) reported in the included studies looking at its association with sedentary behavior in South American adults, January 2010 to December 2018

First author (year) Reference	Population (age) Sample	SB Measure Domain	Outcome measurement	Results		
				Measure of effect (primary outcome)	Interpretation	QA - Score (/20)
<b>Obesity</b>						
Fernandes (2010) 34	Brazilians (≥ 30 years) Men: 925 Women: 1,061	Self-reported TV time	Self-report	aPR for obesity Men: 0.98 (0.84-1.15) Women: 1.42 (1.09-1.83)*	TV time was associated with obesity in women	16
Poterico (2012) 35	Peruvians (30.6 ± 10.1 years) Women: 21,712	Self-reported TV time	Self-report	aOR (95 % CI) to be obese: 2.6 (2.0-3.5)*	TV viewing frequency was associated with obesity	16
Cortes (2013) 33	Brazilians (18-49 years) Women: 13,262	Self-reported TV time	Objective	aPR (CI 95 %) ≥ 5 times/week: Smokers: 1.7 (1.1-2.5)* Non-smokers: 1.1 (0.9-1.2)	Watching TV ≥ 5 times per week was associated with greater prevalence of AO in smoker women	16
Garcia (2014) 32	Brazilians (30-40 years) Men: 33,139 Women: 14,338	Self-reported SA time	Self-report	aOR (CI 95 %) for obesity: Men: 1.27 (1.15-1.41)* Women: 1.24 (1.04-1.48)*	SB was associated with obesity	17
Cristi-Montero (2017) 29	Chileans (46.4 ± 18.6 years) Men: 2,036 Women: 3,004	Self-reported ST	Objective	Reference (high SB/inactive) aOR to have CO: high-SB/active: 0.79 (0.65-0.96)* low-SB/active: 0.71 (0.59-0.84)†	Less sitting time was associated with less chance to have CO	17
Mussi (2017) 31	Brazilians (18-25 years) Men: 26 Women: 161	Self-reported ST	Objective	Area under ROC curve (95 % CI): Obesity = 0.50 (0.30-0.71) AO = 0.66 (0.57-0.75)*	ST during the week was powerful enough to discriminate AO, but not obesity	15
Petermann (2017) 30	Chileans (45.5 ± 18.2 years) Men: 1,045 Women: 1,831	Self-reported ST	Objective	aOR (95 % CI) to be obese in the highest tertile of ST: Men: [1.97 (1.45-2.68)]* Women: [0.88 (0.69-1.12)]	ST was a risk factor for CO among men	16
Martínez (2018) 28	Chilean (47 years) Men: 2,047 Women: 2,993	Self-reported ST	Objective	aOR (95 % CI) for CO: ST ≥ 4 h/day vs. < 4 h/day: 1.15 (1.02-1.30)*	High ST was associated with central obesity	15

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**Table I (Cont.).** Cardiometabolic diseases (primary outcomes) reported in the included studies looking at its association with sedentary behavior in South American adults, January 2010 to December 2018

First author (year) Reference	Population (age) Sample	SB Measure Domain	Outcome measurement	Results		
				measure of effect (primary outcome)	Interpretation	QA - Score (/20)
<b>Diabetes</b>						
Garcia (2014) 32	Brazilians (30-40 years) Men: 33,139; Women: 14,338	Self-reported SA time	Self-report	OR (CI 95 %) for DM: Men: 1.06 (0.88-1.27) Women: 0.86 (0.65-1.13)	SB was not associated with DM	17
Silva (2015) 38	Brazilians (60-80 years) Men: 1,256 Women: 2,009	Self-reported ST	Self-report	aOR (CI 95 %) to have DM: 1.351 (1.057-1.729)*	A daily ST of > 5.5 h was associated with high chances to have DM	16
Cristi-Montero (2017) 29	Chileans (46.4 ± 18.6 years) Men: 2,036 Women: 3,004	Self-reported ST	Objective	Reference (high SB/inactive) OR to have DM: high-SB/active: 0.45 (0.35-0.59) <sup>†</sup> low-SB/active: 0.44 (0.34-0.56)	Less ST was associated with less chance to have DM	17
Diaz-Martinez (2017) 2	Chileans (41.6 ± 18.6 years) Men: 1,783 Women: 2,674	Self-reported ST	Objective	OR (95 % CI) for DM (increase of 1h of ST as independent factor). Men: 1.10 (1.04 – 1.16) <sup>†</sup> Women: 1.08 (1.02 – 1.14) <sup>†</sup>	SB was associated with DM and cardiometabolic risk factors	16
Lemes (2018) 36	Brazilians (68.9 ± 8.4 years) Men: 147 Women: 410	Self-reported SA time TV time	Objective	OR (95 % CI) for DM.: overall SA ≥ 3 h /day vs. < 3 h/day: 1.60 (1.09-2.36) <sup>*</sup> TV time ≥ 3 h/day vs. < 3 h/day: 1.61 (1.11–2.33) <sup>*</sup>	TV time and overall SA was associated with higher prevalence of DM	17
Martinez (2018) 28	Chileans (47 years) Men: 2,047 Women: 2,993	Self-reported ST	Objective	OR (95 % CI) for DM: ST ≥ 4 h/day vs. < 4 h/day: 1.27 (1.06-1.52) <sup>*</sup>	High sitting time was associated with DM	15
Werneck (2018) 37	Brazilians (≥ 18 years) Men: 25,920 Women: 34,282	Self-reported TV time	Self-report	aOR (95 % CI) for DM: men [1.64 (1.23-2.67) <sup>*</sup> ] women [1.33 (1.09-1.63) <sup>*</sup> ]	High levels of TV viewing were associated with greater odds of DM	17

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**Table I (Cont.).** Cardiometabolic diseases (primary outcomes) reported in the included studies looking at its association with sedentary behavior in South American adults, January 2010 to December 2018

First author (year) Reference	Population (age) Sample	SB Measure Domain	Outcome measurement	Results		
				Measure of effect (primary outcome)	Interpretation	QA - Score (/20)
<b>CCD</b>						
Garcia (2014) 32	Brazilians (30-40 years) Men: 33,139 Women: 14,338	Self-reported SA time	Self-report	OR (CI 95 %): for $\geq 2$ CD: Men: one CD = 1.17 (1.09-1.26)*; and $\geq 2$ CD = 1.61(1.46-1.78)*	SB was associated with $\geq 2$ CD	17
Sebastião (2017) 40	Brazilians (70.2 $\pm$ 7.5 years) Men: 134 Women: 221	Self-reported ST	Self-report	NR	ST was not different in individuals presenting none, one or $\geq 2$ CD (DM, hypertension or arthritis)	16
Ribeiro (2018) 39	Brazilians (70.0 $\pm$ 7.6 years) Men: 373 Women: 447	Self-reported ST	Self-report	aOR (95 % CI) to have $\geq 2$ CD: Men: 1.76 (1.10-2.80)* Women: 1.82 (1.15-2.89)*	ST was associated to a higher risk of having $\geq 2$ CD (DM, hypertension or arthritis)	15
Werneck (2018) 37	Brazilians ( $\geq 18$ years) Men: 25,920 Women: 34,282	Self-reported TV time	Self-report	aOR (95 % CI) for HD: men [1.96 (1.43-2.69)*], women [1.30 (1.00-1.68)*]	High levels of TV viewing were associated with greater odds of HD	17
<b>MetS</b>						
Cristi-Montero (2017) 29	Chileans (46.4 $\pm$ 18.6 years) Men: 2,036 Women: 3,004	Self-reported ST	Objective	Reference (high SB/inactive) OR to have MetS: high-SB/active: 0.63 (0.49-0.82) <sup>†</sup> low-SB/active: 0.72 (0.59-0.71) <sup>†</sup>	Less ST was associated with less chance to have MetS	17
Martinez (2018) 28	Chileans (47 years) Men: 2,047 Women: 2,993	Self-reported ST	Objective	OR for MetS: ST $\geq 4$ hr/day vs. $< 4$ hr/day: 1.15 (1.02-1.30)*	High sitting time was associated with MetS	15
Werneck (2018) 37	Brazilians ( $\geq 18$ years) Men: 25,920 Women: 34,282	Self-reported TV time	Self-report	aOR (95 % CI) for hypertension: men [1.36 (1.14-1.63)] women [1.20 (1.05-1.37)]	High levels of TV viewing were associated with greater odds of hypertension	17

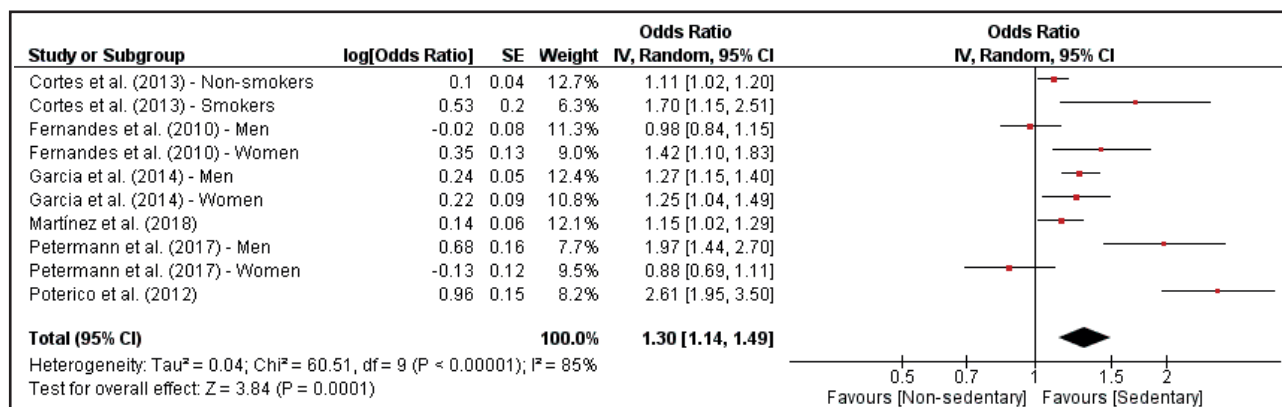
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**Table I (Cont.).** Cardiometabolic diseases (primary outcomes) reported in the included studies looking at its association with sedentary behavior in South American adults, January 2010 to December 2018

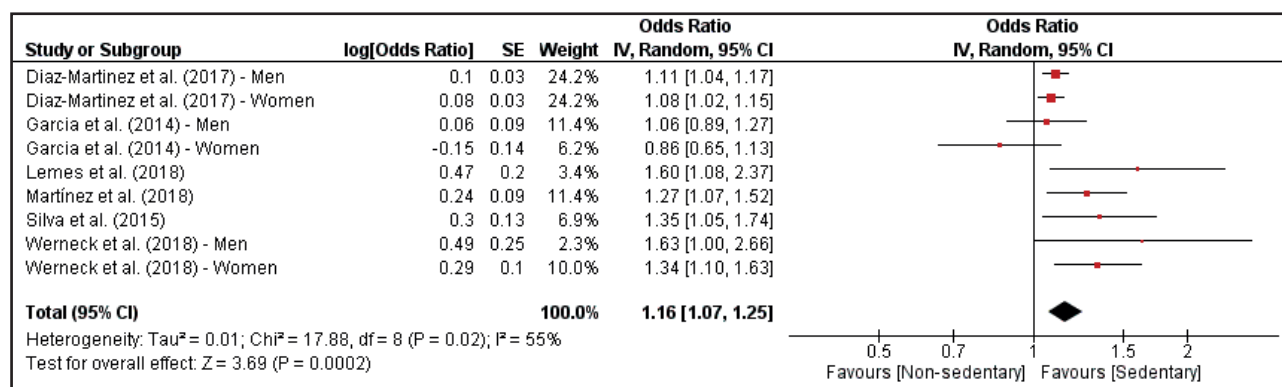
First author (year) Reference	Population (age) Sample	SB Measure Domain	Outcome measurement	Results		
				Measure of effect (primary outcome)	Interpretation	QA - Score (/20)
<b>Hypertension</b>						
Garcia (2014) 32	Brazilians (30-40 years) Men: 33,139 Women: 14,338	Self-reported SA time	Self-report	OR (CI 95 %): for hypertension: Men: 1.00 (0.82-1.22) Women: 1.04 (0.89-1.22)	SB was not associated with hypertension	17
Cristi-Montero (2017) 29	Chileans (46.4 ± 18.6 years) Men: 2,036 Women: 3,004	Self-reported ST	Objective	Reference (high SB/inactive) OR to have hypertension: high-SB/active: 0.52 (0.43-0.63) <sup>†</sup> low-SB/active: 0.60 (0.50-0.72) <sup>†</sup>	Less ST was associated with less chance to have hypertension	17
Martinez (2018) 28	Chileans (47 years) Men: 2,047 Women: 2,993	Self-reported ST	Objective	OR (95 % CI) for hypertension: ST ≥ 4 h/day vs. < 4 h/day: Men: 1.00 (0.82-1.22). Women: 1.04 (0.89-1.22)	SB was not associated with hypertension	15
Werneck (2018) 37	Brazilians (≥ 18 years) Men: 25,920 Women: 34,282	Self-reported TV time	Self-report	aOR (95 % CI) for hypertension: Men [1.36 (1.14-1.63)], Women [1.20 (1.05-1.37)]	High levels of TV viewing were associated with greater odds of hypertension	17

\* $p < 0.05$ ; <sup>†</sup> $p < 0.01$ . Source: prepared by the authors from the study results. AO: abdominal obesity; aOR: adjusted odds ratio; aPR: adjusted prevalence ratio; BMI: body mass index; CI: confidence interval; CO: central obesity; CD: chronic disease; DM: diabetes mellitus; HC: hypercholesterolemia; Li: lower limit; MeIS: metabolic syndrome; NR: not reported; OR: odds ratio; PA: physical activity; QA: quality assessment; ROC: receiver operating characteristic; SA: sedentary activity; SB: sedentary behavior; ST: sitting time; TV: television; TC: total cholesterol; WC: waist circumference.





**Figure 2.** Pooled odds ratios for obesity in association with sedentary behavior. (CI: confidence interval; SE: standard error. Source: prepared by the authors from the study results).



**Figure 3.** Pooled odds ratios for diabetes in association with sedentary behavior. (CI: confidence interval; SE: standard error. Source: prepared by the authors from the study results).

A positive association of ST with fasting insulinemia was observed in Chilean adults (41-43) and in Colombian men (44). Furthermore, SB was positively associated with HOMA-IR in Chilean adults (41-43) and in Colombian men (44). Regarding HbA1c, Chilean ‘high SB-active’ adults showed lower values of HbA1c when compared to those in the ‘low SB-active’ category (29). However, no association of SB with HbA1c was reported for Chilean adults (2).

Chilean adults exhibited a positive association of ST with serum lipids (41-43). Likewise, ST was positively associated with serum TG and HDL-c levels among Colombian men (44). Notwithstanding this, ST during the week or weekend did not discriminate any serum lipid abnormalities in Brazilian women (31). Moreover, Chilean adults in the ‘high SB-active’ or ‘low SB-active’ groups showed no significant associations with an abnormal serum lipid profile (29). Furthermore, Suárez et al. (44) observed that ST was not associated with serum TC and LDL-c levels in Colombian men. Regarding hypercholesterolemia, Garcia et al. (32) found that in Brazilian workers SB at work was positively

associated with hypercholesterolemia. In addition, a higher adjusted prevalence ratio of dyslipidemia was reported among Brazilian women with a more prolonged ST (46).

### SUBGROUP ANALYSES

Subgroup analyses for sex and domain-specific sedentary behavior were performed. Between-sex differences were found in some studies. For instance, obesity (30) and BMI (2) were found to be positively associated with ST in Chilean men only, whereas it was negative in women (28). Waist circumference was found to be positively associated with SB in Chilean women only (2). Among Brazilians, BMI and obesity were positively associated with SB in women only (34). Moreover, SB at work was positively associated with chronic diseases (e.g., obesity, hypertension, CCD, and hypercholesterolemia) especially in men as compared to women (32). Finally, a higher adjusted prevalence ratio of dyslipidemia was reported for Brazilian women but was not reported for men (46).

**Table II.** Related biomarkers (secondary outcomes) of included studies looking at the association of sedentary behavior and cardiometabolic diseases in South American adults, January 2010 to December 2018

First author (year) Reference	Population (age) Sample	SB Measure Domain	Outcome measurement	Results	
				Interpretation	QA - Score (/20)
<b>Body mass index and percentage of body fat</b>					
Fernandes (2010) 34	Brazilians (≥ 30 years) Men: 925; Women: 1,061	Self-reported TV time	Self-report	The highest frequency of TV viewing was significantly associated with BMI in women (aPR: 1.42), but not in men (aPR: 0.98)	15
Celis-Morales (2012) 43	Chileans (37.5 ± 12.8 years) Men: 149; Women: 177	Accelerometer ST Self-reported SB time	Objective	Significant trends to increase BMI and % BF with increasing time spent in SB (accelerometer) and ST (IPAQ)	17
Suárez (2012) 44	Colombians (46.7 ± 6.6 years) Women: 69	Self-reported ST	Objective	Higher ST was significantly correlated with BMI (rho: 0.225) and % BF (rho: 0.249) in men	14
Salas (2016) 42	Chileans (36.6 ± 12.5 years) Men: 137; Women: 177	Accelerometer SB time	Objective	Per one hour decrease in SB, there were significant improvements in BMI (-0.93 and -0.62 kg.m <sup>-2</sup> ) in physically active and inactive and in % BF (-1.04 %) in active men and women	15
Cristi-Montero (2017) 29	Chileans (46.4 ± 18.6 years) Men: 2,036; Women: 3,004	Self-reported ST	Objective	Compared to 'High-SB & Inactive' group, those individuals in 'High-SB & Active' and 'Low-SB & Active' groups showed significant negative associations with BMI (≥ 30.0 kg/m <sup>2</sup> ) (standardized β: -0.182 and -0.156, respectively)	17
Diaz-Martinez (2017) 2	Chileans (41.6 ± 18.6 years) Men: 1,783; Women: 2,674	Self-reported ST	Objective	BMI was positive and significantly associated with ST (> 8 h/day) in men but not women	16
Gonçalves (2017) 45	Brazilians (18-65 years) Men: 521; Women: 890	Self-reported ST	Self-report	Sitting time (> 4 h/day) was not significantly associated with BMI in men and women with overweight classified as sedentary and not active [ > 10 min PA/week - OR: 1.03, 95 % CI); > 150 min PA/week - OR: 1.11, 95 % CI)	15
Leiva (2017) 41	Chileans (37.6 ± 12.9 years) Men: 141; Women: 181	Accelerometer ST	Objective	Per one hour increase in ST, there were significant adverse changes in BMI (0.69 kg/m <sup>2</sup> ) and % BF (1.03 %) in men and women	15
Martínez (2018) 28	Chileans (47 years) Men: 2,047; Women: 2,993	Self-reported ST	Objective	Sitting time was negatively (OR: 0.69; 95 % CI: 0.59-0.81) associated with BMI (> 25 kg/m <sup>2</sup> ) in women, but positively in men (OR: 1.21; 95 % CI: 1.00-1.49)	15

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**Table II (Cont.).** Related biomarkers (secondary outcomes) of included studies looking at the association of sedentary behavior and cardiometabolic diseases in South American adults, January 2010 to December 2018

First author (year) Reference	Population (age) Sample	SB Measure Domain	Outcome measurement	Results	
				Interpretation	QA - Score (/20)
<b>Waist circumference</b>					
Cellis-Morales (2012) 43	Chileans (37.5 ± 12.8 years) Men: 149; Women: 177	Accelerometer ST Self-reported SB time	Objective	Significant trends to increase WC with increasing time spent in sedentary time (accelerometer), but not with increasing ST (IPAQ)	17
Suárez (2012) 44	Colombians (46.7 ± 6.6 years) Women: 69	Self-reported ST	Objective	Sitting time was positively significantly correlated with WC (rho: 0.266) in men	14
Cortés (2013) 33	Brazilians (18-49 years) Women: 13,262	Self-reported TV time	Objective	WC (≥ 80.0 cm) was positively associated with TV time (≥ 5 times/week)	16
Salas (2016) 42	Chileans (36.6 ± 12.5 years) Men: 137; Women: 177	Accelerometer SB time	Objective	Per one hour decrease in SB, there were significant improvements in WC (-2.32 and -1.65 cm) in physically active and inactive men and women	15
Crisli-Montero (2017) 29	Chileans (46.4 ± 18.6 years) Men: 2,036; Women: 3,004	Self-reported ST	Objective	Adults categorized as 'High-SB & Active' or 'Low-SB & Active' showed significant negative associations with WC (standardized β: -0.258 and -0.233, respectively), compared to adults categorized as 'High-SB & Inactive'	17
Díaz-Martínez (2017) 2	Chileans (41.6 ± 18.6 years) Men: 1,783; Women: 2,674	Self-reported ST	Objective	WC was significantly positively associated with ST (> 8 h/day) in women but not men	16
Leiva (2017) 41	Chileans (37.6 ± 12.9 years) Men: 141; Women: 181	Accelerometer ST	Objective	Per one hour increase in ST there was significant adverse change in WC (1.95 cm) in men and women	15
<b>Glucose</b>					
Cellis-Morales (2012) 43	Chileans (37.5 ± 12.8 years) Men: 149; Women: 177	Accelerometer ST Self-reported SB time	Objective	Significant trends to increase fasting glucose with increasing time spent in SB (accelerometer) and ST (IPAQ)	17
Suárez (2012) 44	Colombians (46.7 ± 6.6 years) Women: 69	Self-reported ST	Objective	Sitting time was not significantly correlated with fasting glucose (rho: 0.069) in men	14
Salas (2016) 42	Chileans (36.6 ± 12.5 years) Men: 137; Women: 177	Accelerometer SB time	Objective	Per one hour decrease in SB, there was a significant improvement in glucose (-8.46 and -4.68 mg.dL <sup>-1</sup> ) in physically active and inactive men and women.	15
Crisli-Montero (2017) 29	Chileans (46.4 ± 18.6 years) Men: 2,036; Women: 3,004	Self-reported ST	Objective	Adults categorized as 'High-SB & Active' or 'Low-SB & Active' showed significant negative associations with fasting glucose (standardized β: -0.238 and -0.174, respectively), compared to adults categorized as 'High-SB & Inactive'	17
Díaz-Martínez (2017) 2	Chileans (41.6 ± 18.6 years) Men: 1,783; Women: 2,674	Self-reported ST	Objective	Sitting time (> 8 h/day) was not associated with fasting glucose levels in men and women	16
Leiva (2017) 41	Chileans (37.6 ± 12.9 years) Men: 141; Women: 181	Accelerometer ST	Objective	Per one hour increase in ST there was significant adverse change in glucose (4.79 mg/dL) in men and women	15

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**Table II (Cont.).** Related biomarkers (secondary outcomes) of included studies looking at the association of sedentary behavior and cardiometabolic diseases in South American adults, January 2010 to December 2018

First author (year) Reference	Population (age) Sample	SB Measure Domain	Outcome measurement	Results	
				Interpretation	QA - Score (/20)
<b>Lipid profile, hypercholesterolemia, dyslipidemia</b>					
Celis-Morales (2012) 43	Chileans (37.5 ± 12.8 years) Men: 149; Women: 177	Accelerometer ST Self-reported SB time	Objective	Significant trends to increase TG and reduce HDL-c levels with increasing time spent in SB (accelerometer) and ST (IPAQ). Significant trends to increase TC and LDL-c levels with increasing time spent in SB (accelerometer), but not with increasing ST (IPAQ)	17
Suárez (2012) 44	Colombians (46.7 ± 6.6 years) Women: 69	Self-reported ST	Objective	Sitting time significantly correlated with serum TG (rho: 0.258) and HDL-c (rho: -0.279), but not with TC (rho: 0.017) and LDL-c (rho: 0.052) levels in men	14
Moraes (2013) 46	Brazilians – urban areas 30-65 years Men: 457; Women: 676	Self-reported ST	Objective	Higher adjusted prevalence ratio of dyslipidemia [aPR, 1.2 (1.0-1.6)] in Brazilian women found in the highest tertile of ST (> 5.14 h/day)	15
García (2014) 33	Brazilians (30-40 years) Men: 33,139; Women: 14,338	Self-reported SA time	Objective	Higher time spent in SA (> 4 h/day) at work (i.e. TV viewing and sedentary work) was significantly associated with hypercholesterolemia in male and female workers	17
Salas (2016) 42	Chileans (36.6 ± 12.5 years) Men: 137; Women: 177	Accelerometer SB time	Objective	Per each hour reduced in SB, significant reductions in serum TC (-4.63 mg/dL <sup>-1</sup> ), TG (-6.68 mg/dL <sup>-1</sup> ) and LDL-c (-4.74 mg/dL <sup>-1</sup> ) and increase in HDL-c (2.05 mg/dL <sup>-1</sup> ) levels were observed in physically active and inactive men and women	15
Cristi-Montero (2017) 29	Chileans (46.4 ± 18.6 years) Men: 2,036; Women: 3,004	Self-reported ST	Objective	Individuals categorized as 'High-SB & Active' or 'Low-SB & Active' showed no significant associations with serum lipid profile (e.g., TC, TG, HDL-c) levels, compared to adults categorized as 'High-SB & Inactive'	17
Leiva (2017) 41	Chileans (37.6 ± 12.9 years) Men: 141; Women: 181	Accelerometer ST	Objective	Per one hour increase in ST there were significant adverse changes in TC (9.73 mg/dL), HDL-c (-3.50 mg/dL), LDL-c (10.7 mg/dL) and TG in men and women	15
Mussi (2017) 31	Brazilians (18-25 years) Men: 26; Women: 161	Self-reported ST	Objective	Sitting time during the week or weekend did not discriminate serum lipid (e.g., TG, TC, LDL-c and HDL-c) abnormality among women	15
<b>Insulin, HOMA-IR and HbA1c</b>					
Celis-Morales (2012) 43	Chileans (37.5 ± 12.8 years) Men: 149; Women: 177	Accelerometer ST Self-reported SB time	Objective	Significant trends to increase insulin and HOMA-IR with increasing time spent in SB (accelerometer) and ST (IPAQ)	17
Suárez (2012) 44	Colombians (46.7 ± 6.6 years) Women: 69	Self-reported ST	Objective	Sitting time was significantly correlated with fasting insulin (rho: 0.284) and HOMA-IR (rho: 0.261) in men	14
Salas (2016) 42	Chileans (36.6 ± 12.5 years) Men: 137; Women: 177	Accelerometer SB time	Objective	Per one hour decrease in SB, there were significant improvements in insulin (-2.12 and -1.77 pmol.L <sup>-1</sup> ) and HOMA-IR (-0.81 and 0.56) in physically active and inactive men and women	15
Cristi-Montero (2017) 29	Chileans (46.4 ± 18.6 years) Men: 2,036; Women: 3,004	Self-reported ST	Objective	Adults categorized as 'High-SB & Active' or 'Low-SB & Active' showed significant negative associations with HbA1c (standardized β: -0.286 and -0.183, respectively)	17
Díaz-Martínez (2017) 2	Chileans (41.6 ± 18.6 years) Men: 1,783; Women: 2,674	Self-reported ST	Objective	The time spent sitting (> 8h/day) was not significantly associated with HbA1c levels in men and women	16
Leiva (2017) 42	Chileans (37.6 ± 12.9 years) Men: 141; Women: 181	Accelerometer ST	Objective	Per one hour increase in ST there were significant adverse changes in insulin (2.73 pmol/L) and HOMA-IR (0.75) in men and women	15

aPR: adjusted prevalence ratio; BMI: body mass index; HbA1c: glycated hemoglobin; HOMA-IR: homeostasis model assessment-insulin resistance; HDL-c: high density lipoprotein-cholesterol; IPAQ: International Physical Activity Questionnaire; LDL-c: low density lipoprotein-cholesterol; OR: odds ratio; % BF: percentage of body fat; QA: quality assessment; SA: sedentary activity; SB: sedentary behavior; ST: sitting time; TV: television; TC: total cholesterol; TG: triglycerides; WC: waist circumference. Source: prepared by the authors from the study results.

The investigation of the association of domain-specific SB with CMD and related biomarkers found that 12 studies reported on ST (2,28-31,38-41,44-46) and four on TV time or TV watching frequency (33-35,37). The remaining four studies looked at general measures of SB (32,36,42,43). The results demonstrate equivalent trends for each SB domain.

## DISCUSSION

In this review we thought to systematically review the literature to examine whether domain-specific SB is associated with CMD and its risk factors in South American adults. This is the first review to explore the association of SB with CMD and its risk factors in South American adults. This study summarized the published evidence over the review period (i.e., January 2010 to December 2018), and observed that longer SB (i.e., sitting, TV watching, overall SB time) was associated with CMD (i.e., obesity, DM, and CCD) as well as with its anthropometric (i.e., BMI, WC, and % BF) and metabolic biomarkers (i.e., lipid profile and glucose). Nevertheless, evidence is limited when studies reported the relationship between SB and CMD (i.e., hypertension and MetS) as well as its biomarkers (i.e., HOMA-IR, Bl, dyslipidemia, and hypercholesterolemia). It has to be taken into consideration that reports on the associations of SB with hypertension, MetS, HOMA-IR, insulin, dyslipidemia, and hypercholesterolemia are scarce.

Our results complement the previous evidence from systematic reviews (17,18,47) and meta-analyses (16,19,48), which demonstrate that high SB is associated with CMD and risk factors in different regions of the world. Based on the studies reviewed here, South American adults are likely at larger risk for developing obesity, diabetes, and CCD when incurring in prolonged SB time. Such findings are consistent with those reported about different populations (18,19,48). A significant association of longer time spent in SB was found with obesity (8 studies), DM (6 but 1 study), and CCD (4 studies) in the 20 studies reviewed. For instance, South American (i.e., Chilean) adult men in the highest tercile of ST had a 97 % higher risk for obesity (30). In addition, Lemes et al. (36) reported a 60 % higher risk for diabetes in South American (i.e., Chilean) adults who spent  $\geq 3$  h/day in sedentary activities, whereas those South American (i.e., Brazilian) men and women who reported a daily ST of 4 h had a 76 % and 82 % higher risk of presenting  $\geq 2$  CCDs, respectively (39). However, the magnitude of the risk of developing DM with longer sedentary time is approximately twice as high as in the general population and, in general, longer sedentary time is associated with a 14 % greater risk of cardiovascular disease (19). A significant relationship between increased SB and higher BMI (8 but 1 studies), WC (7 studies), and % BF (4 studies) was also reported in the reviewed studies. These results are similar to those previously reported in different populations (49,50) and, more importantly, are consistent with the association of longer time spent in SB with obesity as observed in the present review.

Concerning sex differences, only seven studies reported distinct associations of SB with CMD and its biomarkers. Based on those

studies, it appears that South American men are at higher risk for obesity and high BMI when spending a lot of time in SB, as compared to women. Such finding is contradictory to the report that women are more inactive (33.9 %) than are men (27.9 %) worldwide (21). Regarding domain-specific SB in South American adults, most studies associated a higher risk for CMD with longer periods of ST (13 studies), which was followed by the extent of TV (6 studies) and SB (4 studies) times. Whether there are distinct health damages for the different specific domains rather than length of exposure is not known, and thus demands further investigation.

Overall, this systematic review presented a positive association between SB and CMD in South American adults. Whether these risks are truly greater in this population group further studies are needed to elucidate, inasmuch as the insufficiency of available direct evidence on this sub-population limits the ability to ascertain such findings. Despite this, the findings presented here are of relevance for South American governments, since they reinforce the need for public policies to face the deleterious consequences of a sedentary lifestyle.

## STUDY LIMITATIONS

This review has some limitations. First, there is a lack of studies examining the relationship of SB with CMD and related biomarkers in South American adults, which make it difficult to generalize our findings. Eleven out of 20 analyzed studies were carried out in Brazilian, seven in Chilean, one in Colombian and one in Peruvian adult men and women. Although the population of these four countries accounts for 73 % (~ 316 million people) of the South American population, no data on adults from the other South American countries were found. Moreover, the selective reporting of positive outcomes in individual studies could potentially reduce the generalizability of our findings. Secondly, the predominant use of self-reported data in individual studies is another limitation, since self-reported data are highly susceptible to biases that might have affected the magnitudes of our results. Only three studies in the present review reported on the use of objective measures (accelerometers) of SB time in Chileans (Leiva et al., 2017; Salas et al., 2016; Celes-Morales et al., 2012), but did not assess the association of SB with CMD as their primary outcome. Finally, despite the quality of the selected studies, all 20 studies were cross-sectional in design, and as such they may include selection and reverse causality biases, as well as residual confounders. Therefore, since there is no temporality described between the sedentary behavior and the outcomes, interpretations should be cautious.

## CONCLUSIONS

In conclusion, spending a long time in an overall SB, mainly in a sitting position or watching TV, was positively associated with the occurrence of CMD (i.e., obesity, diabetes, and  $\geq 2$  CCDs) and related biomarker (i.e., BMI, WC, % BF, lipid profile, and blood glucose) elevations in South American adult men and women.

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