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Sitting less and moving more: the impact of physical activity on mortality in the population of Spain

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Abstract

Background Sitting time (ST) constitutes a significant aspect of sedentary behavior, and its worldwide escalation raises concerns regarding public health. International guidelines recommend limiting sedentary time and replacing it with physical activity (PA) to reduce the risk of diseases and mortality. This study examines the impact of replacing ST with PA on all-cause, cardiovascular disease (CVD), and cancer mortality in a representative cohort of the population of Spain.

Methods We included 30 955 participants aged 15–69 years from two National Health Surveys performed in 2011 and 2017. Data were linked to mortality records as of December 2022. Data on ST, light PA (LPA), and moderate-vigorous PA (MVPA) were collected as part of the International Physical Activity Questionnaire at baseline. Isotemporal substitution analysis from Poisson regression models was used to estimate the relative risk ratio (RR) of replacing ST with LPA or MVPA.

Results During a median follow-up of 5.7 years, 957 deaths were reported. The replacement of 1 h per week of ST with 1 h per week of MVPA was significantly associated with a lower risk of all-cause (3.3%), CVD (6.7%), and cancer mortality (3.1%). Similarly, replacing 1 h per week of ST with 1 h per week of LPA was significantly associated with a lower risk of all-cause (1.6%) and cancer mortality (2.1%). Finally, substituting 1 h per week of LPA with 1 h per week of MVPA was significantly associated with a 7.6% lower risk of CVD mortality.

Conclusions Substituting one hour per week of ST with an equivalent amount of PA was associated with a lower risk of all-cause, CVD, and cancer mortality.

Keywords Sedentarism, Movement, Lifestyles, Cohort study, Public health

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Background

Sedentary behavior (SB) is defined as any waking behavior characterized by an energy expenditure≤1.5 metabolic equivalents (METs) while in a sitting, reclining, or lying posture [1]. Sitting time (ST) involves multiple occupational and non-occupational daily activities and is a major contributor to SB and, thus, it is commonly used as an SB measure in population-based studies [2, 3]. Worldwide, the trend towards SB is increasing [4], likely negatively impacting the world´s population health as time spent in sedentary activities results in detrimental and independent health effects regardless of physical activity levels [5]. Not surprisingly, PA and health international guidelines recommend limiting the amount of sedentary time [6–8] based on the wealth of scientific evidence showing associations between sedentarism and poor cardiometabolic health [9], certain types of cancer [10], and mortality [11].

However, merely reducing sedentary time might not improve mortality, as it may be necessary to replace SB with PA of any intensity [12]. In fact, based on strong evidence suggesting PA´s health benefits [13], PA guidelines recommend replacing sedentary time with additional PA of any intensity [6–8]. Unfortunately, the reality is the low prevalence of sufficient PA worldwide [14], which may significantly reduce the potential benefits of PA on health, as well as increase the risk of non-communicable diseases and mortality [15].

A growing body of research has investigated the replacement of sedentary time with PA using isotemporal substitution models (ISM), which estimate the effect of replacing one behavior (e.g., sitting time) with any PA for the same amount of time [16]. Grgic et al. [17] conducted a systematic review of studies using ISM, and their results suggested the substantial benefits of replacing time spent in SB with PA based on the favorable impact on health-related quality of life, mental health, adiposity, fitness, cardiometabolic biomarkers, chronic diseases, and other medical conditions [17]. In addition, it was observed that replacing SB with different PA levels (light or moderate-vigorous) was associated with a substantial reduction in the mortality risk ranging from 12 to 81% [12, 18–21]. This application of ISM allowed a quantitative approximation of the potential health effects of this behavioral change. These results could inform and make PA guidelines more effective, as well as improve and reinforce public health messages [17] aimed at reducing physical inactivity worldwide.

However, ISM studies with mortality as their outcome are burdened by several limitations and knowledge gaps. First, prospective population-based studies are scarce. Second, the theoretical behavior change most commonly proposed in the ISM studies—replacing behaviors for 30 min per day—may seem unfeasible for a large portion of the population. A proposed change that aligns more closely with PA global recommendations for adults, usually given as weekly recommendations [6–8], may feel more attainable and, thus, make for a more successful public health message. Finally, few of these studies compare the substitution effect of ISM among all-cause, CVD, and cancer mortality, as well as across several sociodemographic determinants.

Therefore, the purpose of this study was to estimate the theoretical impact of replacing one hour per week of SB (i.e., sitting time) with the equivalent of light PA (LPA) or moderate-vigorous PA (MVPA) on all-cause, CVD, and cancer mortality in a representative cohort of the Spanish population. Further, we examined such theoretical effects by sex, age, and educational level.

Methods

Study design and population

The National Health Interview Survey comprises a series of assessments which embody the main source of information on the health of the population of Spain. The survey collects population-based data on health status, behavioral, social, and environmental determinants of health, and use of health services. The participants are selected using a stratified multi-stage sampling and are representative of the non-institutionalized Spanish population [22]. The data for this study came from the 2011 and 2017 surveys, which included 21 007 and 23 089 participants over 15 years of age, respectively. Both surveys used the same sample design and standardized questionnaires administered face-to-face using a Computer-Assisted Personal Interview. Response rates were 66.5% and 69.9% of all selected households in 2011 and 2017 surveys, respectively.

This study was approved by Carlos III Institute of Health Ethical Research Committee (CEI PI 28_2019). All participants gave informed consent to participate in the study before being included.

Variables

Mortality

Survey data were linked to mortality records through December 31, 2022, by the Spanish National Institute of Statistics using the national identification document number. Data on causes of death were collected according to ICD-10 [23]. Cancer mortality and cardiovascular disease mortality (CVD mortality) were defined by the C00-D48 and IC00-I99 codes, respectively.

Physical activity and sitting time

Physical activity and ST were assessed with the International Physical Activity Questionnaire Short-Form (IPAQ-SF). This 9-item questionnaire records the PA performed in the last 7 days corresponding to four intensity

levels (sitting, walking, moderate-intensity, and vigorous-intensity activities) derived from four PA domains (leisure time PA, domestic activities, work-related PA, transport-related PA). The outcomes are the weekly time spent engaged in PA, sitting, MET min/week, and PA categories [24]. For this study, we used three categories from the IPAQ-SF: ST, LPA, and MVPA. To minimize bias from individuals who were inactive because they were sick or physically impaired, participants who reported very poor self-perceived health or severe functional limitations at baseline were excluded from the analyses.

Study covariates

The following demographic and healthy lifestyle variables were included as covariates: age (15–24, 25–34, 35–44, 35–44, 45–54, 55–64, 65–69 years old); sex (women and men); country of birth (Spain and other countries); educational level (elementary or lower, middle school, high school graduate, and university education); tobacco use (never, former, current < 15 cigs/day, and current ≥ 15 cigs/day); alcohol intake based on both frequency of consumption and volume consumed (never drinkers, former drinkers, occasional drinkers, drinkers > 0–20 g/day, and drinkers > 20 g/day); binge drinking (yes/no) defined as the consumption of ≥6 or ≥5 standard drinks (10 g of ethanol) within a 4–6 h period for men and women, respectively; self-reported body mass index (BMI underweight < 18.5 kg/m^2, normal weight 18.5–24.9 kg/m^2, overweight 25.0–29.9 kg/m^2, obesity ≥ 30 kg/m^2, and not available); and level of adherence to a high quality diet based on the Mediterranean Diet Adherence Screener index, ranging from 0 (lowest adherence) to 10 (highest adherence). Participants were classified as having either low, medium, or high adherence [25, 26].

Statistical analysis

Data analyses were conducted on 30 955 individuals from the total sample of 44 096 participants, selected based on age restrictions outlined in the IPAQ-SF (between 15 and 69 years old) and the availability of valid data.

The study involved analyzing the distribution of categorical data and computing proportions along with their corresponding 95% confidence intervals (CI) across categories within the dataset. Additionally, continuous PA variables were represented by weighted means and standard deviations (SD). To ascertain differences between descriptive variables, statistical analyses including t-tests and analysis of variance (ANOVA) were employed.

Three different Poisson regression models were fitted to estimate the incidence rate ratios (IRR) and 95% CI of the association between each PA/ST and the risk of death (all-cause mortality, cancer mortality, and CVD mortality). First, the single model estimated the association between mortality and each PA or ST separately, and is expressed as follows:

Mortality (IRR) = (b_1) LPA + (b_5) covariates.

Second, the partition model represented the effect of increasing the activity type while holding other activity types constant, and is expressed as follows:

Mortality (IRR) = (b_1) LPA + (b_2) MVPA + (b_3) ST + (b_5) covariates.

Third, the hypothetical effect of replacing ST with PA (LPA or MVPA) on mortality was estimated with the ISM. Likewise, the substitution of LPA with MVPA maintaining the ST was also evaluated. This method estimates the effects of replacing one activity for another for the same amount of time (1 h/week, in this case), and is expressed as follows:

Mortality (IRR) = (b_1) LPA + (b_2) MVPA + (b_4) total time + (b_5) covariates.

where the coefficients b_1 and b_2 represent the effects of 1 h/week substitution of ST with LPA or MVPA while the total time remains constant. The analyses were conducted for the whole sample and then stratified by sex. All models were adjusted for sex, age, country of birth, educational level, tobacco use, alcohol intake, binge drinking, BMI, adherence to Mediterranean diet.

Analyses were performed with the STATA version 18.0 (StataCorp LLC, College Station, TX, USA), and the survey command was used to consider the complex design of the survey.

Results

Descriptive characteristics of the sample and time spent on PA levels and ST are shown in Table 1. During a median follow-up of 5.7 years, 957 participants died (310 women and 647 men). The leading causes of death were cancer (460 participants), and CVD (204 individuals). Participants reported an average ST of 33 h/week, 6.2 h/week of LPA, and 2.8 h/week of MVPA.

Table 2 presents the single variable, partition, and isotemporal models examining the associations between PA levels and ST with all-cause, CVD, and cancer mortality. The adjusted partition model, where the models were mutually adjusted for all activity categories, showed that ST was associated with a higher risk for all-cause, CVD, and cancer mortality (1.0%, 1.4%, and 0.7% higher risk, respectively). In contrast, MVPA was associated with a lower risk for all-cause, CVD, and cancer mortality (2.4%, 4.5%, and 2.4% lower risk, respectively). Finally, LPA was not associated to any change in mortality risk.

Based on the isotemporal analysis (adjusted models), substituting ST with PA reduced mortality risk. The replacement of 1 h/week of ST with 1 h/week of MVPA was significantly associated with lower risk for all-cause, CVD, and cancer mortality (3.3%, 6.7%, and 3.1%, respectively). Likewise, replacing 1 h/week of ST with 1 h/week

Table 1 Descriptive characteristics of the sample according to physical activity levels and sitting time

	Total		Light PA	Moderate-vigorous PA	Sitting time
Variable	***N*[a]**	**Proportion %[b]**	**Mean (SD) [b] hours/week**	**Mean (SD) [b] hours/week**	**Mean (SD) [b] hours/week**
Total	30,955		6.2(6.3)	2.8(5.3)	33.0(18.9)
Sex					
Women	16,002	50.0	6.0(6.1)†	2.1(4.4)‡	31.7(18.3)‡
Men	14,953	50.0	6.3(6.6)	3.6(5.9)	34.3(19.4)
Age					
15–24	3030	13.8	5.9(6.3)‡	4.0(5.7)‡	42.2(20.1)‡
25–34	4563	18.7	6.2(6.6)	3.2(5.3)	33.3(20.1)
35–44	7433	23.6	5.8(6.4)	2.9(5.2)	32.0(19.6)
45–54	6916	21.1	6.1(6.2)	2.6(5.2)	32.0(18.8)
55–64	6209	16.1	6.5(6.3)	2.4(5.2)	31.1(16.7)
65–69	2804	6.6	6.8(6.1)	2.2(4.9)	31.1(14.8)
Country of birth					
Spain	27,496	84.1	6.1(6.3)†	2.8(5.2)	33.5(19.0)‡
Other	3459	15.9	6.5(6.6)	2.8(5.5)	28.8(17.0)
Level of education					
Elementary or lower	5207	15.4	6.1(6.4)‡	2.3(5.4)‡	29.5(16.2)‡
Secondary Education	9640	32.2	6.6(6.7)	3.0(5.8)	30.1(17.7)
High school	9877	32.7	6.2(6.4)	3.0(5.2)	33.2(19.2)
University	6231	19.7	5.5(5.7)	2.7(4.3)	39.9(20.2)
Smoking					
Never smokers	14,789	49.4	6.0(6.2)†	2.9(5.2)‡	33.3(18.9)‡
Former smokers	7052	21.5	6.4(6.3)	2.9(5.3)	33.6(19.1)
Smokers 1–14 cig/day	5681	18.5	6.4(6.5)	2.7(5.1)	31.8(18.4)
Smokers ≥ 15 cig/day	3433	10.7	6.0(6.7)	2.5(5.8)	32.1(18.9)
Alcohol intake					
Never drinkers	5508	18.9	6.4(6.4)‡	2.6(5.4)‡	31.1(18.1)‡
Formers drinkers	3596	10.9	5.9(6.1)	2.3(5.0)	31.4(18.2)
Occasional drinkers	9402	31.0	6.0(6.3)	2.7(5.0)	33.3(19.3)
Drinkers > 0–20 g/day	10,503	33.4	6.3(6.3)	3.0(5.3)	34.1(19.0)
Drinkers > 20 g/day	1946	5.9	6.5(6.7)	3.7(6.5)	33.3(18.8)
Binge drinking					
No	28,757	92.7	6.2(6.3)†	2.8(5.2)‡	32.7(18.7)‡
Yes	2198	7.3	5.8(6.4)	3.5(5.8)	36.5(20.2)
Body mass index					
Normal weight	13,705	46.0	6.2(6.3)†	3.1(5.1)‡	33.3(19.2)‡
Overweight	10,782	33.5	6.3(6.4)	2.9(5.5)	32.2(18.4)
Underweight	670	2.5	5.9(6.2)	2.5(4.8)	36.9(20.2)
Obesity	4725	14.7	5.9(6.3)	2.1(5.1)	33.4(18.6)
N/A	1073	3.2	5.2(5.9)	2.1(5.1)	31.0(18.3)
Adherence to Mediterranean Diet					
Very high	6445	18.9	7.3(6.5)‡	3.1(5.3)‡	31.3(17.9)‡
High	5022	15.4	6.3(6.2)	2.7(5.0)	32.3(18.5)
Low	5780	18.3	6.2(6.3)	2.7(5.1)	32.8(18.6)
Very low	13,708	47.4	5.6(6.3)	2.8(5.4)	34.0(19.4)
All-cause mortality					
No	29,998	97.5	6.2(6.3)	2.9(5.3)‡	32.9(18.9)†
Yes	957	2.5	6.2(6.5)	1.8(4.8)	34.8(18.8)
CVD mortality					
No	30,751	99.5	6.2(6.3)	2.8(5.3)†	33.0(18.8)†
Yes	204	0.5	6.8(7.1)	1.3(4.1)	36.7(20.3)
Cancer mortality					

Table 1 (continued)

	Total		Light PA	Moderate-vigorous PA	Sitting time
Variable	***N*[a]**	**Proportion %[b]**	**Mean (SD) [b] hours/week**	**Mean (SD) [b] hours/week**	**Mean (SD) [b] hours/week**
No	30,495	98.8	6.2(6.3)	2.9(5.3)‡	32.9(18.9)
Yes	460	1.2	6.0(6.1)	1.8(4.7)	34.0(18.7)

PA: Physical activity; SD: Standard deviation; CVD: Cardiovascular diseases; N/A: Data not available

[a] Unweighted; [b] %/Weighted means

† P value < 0.05; ‡ P value < 0.001

of LPA was significantly associated with lower risk for all-cause and cancer mortality (1.6 and 2.1%, respectively) with no effect on CVD mortality. In turn, increasing PA intensity did impact CVD mortality. Substituting 1 h/week of LPA with 1 h/week of MVPA was significantly associated with a 7.6% lower risk of CVD mortality.

In Table 3 we reran these analyses stratified by sociodemographic variables. Although replacing 1 h/week of ST with the same amount of time of MVPA had a protective effect independent of sex, age, and educational level, the size of the effect varies. The favorable impact is stronger in women than in men regarding all-cause (8.5% vs. 2.0%) and cancer mortality (11.1% vs. 1.3%). It is also stronger for CVD mortality among individuals with higher versus lower educational level (12.1% vs. 1.4%).

Similarly, the substitution of 1 h/week of ST with 1 h/week of LPA had a stronger protective effect in women than in men but only for cancer mortality (5% vs. 0.8%). Finally, the impact of replacing LPA with MVPA did not vary by sex, age, and educational level in its associations with all-cause, CVD, and cancer mortality (p for interaction > 0.05).

Discussion

Our study provides novel insights into the potential mortality benefits derived from substituting ST with different levels of PA in a population-based cohort of adults residing in Spain. Our results suggest that replacing 1 h/week of ST with an equivalent time of PA reduces the risk for all-cause, CVD, and cancer mortality. The encouraging association was observed when replacing ST with either LPA or MVPA, and also when increasing PA intensity from LPA to MVPA. Thus, although our findings strongly suggest that any increase in PA may benefit health, they also show that the strengths of such associations do vary by type of mortality risk, i.e., all-cause, CVD, or cancer mortality. Further, our stratified results indicate that the magnitude of some of these relationships may vary by sex, age, and educational level.

Our findings support previous research on the beneficial impact on mortality risk stemming from replacing sedentary time with PA [12, 18–21, 27–29]. Nonetheless, we observed a smaller reduction in mortality risk compared to these previous studies, which reported a reduction ranging from 12 to 81%. This discrepancy may be attributed to our use of different methods for estimating SB and PA, as most previous studies utilized objective methods such as accelerometers [12, 18–21, 27, 28].

Nevertheless, their results should be interpreted cautiously, as they involved short follow-up periods, older adults, or limited statistical adjustments for poor health. These factors could result in an overestimation of the association strength between PA and mortality, especially with MVPA [30]. In addition, it has been suggested that self-reported methods may underestimate the strength of these relationships and the true reduction in mortality risk [31, 32]. Therefore, one may argue that had we used objective methods in this study, the associations observed here would have been amplified and thus closer to those referred by these studies.

Furthermore, it is worth noting that our study assessed only ST, whereas other works have included various SB measured by accelerometers or other PA questionnaires. These methods may capture different types of SB related to mortality, such as lying down [33]. Alternatively, the lower impact on mortality observed in our study may be related to the different substitution time proposed. Most ISM studies proposed 30 min/day [12, 19–21, 27, 28], whereas our study proposed 1 h/week. This shorter substitution time could have attenuated the magnitude of these associations, indicating a dose-response association between the PA volume and health outcomes, as reported previously [34, 35].

Our results also suggest that the replacement of 1 h/week of ST with 1 h/week of MVPA versus LPA provides greater mortality risk reduction. This is consistent with previous research reporting a stronger association with mortality when substituting SB with MVPA rather than with LPA [12, 18, 19, 27, 28, 36].

However, we found that the substitution of ST with LPA was not associated to CVD mortality. Although LPA has been associated with improved cardiometabolic health and reduced mortality risk [37], our results indicated that LPA might not be sufficient to counteract the effects of SB on CVD mortality as it falls short of providing the significant cardiovascular benefits that come with

Table 2 Associations among all-cause, cardiovascular disease, and cancer mortality, and physical activity levels and sitting time

	All-cause mortality	CVD mortality	Cancer mortality
	IRR(95%CI)	IRR(95%CI)	IRR(95%CI)
N deaths/total	957/30,955	204/30,955	460/30,955
Single model unadjusted			
MVPA	0.945 (0.922,0.969)	0.900 (0.833,0.971)	0.947 (0.915,0.980)
LPA	0.995 (0.983,1.007)	1.015 (0.989,1.042)	0.992 (0.976,1.007)
ST	1.006 (1.002,1.010)	1.009 (1.001,1.018)	1.004 (0.998,1.010)
Single model adjusted[a]			
MVPA	0.970 (0.953,0.989)	0.941 (0.893,0.993)	0.970 (0.945,0.996)
LPA	0.986 (0.974,0.999)	1.011 (0.983,1.040)	0.979 (0.963,0.996)
ST	1.011 (1.006,1.015)	1.013 (1.004,1.022)	1.009 (1.002,1.016)
Partition model unadjusted			
MVPA	0.946 (0.923,0.970)	0.899 (0.832,0.971)	0.948 (0.916,0.981)
LPA	1.002 (0.991,1.014)	1.027 (1.001,1.054)	0.997 (0.981,1.013)
ST	1.005 (1.001,1.009)	1.010 (1.001,1.019)	1.003 (0.997,1.009)
Partition model adjusted[a]			
MVPA	0.976 (0.958,0.995)	0.945 (0.897,0.997)	0.976 (0.950,1.002)
LPA	0.994 (0.981,1.007)	1.024 (0.995,1.053)	0.986 (0.968,1.003)
ST	1.010 (1.005,1.014)	1.014 (1.005,1.023)	1.007 (1.000,1.014)
Isotemporal unadjusted			
MVPA x ST	0.941 (0.918,0.966)	0.890 (0.823,0.962)	0.946 (0.913,0.979)
LPA x ST	0.997 (0.985,1.009)	1.017 (0.991,1.044)	0.994 (0.979,1.010)
MVPA x LPA	0.944 (0.919,0.971)	0.875 (0.807,0.948)	0.951 (0.915,0.988)
Isotemporal adjusted[a]			
MVPA x ST	0.967 (0.949,0.985)	0.933 (0.885,0.983)	0.969 (0.944,0.995)
LPA x ST	0.984 (0.972,0.997)	1.010 (0.982,1.038)	0.979 (0.962,0.996)
MVPA x LPA	0.982 (0.961,1.004)	0.924 (0.869,0.981)	0.990 (0.959,1.023)

Incidence rate ratio (IRR) and 95% confidence interval (95%CI)

CVD: Cardiovascular diseases; MVPA: moderate-vigorous physical activity; LPA: light physical activity; ST: sitting time

Single model examining the association of each activity individually with all-cause, CVD, and cancer mortality

Partition model examining the association of a 1 h/week increase in each activity while holding other activity types constant with all-cause, CVD, and cancer mortality

Isotemporal model examining the association of replacing 1 h/week of one activity type with 1 h/week of another activity type with all-cause, CVD, and cancer mortality

[a] Adjusted for sex, age, country of birth, educational level, smoking, alcohol intake, binge drinking, body mass index, and adherence to Mediterranean Diet

MVPA. Interestingly, our findings also show that replacing LPA with MVPA was associated with a risk reduction in only CVD mortality. A plausible explanation would be that MVPA activates a range of higher or more CVD-relevant physiological responses than LPA. These responses would, in turn, cause a more significant metabolic favorable impact on cardiovascular health thus counteracting the negative metabolic effects of SB [38]. Thus, these findings highlight the potential beneficial impact of replacing sitting time or LPA with MVPA to lower the risk of CVD-related deaths.

Nevertheless, our results indicate that replacing SB with LPA could also reduce the risk of mortality. Specifically, this substitution was associated with a lower risk for all-cause and cancer mortality. In fact, we observed that substituting ST with LPA might confer protective effects against cancer-related mortality, with the reduction being only slightly under 1% point than that achieved by substituting ST with MVPA. Generally, the associations between PA and cancer mortality are weaker and more heterogeneous compared to other causes of mortality. The heterogeneity might result from grouping different cancer types together. Also, different PA levels could affect individuals differently depending on the cancer type or site [39, 40].

Our results underscore the need for further investigation and are highly relevant for improving public health messaging. This work suggest that small changes in PA and SB can protect against mortality related to a range of chronic diseases, including cancer mortality [6, 35]. This reinforces the World Health Organization's message, based on the current scientific paradigm, that every move counts towards better health [41], and may motivate individuals unable to perform MVPA to engage in LPA. These individuals may find it more feasible to replace SB

Table 3 Isotemporal substitution of sitting time with physical activity levels, and risk for all-cause, cardiovascular diseases, and cancer mortality, by sex, age, and educational level

		ST with MVPA		ST with LPA		LPA wit MVPA	
	N **deaths/total**	**IRR (95%CI)**	***P*** **for interaction**	**IRR (95%CI)**	***P*** **for interaction**	**IRR (95%CI)**	***P*** **for interaction**
All-cause mortality							
Sex							
Women	310/16,002	0.915 (0.871,0.962)		0.975 (0.949,1.001)		0.939 (0.885,0.996)	
Men	647/14,953	0.980 (0.961,0.999)	0.019	0.989 (0.975,1.004)	0.387	0.990 (0.967,1.014)	0.114
Age							
15–54 years	252/21,942	0.972 (0.939,1.006)		0.999 (0.975,1.023)		0.973 (0.934,1.014)	
55–69 years	705/9013	0.963 (0.942,0.985)	0.765	0.977 (0.963,0.991)	0.155	0.986 (0.960,1.013)	0.604
Educational level							
Secondary or higher education	621/25,748	0.964 (0.941,0.987)		0.978 (0.963,0.994)		0.985 (0.957,1.013)	
Primary education or no education	336/5207	0.972 (0.943,1.002)	0.729	0.999 (0.978,1.020)	0.179	0.973 (0.937,1.011)	0.660
CVD mortality							
Sex							
Women	67/16,002	0.853 (0.759,0.958)		1.027 (0.978,1.079)		0.830 (0.726,0.948)	
Men	137/14,953	0.945 (0.893,1.000)	0.108	1.004 (0.971,1.038)	0.579	0.941 (0.881,1.006)	0.101
Age							
15–54 years	49/21,942	0.889 (0.808,0.978)		1.054 (1.001,1.109)		0.843 (0.756,0.941)	
55–69 years	155/9013	0.946 (0.892,1.004)	0.237	0.988 (0.957,1.020)	0.051	0.958 (0.897,1.023)	0.059
Educational level							
Secondary or higher education	128/25,748	0.879 (0.815,0.947)		1.002 (0.967,1.039)		0.877 (0.804,0.957)	
Primary education or no education	76/5207	0.986 (0.929,1.047)	0.036	1.027 (0.980,1.078)	0.612	0.960 (0.885,1.041)	0.133
Cancer mortality							
Sex							
Women	163/16,002	0.889 (0.818,0.968)		0.950 (0.917,0.984)		0.936 (0.850,1.032)	
Men	297/14,953	0.987 (0.961,1.014)	0.031	0.992 (0.972,1.012)	0.048	0.995 (0.962,1.030)	0.316
Age							
15–54 years	107/21,942	0.946 (0.882,1.015)		0.983 (0.952,1.016)		0.962 (0.889,1.042)	
55–69 years	353/9013	0.977 (0.950,1.006)	0.353	0.977 (0.957,0.998)	0.929	1.000 (0.963,1.038)	0.406
Educational level							
Secondary or higher education	310/25,748	0.962 (0.931,0.995)		0.970 (0.949,0.991)		0.992 (0.954,1.032)	
Primary education or no education	150/5207	0.981 (0.937,1.028)	0.561	0.999 (0.969,1.029)	0.138	0.983 (0.925,1.044)	0.766

Isotemporal substitution examining the association of replacing 1 h/week of one activity type with 1 h/week of another activity type

MVPA: moderate-vigorous physical activity; LPA: light physical activity; ST: sitting time; CVD: Cardiovascular disease

Incidence rate ratio (IRR) and 95% confidence interval (95%CI). P value for interactions with sex, age, and educational level categories

All models were adjusted for sex, age, country of birth, educational level, smoking, alcohol intake, binge drinking, body mass index, and adherence to Mediterranean Diet

with LPA, rather than with MVPA, thus improving their health.

Our analyses stratified by sociodemographic variables show that higher educated individuals could derive more benefits from substituting ST with MVPA than their lower educated counterparts. We would argue that those with higher educational level often hold higher-ranking positions involving prolonged ST and thus at a higher mortality risk [42]. Thereby, substituting sedentary time with PA might help attenuate this risk in this subpopulation [43].

Further, health-related benefits of PA differ by PA domains, with greater benefits associated with PA performed during leisure time (LTPA) [44, 45]. Considering the educational disparities in reported PA domains—where higher educated individuals are more likely to engage in LTPA [46, 47] than others—could help explain the observed differences in benefits.

Reported sex differences in response to PA, reveal that women experience more significant reductions than men in overall and cardiovascular mortality risk at equivalent levels of LTPA [48, 49]. To the best of our knowledge, only two studies have analyzed the substituting effects of replacing SB with PA on mortality risk by sex. One study [27] found similar results across sexes when replacing 30 min/day of ST with LPA or MVPA for all-cause, CVD, and cancer mortality. However, another study [28] showed that replacing 30 min/day of SB with an equal amount of time of MVPA was associated with a lower risk for all-cause mortality in men, but not in women. Our results indicated that the effects of replacing 1 h/week of SB with 1 h/week of PA (LPA or MVPA) might confer more protection against all-cause, CVD, and cancer mortality in women than in men. Overall, this indicates the importance of considering and further exploring sex interaction effects in these associations in future studies.

This study has several strengths. We used data from two nationally representative samples of the population residing in Spain over 15 years of age, and followed-up for a median of 5.7 years. To the best of our knowledge, this is the first study to estimate the substitution effects of replacing ST time with an equal amount of PA time in the population of a Southern European country. In addition, we controlled for a wide range of potential confounding variables and excluded participants reporting very poor self-perceived health or severe functional limitations at baseline. Furthermore, unlike previous studies, our proposed short substitution time of ST for PA (1 h/week) to achieve mortality benefits makes our findings easily transferable to PA guidelines [6–8] and may inform a more efficacious public health message.

However, our study was not without limitations. Both PA and ST were self-reported measures, susceptible to recall bias, which may have underestimated SB and overestimated PA [50, 51]. Although the IPAQ-SF might overestimate PA [52], it is recommended as a cost-effective method for large-scale monitoring of PA in the EU [53] given its acceptable measurement properties [24]. In contrast, the single-item SB question from the IPAQ-SF had low criterion validity and provided limited information [54]. Having said that, single-item measures can be a valid screening tool to determine whether respondents´ activity levels are sufficient to provide health benefits [55]. Moreover, objective methods are not without limitations [56], they present their own challenges, and they are difficult to implement in the context of large-scale epidemiological studies [57]. Further, PA and ST were reported only at baseline, and were not re-assessed, so follow-up data on these behaviors were not available. In addition, these findings are based on theoretical models. However, ISM has been suggested as a useful method to discern the morbidity and mortality benefits that could be achieved when SB is replaced with PA [58]. Finally, while our study was conducted in a representative Spanish population, the generalizability of the findings to other countries or cultural contexts may not be directly applicable. However, these findings may contribute to the public health message regarding the amount of time spent in SB that needs to be replaced with PA to confer health benefits.

Conclusions

Our findings provide supporting evidence to support the message that less sitting time and more physical activity diminishes mortality risk. Our results indicate that replacing 1 h per week of sitting time with the same time of light physical activity or moderate-to-vigorous physical activity is significantly associated with a reduction in all-cause, CVD, and cancer mortality risk. Additionally, our results indicate that the magnitude of these effects may vary according to certain sociodemographic variables, especially by sex. Future research should focus on the mechanisms by which the substitution of ST with different PA levels reduces the risk of mortality for various causes of death, as well as the source of the sex difference.

Abbreviations

ST	Sitting time
PA	Physical activity
CVD	Cardiovascular diseases
LPA	Light physical activity
MVPA	Moderate-vigorous physical activity
RR	Risk ratio
IRR	Incidence risk ratio
METs	Metabolic equivalent task
ISM	Isotemporal substitution models
IPAQ-SF	International Physical Activity Questionnaire Short-Form
BMI	Body mass index

Author contributions

MAC participated in the conceptualization, methodology, formal analysis, data curation, and writing of the original draft. IG participated in the conceptualization, methodology, formal analysis, data curation, writing of the original draft, resources and supervision. CO participated in the data curation, analysis, manuscript reviewing and editing. BG, AM, and MN participated in manuscript reviewing and editing. All authors have read and approved the final version of the manuscript and agree with the order of presentation of the authors.

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Data availability
The data supporting the findings of this study are available from the Spanish Ministry of Health and the Spanish National Institute of Statistics. Access to these data is restricted, as they were used under specific collaboration agreements and conventions for this study and are therefore not publicly available.

Declarations

Ethics approval and consent to participate
The study was approved by Carlos III Institute of Health Ethical Research Committee (CEI PI 28_2019). All participants gave informed consent to participate in the study before being included.

Consent for publication
Not applicable.

Disclaimer
This article presents independent research. The views expressed are those of the authors and not necessarily those of the Institute of Health Carlos III.

Competing interests
The authors declare no competing interests.

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