Leisure-time and transport-related physical activity and the risk of mortality: the CRONICAS Cohort Study

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Short title:

Physical activity and all-cause mortality

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Conflict of interest

The authors declare that no conflict of interest exist.

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ABSTRACT (196 words)

Background:

The long-term health association of the leisure-time and transport-related physical activity domains of the International Physical Activity Questionnaire (IPAQ) have not been established in Latin American settings. We aimed to quantify the 7-year all-cause mortality risk associated with levels of leisure-time and transport-related physical activity.

Methods:

Ongoing prospective cohort study conducted in four sites in Peru. People ≥ 35 years were randomly selected from the general population in each study site. The exposures were leisure-time and transport-related physical activity (IPAQ) at baseline. The outcome was all-cause mortality based on information retrieved from national records. Cox regression and sensitivity analyses were conducted.

Results:

There were 3601 people (mean age 55.8 years, 51.5% women). Greater levels of physical activity were associated with lower risk of all-cause mortality, an observation confirmed in sensitivity analyses. Compared to those with low levels of physical activity, leisure-time (≥ 500 MET-min/week) and transport-related (500-1499 and ≥ 1500 MET-min/week) physical activity were associated with 70% (95% CI: 3%-90%), 43% (95% CI: 18%-61%), and 42% (95% CI: 8%-63%) lower all-cause mortality, respectively.

Conclusions:

Greater levels of leisure-time and transport-related physical activity were associated with a strong reduction in the risk of all-cause mortality across different geographical sites.

Keywords:

Mortality, physical activity, leisure activities, transportation, Peru

INTRODUCTION

Physical activity has been associated with important health benefits [1, 2], including, but not limited to a reduction in overweight and obesity rates, and lower risk of cancer as well as mortality [3-5]. Low physical activity continues being an important risk factor contributing to global mortality [6] as the annual rate of physical activity worldwide has not changed during the last decades. As a consequence, the World Health Organization Global Action Plan for the Prevention and Control of Noncommunicable Diseases (NCD) incorporated an aim to reduce modifiable risk factors, including tobacco use, unhealthy diet and physical inactivity, for NCDs and underlying social determinants by creating health-promoting environments [7, 8].

According to the US Department of Health and Human Services, adults should do at least 150 to 300 minutes a week of moderate-intensity, or 75 to 150 minutes a week of vigorous-intensity aerobic physical activity or an equivalent combination of moderate- and vigorous-intensity aerobic activity [9]. However, existing literature shows high levels of physical inactivity, especially in low- and middle-income countries [10]. In Peru, for example, in a nationally representative sample, low levels of physical activity were reported in 62% of adults aged 18 to 59 years [11]. Moreover, the baseline assessment of the CRONICAS Cohort Study, conducted in resource-constrained settings with varying degrees of urbanization and altitude, found that physical inactivity was present in 94% of individuals when measured by the leisure-time domain of the International Physical Activity Questionnaire (IPAQ) [12].

The IPAQ is a widely used tool for assessing and comparing physical activity levels in different populations. Whereas the IPAQ has been validated in different Latin American countries, the application of the full questionnaire has time and resource challenges, as well as limited correlation when contrasted with objective physical activity data [13, 14]. To overcome this, the leisure-time and transport-related domains of the IPAQ have been encouraged in Colombian and Brazilian populations for population-based surveillance and research [15]. Such recommendation may apply to similar populations, including Peru, but the public health implications of using these two IPAQ domains needs to be verified. Moreover, the long-term associations on important outcomes have not been determined yet in Latin American populations. Existing information regarding health benefits of physical activity on all-cause mortality comes mainly from data from high-income countries [16, 17], whereas only two reports were included from resource-constrained settings (Iran and China), and none from Latin America.

As a result, this study aimed to evaluate the association between physical activity levels, assessed by using the leisure-time and transport-related domains of the IPAQ, on all-cause mortality in resource-constrained settings in Peru, using a cohort with 7 years of follow-up.

METHODS

Study design

Data from the CRONICAS Cohort Study was used, and its methodological details have been described elsewhere [18]. Briefly, individuals from four Peruvian sites located in three different regions, differing by level of altitude and urbanization, were included. The study sites were Pampas de San Juan de Miraflores, a highly-urbanized, at the sea level setting, in Lima; Puno, a high-altitude region in the Peruvian highlands (3825 meters above sea level), and split into rural and urban settings; and Tumbes, a semiurban low-altitude (sea level), coastal region where rural areas are intermixed with rapidly-growing urban areas. For this

manuscript, baseline data, collected between 2010 and 2012, and mortality records, retrieved in 2018, were analyzed.

Study participants

A sex- and age-stratified (35-44, 45-54, 55-64, and 65+ years) random sample was taken for each of the study sites. The sampling frame for this selection was based on information from the most updated census in each site (2010). Individuals were selected by computer from the census list with replacement in case of rejecting participation.

Subjects aged ≥ 35 years and with full-time residence in the study area were invited to participate. Women who were pregnant, those cognitively incapable of providing informed consent, or those bedridden or with physical disability preventing measurements of blood pressure or anthropometrics were excluded. Only one participant per household was enrolled into the study.

Definition of variables

Outcome: All cause-mortality was the outcome of interest and was defined by the occurrence of any fatal event between baseline enrollment and any point during follow-up. In 2018, the vital status of participants (dead or alive) was retrieved from national vital registries. For this evaluation, participants were not directly contacted as only vital status and date of death or censoring was required. If a participant had died, the date of death was used for analysis purposes; but if participant was alive, then the date on which the search in the National Registry of Identification and Civil Status (RENIEC in Spanish) database was conducted was considered as the censoring date. The time between baseline assessment and the date of death or censorship was then estimated in years.

Exposure: At the cohort baseline, the leisure-time and transport-related domains of the IPAQ were applied. The decision of using these domains was based on guidance derived from research and evaluation conducted in Latin American countries such as Brazil and Colombia [15]. We used the Spanish version of the IPAQ adapted for similar countries such as Colombia (<http://www.ipaq.ki.se/>). We defined low and high levels of physical activity for each of these two domains based on specific cutoffs.

In the case of leisure-time physical activity, those with <600 MET-min/week during leisure time were defined as doing none or very little physical activity (i.e., low level), whereas those ≥ 600 MET-min/week were considered as doing high level of leisure-time physical activity. Similarly, for transport-related physical activity, low level was defined as reporting not doing any transport-related physical activity and, conversely, any single walk or cycle trip for 10 minutes or more was considered as high transport-related physical activity [19].

In addition, leisure-time physical activity was also split into three groups: <150 MET-min/week, between 150 and 499 MET-min/week, and ≥ 500 MET-min/week. This additional definition was based on the distribution of the variables as more than 80% of study subjects had <150 MET-min/week and to evaluate dose-response. Similarly, transport-related physical activity domain was also split into three categories but with different cut-offs: <500 MET-min/week, between 500 and 1499 MET-min/week, and ≥ 1500 MET-min/week.

Other study variables: Baseline demographic, socioeconomic, and behavioral risk factor variables were included in the analysis as potential confounders of the association of interest. These variables were: sex (male vs. female); age (35-44, 45-54, 55-64, and 65+ years); years of education (<7 , 7-11, and 12+ years); socioeconomic position, based on a wealth index using household assets and facilities separately for each study site and then combined into a single variable and presented in tertiles [20]; and study site (highly-urbanized Lima, urban Puno, rural Puno, and semiurban Tumbes). Behavioral risk factors included daily smoking defined as at least one cigarette per day (yes vs. no) [21]; alcohol drinking, based on the consumption of at least 6 drinks of beer or any equivalent beverage once or more per month (high vs. low) [22]; and body mass index, with the traditional cutoffs

for normal ($\text{BMI} < 25 \text{ kg/m}^2$), overweight ($25 \text{ kg/m}^2 \leq \text{BMI} \leq 30 \text{ kg/m}^2$), and obesity ($\text{BMI} \geq 30 \text{ kg/m}^2$). In addition, hypertension, defined as systolic blood pressure $\geq 140 \text{ mm Hg}$, diastolic blood pressure $\geq 90 \text{ mm Hg}$, or self-report of physician diagnosis or current use of antihypertensive medication (yes vs. no) [23]; total cholesterol levels, defined as normal (total cholesterol $< 200 \text{ mg/dL}$), high-normal ($200 - 239 \text{ mg/dL}$), and high ($\geq 240 \text{ mg/dL}$); and type 2 diabetes status, defined as fasting glucose $\geq 126 \text{ mg/dL}$, or self-report of physician diagnosis or currently receiving antidiabetic drugs [24], were also included.

Total serum cholesterol and plasma glucose were measured after 8-12 hours of fasting. Cholesterol was measured using a Cobas Modular Platform automated analyzer with Roche Diagnostic reagents, whereas glucose was measured using an enzymatic colorimetric method (GOD-PAP, Modular P-E/Roche-Cobas). All samples were analyzed in a single facility, and quality assurance was verified regularly and monitored by Bio-Rad.

Statistical methods

Analyses were conducted using STATA 16 for Windows (StataCorp, College Station, TX, US). Initially, a description of the sample of participants at baseline was conducted. Median and interquartile range for numerical variables, especially for MET-min/week estimations, and proportions for categorical ones were used. The prevalence of low physical activity levels in each IPAQ domain was estimated with their respective 95% confidence intervals (95% CI). Comparisons between population characteristics were also pursued using the nonparametric quality-of-median test for numerical variables and the Chi-squared test for categorical ones.

Mortality rates for the overall sample as well as by physical activity levels were estimated by using person-time and incidence rates. These estimates were reported by 1,000 person-years of follow-up. Crude and adjusted Cox proportional hazard models were built to separately assess the association between each of the definitions of leisure-time and transport-related physical activity and all-cause mortality, reporting hazard ratios (HR) and 95% CI.

Sensitivity analyses were also pursued by including models and estimations utilizing different cutoffs of physical activity levels. In addition, models were built by excluding deaths occurring within the first two years of follow-up, by excluding hypertension and type 2 diabetes cases at baseline, comparing those who did not report physical activity vs. those reporting any physical activity, and using 500 MET-min/week as a cutoff for defining physically active. All these analyses are presented as supplemental material and, for sake of consistency, were done separately for each IPAQ domain.

Ethics

All participants provided oral informed consent because of high illiteracy rates, mainly in rural areas. The study was approved by the Institutional Review Boards (IRB) at Universidad Peruana Cayetano Heredia (UPCH) and A.B. PRISMA, in Lima, Peru, and the Johns Hopkins University, in Baltimore, US. Follow-up assessment to evaluate vital status of participants in 2018 was approved by the IRB at UPCH.

RESULTS

Participant characteristics at baseline

A total of 6872 subjects were contacted, and 4325 were initially enrolled in the cohort. However, 38 had incomplete survey and 686 individuals were not further available. Thus, 3601 participants had information for analysis. Of them, 10 physical activity records were incomplete at baseline. Then, data of 3591 (99.7%) individuals, mean age 55.8 (SD ± 12.7) years, 51.5% females, and 1638 (45.7%) had < 7 years of education, were analyzed.

Physical activity levels

Leisure-time physical activity was low in 94.9% (95% CI: 94.1% - 95.5%) of study subjects, and 2986 (83.2%; 95% CI: 81.9% - 84.4%) had levels <150 MET-min/week. In bivariate analyses, low levels of leisure-time physical activity were more frequent among females ($p<0.001$), older individuals ($p=0.02$), less educated ($p<0.001$), those with low socioeconomic position ($p<0.001$), and those from rural and semiurban settings ($p<0.001$). However, heavy drinking was associated with greater level of leisure-time physical activity ($p<0.001$). Details are presented in Table 1 and Supplemental Tables 1 and 2.

On the other hand, only 34.3% (95% CI: 32.7% - 35.9%) reported low levels of transport-related physical activity, and 978 (27.3%; 95% CI: 25.8% - 28.7%) had levels <500 MET-min/week. Low levels of transport-related physical activity were more common among females ($p<0.001$), older individuals ($p<0.001$), those less educated ($p<0.001$), among those with low socioeconomic position ($p<0.001$), in semiurban sites ($p<0.001$), those with hypertension, and with type 2 diabetes ($p=0.002$). See details in Table 2 and Supplemental Tables 1 and 3.

Risk of mortality by physical activity levels

The vital status of 3321 (92.5%) subjects was confirmed, with a mean time of follow-up of 7.0 (SD ± 1.0) years, and completing a total of 23,166.4 person-years. A total of 199 (6.0%) deaths were recorded during the study period, with an all-cause mortality rate of 8.6 (95% CI: 7.5 – 9.9) per 1,000 person-years.

Leisure-time physical activity and all-cause mortality

Crude mortality rate was lower among those with high levels of leisure-time physical activity compared to those with low levels, but this association was attenuated in the multivariable model (HR = 0.45; 95% CI: 0.14 – 1.41). Nevertheless, individuals with ≥ 500 MET-min/week of leisure-time physical activity had a reduction of 70% in the risk of all-cause mortality compared to those with <150 MET-min/week (HR = 0.30; 95% CI: 0.10 – 0.97). See details in Figure 1 and Supplemental Table 4. When sensitivity analyses were conducted, results were consistent with the findings reported here, although some of them were not significant (Supplemental Table 5).

Transport-related physical activity and all-cause mortality

Regardless of the definition used, higher crude mortality rates were observed among those with low levels of transport-related physical activity. In multivariable model, those with greater levels of transport-related physical activity had, on average, 43% to 47% reduction in the risk of all-cause mortality compared to the reference group (Figure 1 and Supplemental Table 4). Similarly, sensitivity analyses yielded results that were consistent with these findings (Supplemental Table 6).

DISCUSSION

Main findings

Greater levels of physical activity, assessed using the leisure-time and transport-related IPAQ domains, were associated with a reduction of the risk of all-cause mortality, especially among those with at least 500 MET-min/week, which is considered a good goal for optimal cardiovascular health [9], including those with cardiovascular conditions [25]. In terms of the magnitude of the association, our estimates are higher than previous studies using self-reported physical activity and already described in the literature [5, 26, 27], which may contribute to a better understanding of the higher burden of NCDs in low-resource settings. Our results also highlight that 95% of individuals were in the low-level category of leisure-time physical activity, and a third had low level of transport-related physical activity. These

population patterns point towards major gaps that require attention in the field of health promotion, including the role of physical activity, in order to accrue progress towards the monitoring international indicators including the World Health Organization's (WHO) Global Action Plan for the Prevention and Control of Noncommunicable Diseases [7].

Comparison with previous studies

A systematic review and meta-analysis examined the association between accelerometer-assessed physical activity and all-cause mortality, and concluded that, regardless of intensity, any physical activity was associated with lower risk of mortality with a non-linear dose-response [26]. Similarly, another meta-analysis showed that time spent in daily device-measured light-intensity physical activity has been associated with reduced risk of mortality in adults [28]. Previous studies have reported a non-linear dose-response association between physical activity and mortality [5, 26, 27], and such finding is consistent regardless the use of self-reported or device-measured physical activity. However, such dose-response finding was not evident in our results, possibly because of the limited number of events, as only 6% of participants died during the 7 years of follow-up, or because of the notorious proportion of low levels of physical activity in our population, especially in the case of leisure-time physical activity.

From the leisure-time physical activity perspective, a large pooled 10-year follow-up cohort analysis showed that even low levels of leisure-time physical activity of moderate to vigorous intensity, equivalent to less than half the WHO recommendation, were associated with reduced risk of mortality compared to no such activity [4]. Similarly, in a prospective cohort of participants from 17 different countries, including Argentina, Brazil, Chile and Colombia, reported that higher recreational and non-recreational physical activity were associated with a lower risk of mortality and cardiovascular events among subjects from low-income, middle-income, and high-income countries [29]. However, only pooled data was available and findings for each country were not reported.

Most of the studies focused on transport-related physical activity were based on cycling and walking. A systematic review reported that both cycling and walking reduced the risk of all-cause mortality, adjusted for other physical activity domains, defining a cutoff of 675 MET-min/week [27]. Active commuting has been also associated with lower risk of cardiovascular disease, cancer, and all-cause mortality [30]. Thus, our findings using the transport-related IPAQ domain are in line with previous reports regarding this topic and confirm the direction of the association. Importantly, we contribute to the global literature of physical activity and NCDs by providing information from several resource-constrained Latin American settings. In addition, the observed associations with all-cause mortality described in here are much higher than previous studies assessing physical activity through self-report.

Relevance to public health

Our results suggest that leisure-time and transport-related physical activity domains of the IPAQ may be relevant for the Peruvian and similar low-resource contexts. First, the surveillance of physical activity can prioritize the utilization of the leisure and transport domains as a pragmatic approach. Second, the substantial low levels of physical activity reported in our study emphasize the immense window for improvement. In light of our findings, there is a clear need and opportunity to encourage leisure-time physical and transport-related physical activity, particularly in resource-constrained settings.

Our results suggest that increasing physical activity to levels associated with lower mortality risk seems to be achievable for any individual from the general population. As a matter of fact, to place these recommendations in perspective, improving physical activity could be achieved by walking for 30 minutes for 5 days at a usual pace (3 METs), or cycling 25 minutes for 6 days at a usual pace (3.5 METs) [31].

According to the Global Burden of Disease, worldwide, the implementation of appropriate interventions to change behaviors, especially those related to physical activity, diet quality, and caloric intake are limited by different challenges [6]. Strategies to encourage physical activity should target all age groups, and should be supportive, i.e., including friend, families, or even peers and professionals, and facilitate the access to indoor and outdoor recreation facilities [9]. In addition, such strategies should be implemented including the use of mobile technologies [32], but also improving the built environment to secure the safety of pedestrians and cyclists [33, 34], which are common concerns in limited-resources settings.

Strengths and limitations

This study utilized information of a well-established cohort of participants across different settings in Peru, with high rates of follow-up and exploring a robust long-term outcome such as mortality, important features to inform relevant decision-making. In addition, our study used two domains of the IPAQ, rather than the full instrument, as previously recommended for Latin American settings [15]. We also provide longitudinal estimates of associations and providing a pragmatic low-cost way to support the NCD surveillance efforts.

However, there are some limitations that should be highlighted. First, physical activity was measured only at baseline and, therefore, changes in the patterns or profiles of physical activity over time were not considered and may affect the reported association. Despite this, establishing this association is of essence to support the wider NCD prevention agenda, particularly given mortality risks in a population understudied such as the Latin American region. Second, reverse causality may be present as some conditions before death may limit physical activity and we performed several sensitivity analyses excluding data of deaths occurred within the first 2 years of follow-up. Our sensitivity analyses results (Supplemental Tables 4 and 5) were consistent in direction and magnitude with our estimates herein reported as well as those previously published. Third, all-cause mortality was the outcome of interest, which is a robust indicator but does not allow for further exploration such as cardiovascular or cancer mortality, as that information was not available. Fourth, only two domains of the IPAQ were assessed and total physical activity was not available to be used as potential variable of control. Finally, some residual confounding may be present as variables associated with diet patterns were not available for this analysis.

Conclusions

Greater levels of leisure-time and transport-related physical activity, measured with the IPAQ were associated with a strong reduction in the risk of all-cause mortality across different geographical sites. These findings suggest the need to actively encourage leisure-time physical and transport-related physical activity in Peru and similar low-resource settings.

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FIGURES AND TABLES

Figure 1: All-cause mortality risk by physical activity levels: forest plot of adjusted models

HR = Hazard ratio.

Model adjusted by sex, age, years of education, socioeconomic position, study site, daily smoking, drinking, obesity, hypertension, total cholesterol, and type 2 diabetes status.

Table 1: Characteristics of the study population by leisure-time physical activity

Variables	Leisure-time physical activity		p-value
	Moderate/high (n = 185)	Low (n = 3406)	
Sex			<0.001
Female	59 (3.2%)	1787 (96.8%)	
Male	126 (7.2%)	1615 (92.8%)	
Age			0.02
35 – 44 years	41 (4.8%)	816 (95.2%)	
45 – 54 years	55 (6.0%)	866 (94.0%)	
55 – 64 years	58 (6.4%)	854 (93.6%)	
65+ years	31 (3.5%)	866 (96.5%)	
Years of education			<0.001
< 7 years	52 (3.2%)	1587 (96.8%)	
7 – 11 years	54 (4.7%)	1101 (95.3%)	
12+ years	79 (9.9%)	719 (90.1%)	
Socioeconomic position			<0.001
Low	23 (1.9%)	1191 (98.1%)	
Middle	59 (5.0%)	1125 (95.0%)	
High	103 (8.6%)	1094 (91.4%)	
Study site			<0.001
Lima (highly urbanized)	67 (6.1%)	1037 (93.9%)	
Urban Puno (urbanized)	55 (7.3%)	704 (92.7%)	
Rural Puno (rural)	16 (2.3%)	680 (97.7%)	
Tumbes (semiurban)	47 (4.6%)	985 (95.4%)	
Daily smoking			0.25
No	182 (5.2%)	3299 (94.8%)	
Yes	3 (2.8%)	106 (97.3%)	
Drinking			0.04
Low	169 (5.0%)	3231 (95.0%)	
High	46 (8.4%)	175 (91.6%)	
Body mass index			0.06
Normal	47 (5.0%)	900 (95.0%)	
Overweight	89 (6.4%)	1313 (93.6%)	
Obesity	36 (4.2%)	831 (95.9%)	
Hypertension			0.22
No	135 (5.7%)	2247 (94.3%)	
Yes	40 (4.6%)	836 (95.4%)	
Total cholesterol			0.82
<200 mg/dL	87 (5.3%)	1567 (94.7%)	
200 – 239 mg/dL	53 (5.5%)	917 (94.5%)	
240 mg/dL and over	23 (4.7%)	468 (95.3%)	
Type 2 diabetes			0.60
No	147 (5.2%)	2710 (94.8%)	
Yes	16 (5.9%)	256 (94.1%)	

Comparisons were done using Chi-squared test. Percentages are in rows.
 Low level of leisure time physical activity was defined as doing none or very little physical activity (i.e., <600 MET-min/week) during leisure time.

Table 2: Characteristics of the study population by transport-related physical activity

Variables	Transport-related physical activity		p-value
	Moderate/high (n = 2360)	Low (n = 1231)	
Sex			<0.001
Female	1067 (57.8%)	779 (42.2%)	
Male	1289 (74.0%)	452 (26.0%)	
Age			<0.001
35 – 44 years	602 (70.3%)	255 (29.7%)	
45 – 54 years	667 (72.4%)	254 (27.6%)	
55 – 64 years	617 (67.7%)	295 (32.3%)	
65+ years	472 (52.6%)	425 (47.4%)	
Years of education			<0.001
< 7 years	903 (55.1%)	735 (44.9%)	
7 – 11 years	824 (71.5%)	328 (28.5%)	
12+ years	631 (79.1%)	167 (20.9%)	
Socioeconomic position			<0.001
Low	709 (58.5%)	504 (41.5 %)	
Middle	770 (65.1%)	413 (34.9%)	
High	881 (73.7%)	314 (26.3%)	
Study site			<0.001
Lima (highly urbanized)	863 (78.2%)	241 (21.8%)	
Urban Puno (urbanized)	571 (75.2%)	188 (24.8%)	
Rural Puno (rural)	501 (72.0%)	195 (28.0%)	
Tumbes (semiurban)	425 (41.2%)	607 (58.8%)	
Daily smoking			<0.37
No	2283 (65.6%)	1198 (34.2%)	
Yes	76 (69.7%)	33 (30.3%)	
Drinking			0.006
Low	2217 (65.2%)	1183 (34.8%)	
High	143 (74.9%)	48 (25.1%)	
Body mass index			0.10
Normal	605 (63.9%)	342 (36.1%)	
Overweight	935 (66.7%)	467 (33.3%)	
Obesity	542 (62.5%)	325 (37.5%)	
Hypertension			<0.001
No	1610 (67.6%)	772 (32.4%)	
Yes	508 (58.0%)	368 (42.0%)	
Total cholesterol			0.01
<200 mg/dL	1105 (66.8%)	549 (33.2%)	
200 – 239 mg/dL	598 (61.7%)	372 (38.3%)	
240 mg/dL and over	302 (61.5%)	189 (38.5%)	
Type 2 diabetes			0.002
No	1864 (65.2%)	993 (34.8%)	
Yes	152 (55.9%)	120 (44.1%)	

Comparisons were done using Chi-squared test. Percentages are in rows.
 Low level of transport-related physical activity was defined as not reporting walking or cycling trips in the transport domain of the IPAQ.

SUPPLEMENTAL MATERIAL

Supplemental Table 1: Characteristics of the study population by level of physical activity

Variables	LTPA (MET-min/week) Median (IQR)	p-value	TRPA (MET-min/week) Median (IQR)	p-value
Sex		<0.001		<0.001
Female	0 (0)		773 (347 – 1333)	
Male	0 (0 – 132)		1127 (631 – 2062)	
Age		0.009		<0.001
35 – 44 years	0 (0 – 40)		1026 (565 – 1911)	
45 – 54 years	0 (0 – 33)		1053 (579 – 1975)	
55 – 64 years	0 (0)		933 (480 – 1813)	
65+ years	0 (0)		693 (297 – 1235)	
Years of education		<0.001		<0.001
< 7 years	0 (0)		702 (311 – 1253)	
7 – 11 years	0 (0 – 33)		1049 (582 – 1943)	
12+ years	0 (0 – 198)		1180 (702 – 2076)	
Socioeconomic position		<0.001		<0.001
Low	0 (0)		773 (391 – 1315)	
Middle	0 (0)		924 (462 – 1680)	
High	0 (0 – 160)		1120 (622 – 2079)	
Study site		<0.001		<0.001
Lima	0 (0 – 99)		1318 (693 – 2373)	
Urban Puno	0 (0 – 99)		1071 (640 – 1746)	
Rural Puno	0 (0)		924 (570 – 1464)	
Tumbes	0 (0)		508 (199 – 1013)	
Daily smoking		0.29		0.12
No	0 (0)		924 (471 – 1676)	
Yes	0 (0 – 80)		1191 (499 – 2027)	
Drinking		0.05		<0.001
Low	0 (0)		918 (462 – 1663)	
High	0 (0 – 99)		1235 (640 – 2587)	
Body mass index		0.04		0.04
Normal	0 (0)		853 (462 – 1516)	
Overweight	0 (0 – 33)		954 (480 – 1893)	
Obesity	0 (0)		924 (391 – 1653)	
Hypertension		0.78		<0.001
No	0 (0)		942 (499 – 1787)	
Yes	0 (0)		775 (323 – 1511)	
High total cholesterol		0.62		0.08
<200 mg/dL	0 (0)		936 (471 – 1795)	
240 – 239 mg/dL	0 (0 – 33)		853 (405 – 1664)	
240 mg/dL and over	0 (0)		876 (405 – 1582)	
Type 2 diabetes		0.88		0.01
No	0 (0)		933 (462 – 1737)	
Yes	0 (0)		782 (323 – 1409)	

Comparisons were done using the nonparametric equality-of-medians test.

Supplemental Table 2: Characteristics of the study population by leisure-time physical activity

Variables	Leisure-time physical activity			p-value
	<150 MET-min/week (n = 2982)	150-499 MET-min/week (n = 337)	500+ MET-min/week (n = 268)	
Sex				<0.001
Female	1656 (55.5%)	109 (32.3%)	81 (30.2%)	
Male	1326 (44.5%)	228 (67.7%)	187 (69.8%)	
Age				0.005
35 – 44 years	694 (23.3%)	94 (27.9%)	69 (25.8%)	
45 – 54 years	748 (25.1%)	90 (26.7%)	83 (31.0%)	
55 – 64 years	763 (25.6%)	76 (22.6%)	73 (27.2%)	
65+ years	777 (26.0%)	77 (22.8%)	43 (16.0%)	
Years of education				<0.001
< 7 years	1462 (49.0%)	107 (31.8%)	69 (25.8%)	
7 – 11 years	947 (31.8%)	122 (36.2%)	83 (31.0%)	
12+ years	574 (19.2%)	108 (32.0%)	116 (43.2%)	
Socioeconomic position				<0.001
Low	1095 (36.7%)	81 (24.0%)	37 (13.8%)	
Middle	996 (33.4%)	103 (30.6%)	84 (31.3%)	
High	895 (29.9%)	153 (45.4%)	147 (54.9%)	
Study site				<0.001
Lima (highly urbanized)	875 (29.3%)	134 (39.8%)	95 (35.5%)	
Urban Puno (urbanized)	592 (19.8%)	86 (25.5%)	81 (30.2%)	
Rural Puno (rural)	638 (21.4%)	30 (8.9%)	28 (10.5%)	
Tumbes (semiurban)	881 (29.5%)	87 (25.8%)	64 (23.8%)	
Daily smoking				0.07
No	2899 (97.1%)	320 (95.0%)	262 (97.8%)	
Yes	86 (2.9%)	17 (5.0%)	6 (2.2%)	
Drinking				0.09
Low	2838 (95.0%)	314 (93.2%)	248 (92.5%)	
High	148 (5.0%)	23 (6.8%)	20 (7.5%)	
Body mass index				0.17
Normal	788 (29.6%)	87 (28.7%)	72 (29.3%)	
Overweight	1146 (43.0%)	133 (43.9%)	123 (50.0%)	
Obesity	733 (27.5%)	83 (27.4%)	51 (20.7%)	
Hypertension				0.06
No	1969 (72.9%)	216 (70.1%)	197 (78.8%)	
Yes	731 (27.1%)	92 (29.9%)	53 (21.2%)	
High total cholesterol				0.94
<200 mg/dL	1367 (52.9%)	157 (52.9%)	130 (55.3%)	
240 – 239 mg/dL	804 (31.1%)	94 (31.6%)	72 (30.7%)	
240 mg/dL and over	412 (16.0%)	46 (15.5%)	33 (14.0%)	
Type 2 diabetes				0.91
No	2370 (91.4%)	271 (90.6%)	216 (91.5%)	
Yes	224 (8.6%)	28 (9.4%)	20 (8.5%)	

Comparisons were done using Chi-squared test.

Supplemental Table 3: Characteristics of the study population by transport-related physical activity

Variables	Transport-related physical activity			p-value
	<500 MET-min/week (n = 2982)	500-1499 MET-min/week (n = 337)	1500+ MET-min/week (n = 268)	
Sex				<0.001
Female	630 (64.4%)	820 (52.3%)	396 (38.0%)	
Male	348 (35.6%)	747 (47.7%)	646 (62.0%)	
Age				<0.001
35 – 44 years	184 (18.8%)	376 (24.0%)	297 (28.5%)	
45 – 54 years	201 (20.6%)	412 (26.3%)	308 (29.5%)	
55 – 64 years	238 (24.4%)	397 (25.4%)	277 (26.5%)	
65+ years	354 (36.2%)	381 (24.3%)	162 (15.5%)	
Years of education				<0.001
< 7 years	602 (61.5%)	712 (45.4%)	324 (31.1%)	
7 – 11 years	252 (25.8%)	496 (31.7%)	404 (38.7%)	
12+ years	124 (12.7%)	359 (22.9%)	315 (30.2%)	
Socioeconomic position				<0.001
Low	405 (41.4%)	562 (35.8%)	246 (23.6%)	
Middle	328 (33.5%)	511 (32.6%)	344 (32.9%)	
High	245 (25.1%)	496 (31.6%)	454 (43.5%)	
Study site				<0.001
Lima (highly urbanized)	187 (19.1%)	431 (27.4%)	486 (46.5%)	
Urban Puno (urbanized)	148 (15.1%)	367 (23.4%)	244 (23.4%)	
Rural Puno (rural)	133 (13.6%)	395 (25.2%)	168 (16.1%)	
Tumbes (semiurban)	510 (52.2%)	376 (24.0%)	146 (14.0%)	
Daily smoking				0.12
No	950 (97.1%)	1528 (97.5%)	1003 (96.1%)	
Yes	28 (2.9%)	40 (2.5%)	41 (3.9%)	
Drinking				<0.001
Low	942 (96.3%)	1496 (95.4%)	962 (92.2%)	
High	36 (3.7%)	73 (4.7%)	82 (7.9%)	
Body mass index				0.002
Normal	284 (31.2%)	423 (30.9%)	240 (25.6%)	
Overweight	362 (39.8%)	585 (42.8%)	455 (48.5%)	
Obesity	264 (29.0%)	359 (26.3%)	244 (25.9%)	
Hypertension				<0.001
No	602 (65.8%)	1050 (75.4%)	730 (76.8%)	
Yes	313 (34.2%)	342 (24.6%)	221 (23.2%)	
High total cholesterol				0.02
<200 mg/dL	441 (49.3%)	702 (53.7%)	511 (56.0%)	
240 – 239 mg/dL	308 (34.5%)	386 (29.5%)	276 (30.2%)	
240 mg/dL and over	145 (16.2%)	220 (16.8%)	126 (13.8%)	
Type 2 diabetes				0.02
No	800 (89.3%)	1201 (91.5%)	856 (93.0%)	
Yes	96 (10.7%)	112 (8.5%)	64 (7.0%)	

Comparisons were done using Chi-squared test.

Supplemental Table 4: All-cause mortality risk by physical activity levels: crude and adjusted models

	Mortality rate (95% CI)	Crude model HR (95% CI)	Adjusted model* HR (95% CI)
Leisure-time physical activity			
<i>Definition 1: categories</i>			
Low level	8.9 (7.7 – 10.2)	1 (Ref)	1 (Ref)
High level	4.0 (1.6 – 9.5)	0.45 (0.19 – 1.09)	0.45 (0.14 – 1.41)
<i>Definition 2: MET-min/week</i>			
<150 MET-min/week	9.4 (8.1 – 10.9)	1 (Ref)	1 (Ref)
150 – 499 MET-min/week	6.5 (3.9 – 10.8)	0.69 (0.41 – 1.18)	0.85 (0.49 – 1.50)
≥500 MET-min/week	2.8 (1.2 – 6.6)	0.30 (0.12 – 0.72)	0.30 (0.10 – 0.97)
Transport-related physical activity			
<i>Definition 1: categories</i>			
Low level	13.6 (11.3 – 16.4)	1 (Ref)	1 (Ref)
High level	5.9 (4.8 – 7.3)	0.43 (0.32 – 0.57)	0.53 (0.38 – 0.74)
<i>Definition 2: MET-min/week</i>			
<500 MET-min/week	14.0 (11.4 – 17.2)	1 (Ref)	1 (Ref)
500 – 1499 MET-min/week	7.3 (5.8 – 9.2)	0.52 (0.38 – 0.71)	0.57 (0.39 – 0.82)
≥1500 MET-min/week	5.3 (3.8 – 7.4)	0.37 (0.25 – 0.55)	0.58 (0.37 – 0.92)

Mortality rate was calculated by 1000 person-years of follow-up. Bold estimates are significant (p<0.05).

Low level of leisure time physical activity was defined as doing none or very little physical activity (i.e., <600 MET-min/week) during leisure time. Low level of transport-related physical activity was defined as not reporting walking or cycling trips in the transport domain of the IPAQ.

* Model adjusted by sex, age, years of education, socioeconomic position, study site, daily smoking, drinking, obesity, hypertension, total cholesterol, and type 2 diabetes status.

Supplemental Table 5: All-cause mortality risk by leisure-time physical activity: sensitivity analysis

	Mortality rate (95% CI)	Crude model	Adjusted model*
		HR (95% CI)	HR (95% CI)
Excluding deaths occurring within first 2 years of follow-up			
Definition 1:			
Low level	7.0 (5.9 – 8.2)	1 (Ref)	1 (Ref)
High level	1.6 (0.4 – 6.4)	0.23 (0.06 – 0.92)	0.36 (0.09 – 1.46)
Definition 2:			
<150 MET-min/week	7.4 (6.3 – 8.7)	1 (Ref)	1 (Ref)
150 – 499 MET-min/week	4.8 (2.6 – 8.6)	0.64 (0.35 – 1.19)	0.77 (0.41 – 1.46)
≥500 MET-min/week	1.1 (0.3 – 4.4)	0.15 (0.04 – 0.60)	0.24 (0.06 – 0.98)
Excluding hypertension and type 2 diabetes cases at baseline			
Definition 1:			
Low level	8.1 (7.0 – 9.4)	1 (Ref)	1 (Ref)
High level	6.6 (5.5 – 7.9)	0.30 (0.10 – 0.94)	0.17 (0.02 – 1.20)
Definition 2:			
<150 MET-min/week	8.2 (7.0 – 9.5)	1 (Ref)	1 (Ref)
150 – 499 MET-min/week	6.7 (5.6 – 8.0)	0.66 (0.38 – 1.17)	0.88 (0.48 – 1.61)
≥500 MET-min/week	6.6 (5.5 – 7.9)	0.20 (0.06 – 0.61)	0.11 (0.02 – 0.79)
Comparing those who reported no LTPA vs any LTPA			
No LTPA	7.5 (6.3 – 8.9)	1 (Ref)	1 (Ref)
Any LTPA	4.2 (2.8 – 6.3)	0.56 (0.36 – 0.87)	0.64 (0.39 – 1.04)
Using 500-MET-min/week as cutoff			
< 500 MET-min/week	7.1 (6.1 – 8.4)	1 (Ref)	1 (Ref)
≥ 500 MET-min/week	1.1 (0.3 – 4.4)	0.16 (0.04 – 0.63)	0.25 (0.06 – 1.01)

LTPA = Leisure-time physical activity. Mortality rate was calculated by 1000 person-years of follow-up. Bold estimates are significant ($p < 0.05$). Models were built using deaths occurring after 2 years of follow-up.

* Model adjusted by sex, age, years of education, socioeconomic position, study site, daily smoking, drinking, obesity, hypertension, total cholesterol, and type 2 diabetes status, except for the case when hypertension and type 2 diabetes cases were excluded at baseline.

Supplemental Table 6: All-cause mortality risk by transport-related physical activity: sensitivity analysis

	Mortality rate (95% CI)	Crude model HR (95% CI)	Adjusted model* HR (95% CI)
Excluding deaths occurring within first 2 years of follow-up			
Definition 1:			
Low level	11.0 (8.9 – 13.6)	1 (Ref)	1 (Ref)
High level	4.4 (3.4 – 5.6)	0.39 (0.28 – 0.53)	0.50 (0.34 – 0.74)
Definition 2:			
<500 MET-min/week	11.4 (9.0 – 14.3)	1 (Ref)	1 (Ref)
500 – 1499 MET-min/week	5.4 (4.2 – 7.1)	0.47 (0.33 – 0.67)	0.58 (0.38 – 0.89)
≥1500 MET-min/week	4.0 (2.7 – 5.8)	0.34 (0.22 – 0.53)	0.59 (0.35 – 0.98)
Excluding hypertension and type 2 diabetes cases at baseline			
Definition 1:			
Low level	8.3 (7.1 – 9.7)	1 (Ref)	1 (Ref)
High level	6.6 (5.6 – 7.9)	0.42 (0.31 – 0.56)	0.52 (0.36 – 0.74)
Definition 2:			
<500 MET-min/week	8.0 (6.9 – 9.4)	1 (Ref)	1 (Ref)
500 – 1499 MET-min/week	7.0 (5.9 – 8.3)	0.50 (0.36 – 0.70)	0.54 (0.36 – 0.80)
≥1500 MET-min/week	6.6 (5.6 – 7.9)	0.37 (0.25 – 0.55)	0.54 (0.33 – 0.87)
Comparing those who reported no TRPA vs any TRPA			
No TRPA	32.6 (22.0 – 48.3)	1 (Ref)	1 (Ref)
Any TRPA	5.8 (4.9 – 6.9)	0.17 (0.11 – 0.26)	0.27 (0.16 – 0.43)
Using 500-MET-min/week as cutoff			
< 500 MET-min/week	11.4 (9.0 – 14.3)	1 (Ref)	1 (Ref)
≥ 500 MET-min/week	4.9 (3.9 – 6.0)	0.42 (0.31 – 0.58)	0.57 (0.39 – 0.84)

TRPA = Transport-related physical activity. Mortality rate was calculated by 1000 person-years of follow-up. Bold estimates are significant (p<0.05). Models were built using deaths occurring after 2 years of follow-up.

* Model adjusted by sex, age, years of education, socioeconomic position, study site, daily smoking, drinking, obesity, hypertension, total cholesterol, and type 2 diabetes status, except for the case when hypertension and type 2 diabetes cases were excluded at baseline.