



RESEARCH ARTICLE

Preventable Ischaemic Heart Disease and Stroke Deaths Attributable to Insufficient Physical Activity: A Comparative Risk Assessment Analysis in the Argentinian Population

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Abstract

Background: Physical inactivity is estimated to be the 9th leading risk factor for all-cause mortality in Argentina. However, its impact on specific causes of death has not been evaluated using nationally representative data.

Design: We conducted a comparative risk assessment analysis to estimate the proportion and number of IHD and stroke deaths in Argentina that are attributable to different non-optimal levels of physical activity (PA).

Methods: We obtained data on prevalence of different levels of PA from the Argentinian National Survey of Risk Factors in 2013 and used relative risks for IHD and stroke mortality from previous meta-analyses. Deaths due to IHD and stroke, by age and sex, were obtained from the national death registry for the year 2010. We considered 4 categories of PA based on the metabolic equivalent tasks per minute per week (METs.min/week): inactive, < 600, ≥ 600 to < 1,600 and ≥ 1,600.

Results: In Argentina, 76.8% (CI 95%; 75.8%-77.7%) of the population older than 30-years-old engaged in < 1,600 METs.min/week. This level of insufficient activity contributed to 26% of CVD deaths (IHD or stroke) (11,234 of 43,796 deaths; 6,013 in men and 5,221 in women); 29% (7,292) of IHD deaths; and 21% (3,942) of stroke deaths. The impact of insufficient PA was higher in individuals younger than 70-years-old due to stronger associations between non-optimal PA and mortality from IHD and stroke.

Conclusions: A non-optimal level of PA contributes substantially to the mortality burden of cardiovascular diseases in Argentina, especially in individuals under 70-years-old. More substantial resources should be directed toward enhancing built and social environments which are essential to effectively increase PA, to improve health-related quality of life and reduce the burden of cardio-metabolic diseases in Argentina.

Keywords

Physical activity, Mortality, Ischaemic heart disease, Stroke, Comparative risk assessment, Burden of disease, Latin America

Introduction

There is substantial evidence from epidemiological studies to support that physical activity (PA) is causally associated with morbidity and mortality from cardiovascular diseases (CVD) [1-3].

For example, a recent meta-analysis of 33 prospective cohort studies found a dose-response relationship between physical activity and risk of ischaemic heart disease (IHD). Individuals who expended at least 600 or 1200 of metabolic equivalent tasks (MET) minute per week had respectively a 14% and 20% lower IHD risk compared with those reporting no leisure time physical activity [1]. These benefits are thought to be mediated through blood pressure reduction [4], weight loss, and improved insulin sensitivity, lipid profile and endothelial function [5,6]. According to the Global Burden of Disease study 2010, and despite the current international guidelines [7], low PA (< 600 METs.min/week) is the 9th most important risk factor for deaths in Argentina [8]. However the impact of insufficient PA on deaths from different causes as well as the impact of different non-optimal levels of PA on cardiovascular mortality remains unknown. Previous studies have estimated the

impact of non-optimal levels of PA on CVD mortality in the US [9], other high-income countries [10] and one study in Argentina. However, this study only accounted for the impact of engaged in less than 600 METs.min/week [11]. Considering the growing burden of cardiovascular disease and costs in developing countries, especially for transitional countries like Argentina, it is critical to provide local decision-makers with accurate data about the actual proportion of the cardiovascular disease burden attributable to one of the most important modifiable risk factors.

Hence, we aimed to estimate the proportion and number of IHD and stroke deaths in Argentina that are attributable to different non-optimal levels of PA (< 1600 METs.min/week) using nationally representative data and age-specific relative risks derived from important observational studies.

Methods

We conducted a population-level comparative risk assessment (CRA) analysis to estimate the number of deaths that would be prevented if current levels of PA were changed to a hypothetical alternative distribution. The inputs for the analysis were (1) the current population distribution of PA in Argentina (2) the etiological effect of PA on IHD and stroke mortality (relative risks), (3) a reference or optimal level for PA, and (4) the total number of IHD and stroke deaths.

Data sources

Population: To examine the levels of PA in the population aged 30 years and older, we used data from the third Argentinian National Survey of Risk Factors (AN-SRF) conducted in 2013. The target population for this survey comprised persons aged 18 years and more living in private households located in urban areas of 5,000 or more inhabitants from 6 different regions: Gran Buenos Aires, Pampeana, Noroeste, Noreste, Cuyo and Patagonia. The sample was selected through a probabilistic multi-stage process to ensure national representativeness. The surveys were based on a complex sample design and system of weighting that allowed computing population-based estimates of health conditions and behaviors. The response rate was 79.8%. Risk factors and socioeconomic factors were self-reported by participants during in-person interviews. Further methodological features of the ANRFS have been published elsewhere [12].

Risk factor exposure

Data on physical activity was collected by trained interviewers using an adapted short form of the international physical activity questionnaire (IPAQ) [13]. The IPAQ short form showed to produce repeatable data, the 75% of the reported test-retest Spearman's reliability coefficients were acceptable, averaging 0.8 [14].

The questionnaire asked about frequency (days per week) and duration (minutes per day) of vigorous/ mod-

erate intensity activities and walking during the last 7 days.

We estimated energy expended on the assessed PA in METs. One MET is defined as the energy it takes to sit quietly, which is about one calorie per kilogram (2.2 pounds) of body weight per hour for an average adult (e.g. 1 MET = 1 kcal/kg/hour). We categorized PA in three groups according to intensity: light activities < 3.0 METs, moderate activities 3.0-6.0 METs and vigorous activities > 6 METs [15]. We assigned average METs of 4 for moderate intensity activities, 8 for vigorous intensity activities, and 3.3 for walking following the IPAQ's guidelines for data processing and analysis [16].

Total walking MET.min/week score was calculated as $3.3 \times \text{walking minutes} \times \text{walking days}$ in the last 7 days. Total moderate MET.min/week score was calculated as $4 \times \text{moderate intensity minutes} \times \text{moderate intensity days}$ in the last 7 days. Total vigorous MET.min/week score was calculated as $8 \times \text{vigorous intensity minutes} \times \text{vigorous intensity days}$ in the last 7 days. Finally, total physical activity MET-minutes/week score was computed as the sum of the total MET.min/week spent in walking, moderate and vigorous activities. Only activities performed for 10 or more minutes were included. If the reported duration of a specific intensity of activity exceeding 180 minutes per day, we set it to 180 [16]. As distribution of MET.min/week is skewed to the right, based on the current recommendations [7] a previous similar study [9], we categorized total MET.min/week into four categories: inactive: those who reported no moderate or vigorous activities; insufficiently active: those with calculated moderate or vigorous PA of < 600 MET.min/week; sufficiently active: those with 600 to 1600 MET.min/week; and highly active: those with ≥ 1600 MET.min/week. We accounted for complex survey design and sampling weights in estimating prevalence of these categories nationally.

Etiological effects of risk factors on disease-specific mortality

We obtained the relative risks (RR) for stroke and IHD mortality for each exposure category of PA based on a previous analysis that used the highly active category as the reference group. This analysis provided the set of age-specific relative risks categorized in: 30-69, 70-79 and ≥ 80 years, therefore the present analysis had the restriction of using the same age categories [9,17]. The RRs used for PA were assumed to be the same for men and women as there is insufficient evidence for different proportional effects by gender. We used a separate set of relative risks which had as the reference group the PA level recommended by public health guidelines [7] (≥ 600 METs.min/week) (Table 1).

Disease-specific deaths

The number of disease-specific deaths, by age and

Table 1: Relative risk (95% confidence interval) estimates for categories of physical activity on disease-specific mortality, by age [9,17].

| | Highly active | Sufficiently active | Insufficiently active | Inactive |
|---------------|---------------|---------------------|-----------------------|------------------|
| IHD | | | | |
| 30-69 | 1.00 | 1.15 (1.04-1.28) | 1.66 (1.14-2.41) | 1.97 (1.56-2.47) |
| 70-79 | 1.00 | 1.15 (1.00-1.32) | 1.51 (1.00-2.27) | 1.73 (1.36-2.19) |
| ≥ 80 | 1.00 | 1.15 (0.94-1.41) | 1.38 (0.86-2.21) | 1.50 (1.14-1.96) |
| Stroke | | | | |
| 30-69 | 1.00 | 1.12 (0.62-2.04) | 1.23 (0.41-3.68) | 1.72 (1.09-2.7) |
| 70-79 | 1.00 | 1.12 (0.54-2.32) | 1.21 (0.36-4.08) | 1.55 (0.96-2.5) |
| ≥ 80 | 1.00 | 1.12 (0.36-3.53) | 1.18 (0.23-6.05) | 1.39 (0.80-2.4) |
| IHD | | | | |
| 30-69 | 1.00 | 1.00 | 1.44 (1.28-1.62) | 1.71 (1.58-1.85) |
| 70-79 | 1.00 | 1.00 | 1.31 (1.17-1.48) | 1.50 (1.38-1.61) |
| ≥ 80 | 1.00 | 1.00 | 1.20 (1.07-1.35) | 1.30 (1.21-1.41) |
| Stroke | | | | |
| 30-69 | 1.00 | 1.00 | 1.10 (0.89-1.37) | 1.53 (1.31-1.79) |
| 70-79 | 1.00 | 1.00 | 1.08 (0.87-1.33) | 1.38 (1.18-1.60) |
| ≥ 80 | 1.00 | 1.00 | 1.05 (0.85-1.30) | 1.24 (1.06-1.45) |

Inactive: no moderate or vigorous activities; Insufficiently active: < 600 MET/minutes/week; Sufficiently active: ≥ 600 MET/minutes/week; Highly active: ≥ 1600 MET/minutes/week; IHD: ischaemic heart disease

sex, were obtained from the Directorate of Health Statistics of the National Ministry of Health for the year 2010 [18]. We included deaths from stroke (ICD10 code: I60-I69), IHD (ICD10 code: I20-I25) and 80% of sudden death (ICD10 code: R96) assuming that this percentage of sudden deaths were due to IHD [19]. We incorporated a correction factor for “garbage coding”, by increasing the number of IHD deaths by 21.5%, which was the percentage globally used in the GBD 2010 study [20]. Garbage codes are deaths that have been coded to an intermediate, immediate, or ill-defined cause and must instead be attributed to the underlying causes. In addition, we corrected the number of deaths for underreporting of deaths which is estimated to be 1% [21].

Data analysis: We computed the proportional reduction in disease-specific deaths that would occur if PA level were increased to an alternative level with lower risk (i.e. ≥ 1600 or ≥ 600 METs.min/week separately), through calculating the population attributable fraction (PAF) using the following formula

$$\sum_i p_i^* (RR_i - 1) / (\sum_i P_i^* (RR_i - 1) + 1)$$

Where

- i is the index categories of PA.
- P_i is the prevalence of PA in category i .
- RR_i is the relative risk of the disease in category i compared with the reference category.

We conducted all analyses separately by sex and age group (30-69, 70-79 and +80 years). We restricted analyses to ≥ 30 y because there are limited data on the mortality effects of these risk factors at younger ages and also because there are very few deaths from IHD and stroke in those aged 30 or younger.

The number of attributable deaths was simply calculated by multiplying PAFs for each outcome and age-sex

group by the observed number of IHD or stroke deaths in that age-sex category. We also report proportion and number of IHD or stroke deaths (hereafter denoted by CVD) that were attributable to non-optimal PA.

Results

The population of the third ANSRF survey was constituted by 32,365 participants. After exclusion of individuals younger than 30-years-old, the final sample consisted in 24,427 participants of which 10,640 (43.6%) were men and 13,787 (56.4%) were women. The demographic characteristics and cardiovascular risk profile of the general population ≥ 30-years-old in Argentina are presented in Table 2. Approximately, 86% of individuals were aged between 30 to 69-years-old and 50% did not graduate from primary school. The prevalence of current smokers was 28.1% in men and 19.6% in women, obesity 23.6% (26.4% in men; 21.1% in women), diabetes 12.2% and hypertension 40.2% being in these cases similar between men and women. The 4.8% reported history of myocardial infarction and 2.5% history of stroke.

In the year 2013, only 23.3% (CI 95%; 22.3-24.3) of the Argentinian residents older than 30 years were highly active (i.e. had ≥ 1,600 METs.min/week of activity) and 47.5% (CI 95%; 46.3-48.7) reached the recommended minimum levels of PA (> 600 METs.min/week). Energy expenditure was lower in older ages in both sexes as expected (Table 3). Energy expenditure was lower in women than men in all age groups, as was the prevalence of highly active category.

In the year 2010, 43,796 Argentinian residents older than 30 years died due to IHD or stroke, 23,625 in men and 20,171 in women [18]. In men, the largest number of CVD deaths was observed between 30 and 69 years, while in women the largest share was in those aged 80

Table 2: General characteristics and risk factors among population aged 30 years and older in Argentina in 2013.

| | Overall (n 24,427) | Men (n 10,640) | Women (n 13,787) |
|--------------------------------------|--------------------|-------------------|-------------------|
| Age groups, % (95% CI) | | | |
| 30-69 yr | 86 (85.6, 87.2) | 88.7 (87.5, 89.7) | 84.4 (83.2, 86.0) |
| 70-79 yr | 9.2 (8.5, 9.8) | 7.9 (7.0, 8.9) | 10.3 (9.4, 11.2) |
| ≥ 80 yr | 4.5 (4.0, 4.9) | 3.4 (2.8, 4.2) | 5.3 (4.7, 6.1) |
| Educational level, % (95% CI) | | | |
| < 7 years | 11.9 (11.1, 12.7) | 11.4 (10.3, 12.7) | 12.3 (11.3, 13.3) |
| 7 to 11 years | 38.6 (37.4, 39.8) | 40.3 (38.5, 42.1) | 37.1 (35.5, 38.6) |
| ≥ 12 years | 49.5 (48.3, 50.7) | 48.2 (46.4, 50.1) | 50.5 (48.9, 52.2) |
| Risk factors, % (95% CI) | | | |
| Current smoker | 23.5 (22.5, 24.6) | 28.1 (26.4, 29.7) | 19.6 (18.3, 20.9) |
| Overweight | 37.8 (36.6, 38.9) | 44.4 (42.6, 46.2) | 32.1 (30.5, 33.5) |
| Obesity | 23.6 (22.5, 24.6) | 26.4 (24.8, 28.1) | 21.1 (19.8, 22.4) |
| Diabetes | 12.2 (11.5, 13.0) | 11.4 (10.4, 12.6) | 12.8 (11.8, 13.9) |
| Hypertension | 40.2 (38.9, 41.4) | 37.1 (35.2, 38.9) | 42.7 (41.1, 44.4) |
| Hypercholesterolemia | 32.8 (31.5, 34.1) | 32.7 (30.6, 34.8) | 32.8 (31.1, 34.5) |
| History of CVD, % (95% CI) | | | |
| Myocardial infarction | 4.8 (4.3, 5.3) | 4.9 (4.2, 5.7) | 4.7 (4.1, 5.6) |
| Stroke | 2.5 (2.2, 2.9) | 2.9 (2.3, 3.6) | 2.2 (1.8, 2.8) |

Data are weighted percentages; Current smokers are those who have smoked at least 100 cigarettes during their lifetime; Educational level was defined by years of schooling; Body mass index (BMI) was calculated by self-reported weight divided by self-reported height in meters squared (kg/m^2), participants were categorized into overweight (25.0-29.9 kg/m^2) and obese ($\geq 30.0 \text{ kg}/\text{m}^2$); Hypertension, diabetes and hypercholesterolemia: self-reported history of these conditions; Myocardial infarction and stroke: self-reported history of these conditions; CVD: cardiovascular disease

Table 3: National prevalence (95% confidence interval) of physical activity categories by age and sex [12].

| Age group | Highly active | Sufficiently active | Insufficiently active | Inactive |
|----------------------------|------------------|---------------------|-----------------------|------------------|
| Overall^a | 23.3 (22.3-24.3) | 24.2 (23.2-25.3) | 24.8 (23.7-25.9) | 27.7 (26.7-28.9) |
| Men | 27.2 (25.6-28.8) | 24.0 (22.5-25.6) | 21.8 (20.3-23.5) | 27.0 (25.3-28.7) |
| 30-69 | 28.8 (27.1-30.6) | 24.1 (22.5-25.8) | 21.0 (19.4-22.7) | 26.1 (24.3-27.9) |
| 70-79 | 17.2 (13.5-21.7) | 25.7 (21.1-31.0) | 26.6 (21.3-32.6) | 30.5 (24.9-36.8) |
| ≥ 80 | 7.8 (4.8-12.4) | 18.0 (12.6-25.2) | 31.9 (22.5-43.1) | 42.3 (33.2-52.0) |
| Women | 19.9 (18.7-21.2) | 24.4 (23.1-25.8) | 27.3 (25.9-28.8) | 28.4 (27.0-30.0) |
| 30-69 | 21.8 (20.4-23.2) | 25.5 (24.0-27.1) | 27.0 (25.4-28.6) | 25.7 (24.2-27.3) |
| 70-79 | 11.6 (8.9-15.0) | 19.0 (15.7-22.8) | 31.5 (27.2-36.2) | 37.8 (33.3-42.5) |
| ≥ 80 | 5.7 (3.6-8.8) | 18.1 (13.0-24.6) | 23.7 (18.7-29.6) | 52.5 (45.7-59.3) |

Inactive: those who reported no moderate or vigorous activities; Insufficiently active < 600 MET/minutes/week; sufficiently active ≥ 600 MET/minutes/week; highly active ≥ 1600 MET/minutes/week; ^a: In the population older than 30-years-old

Table 4: Population attributable fractions (PAF) and deaths attributable to physical activity < 1600 METs.min/week by sex and age.

| | IHD | | | Stroke | | | IHD and stroke | | |
|---------------------|----------------------|---------|---------------------|----------------------|---------|---------------------|----------------------|---------|---------------------|
| | Observed deaths [18] | PAF (%) | Attributable deaths | Observed deaths [18] | PAF (%) | Attributable deaths | Observed deaths [18] | PAF (%) | Attributable deaths |
| Both genders | | | | | | | | | |
| 30-69 | 8710 | 30 | 2649 | 5461 | 21 | 1162 | 14171 | 27 | 3811 |
| 70-79 | 6416 | 30 | 1921 | 4985 | 22 | 1081 | 11402 | 26 | 3002 |
| ≥ 80 | 10016 | 27 | 2722 | 10446 | 21 | 1699 | 18223 | 24 | 4422 |
| All adults | 25142 | 29 | 7292 | 18654 | 21 | 3942 | 43796 | 26 | 11234 |
| Men | | | | | | | | | |
| 30-69 | 6579 | 30 | 1968 | 3423 | 21 | 716 | 10002 | 27 | 2684 |
| 70-79 | 3990 | 29 | 1146 | 2688 | 21 | 552 | 6678 | 25 | 1698 |
| ≥ 80 | 4000 | 26 | 1056 | 2945 | 20 | 576 | 6945 | 23 | 1632 |
| All adults | 14569 | 29 | 4170 | 9056 | 20 | 1843 | 23625 | 25 | 6013 |
| Women | | | | | | | | | |
| 30-69 | 2131 | 32 | 681 | 2038 | 22 | 446 | 4169 | 27 | 1127 |
| 70-79 | 2426 | 32 | 775 | 2298 | 23 | 529 | 4724 | 28 | 1304 |
| ≥ 80 | 6016 | 28 | 1667 | 5262 | 21 | 1124 | 11278 | 25 | 2790 |
| All adults | 10573 | 30 | 3122 | 9598 | 22 | 2099 | 20171 | 26 | 5221 |

IHD: Ischaemic heart disease; PAF: population attributable fraction

years or older. IHD had a larger share with 25,142 deaths (14,569 in men and 10,573 in women) compared with stroke that caused 18,654 deaths (9,598 in women and 9,056 in men) (Table 4).

Non-optimal levels of PA (engaging in less than 1600 MET.min/week), was responsible for an estimated 11,234 CVD deaths (26%) of which 7,292 were IHD deaths and 3,942 were stroke deaths (Figure 1). The proportional impact of non-optimal PA on IHD (29%) was higher than that for stroke (21%), because the etiological effect (RRs) of non-optimal PA on IHD mortality was stronger (Table 4). A quarter of CVD deaths in men

and women were attributable to non-optimal PA. The proportional impact of non-optimal PA on CVD mortality decreased in older age groups, due to lower RRs and despite higher prevalence of non-optimal PA. Therefore, the higher number of attributable deaths in older ages were mainly a consequence of the larger number of CVD deaths.

Engaging in less than recommended levels of PA (< 600 METs.min/week) was responsible for 7,278 (17%) of CVD deaths (43,796) in Argentina in 2010, 4,907 attributable deaths were from IHD (20% of all IHD deaths) and 2,371 were from stroke (13%) deaths (Table 5 and

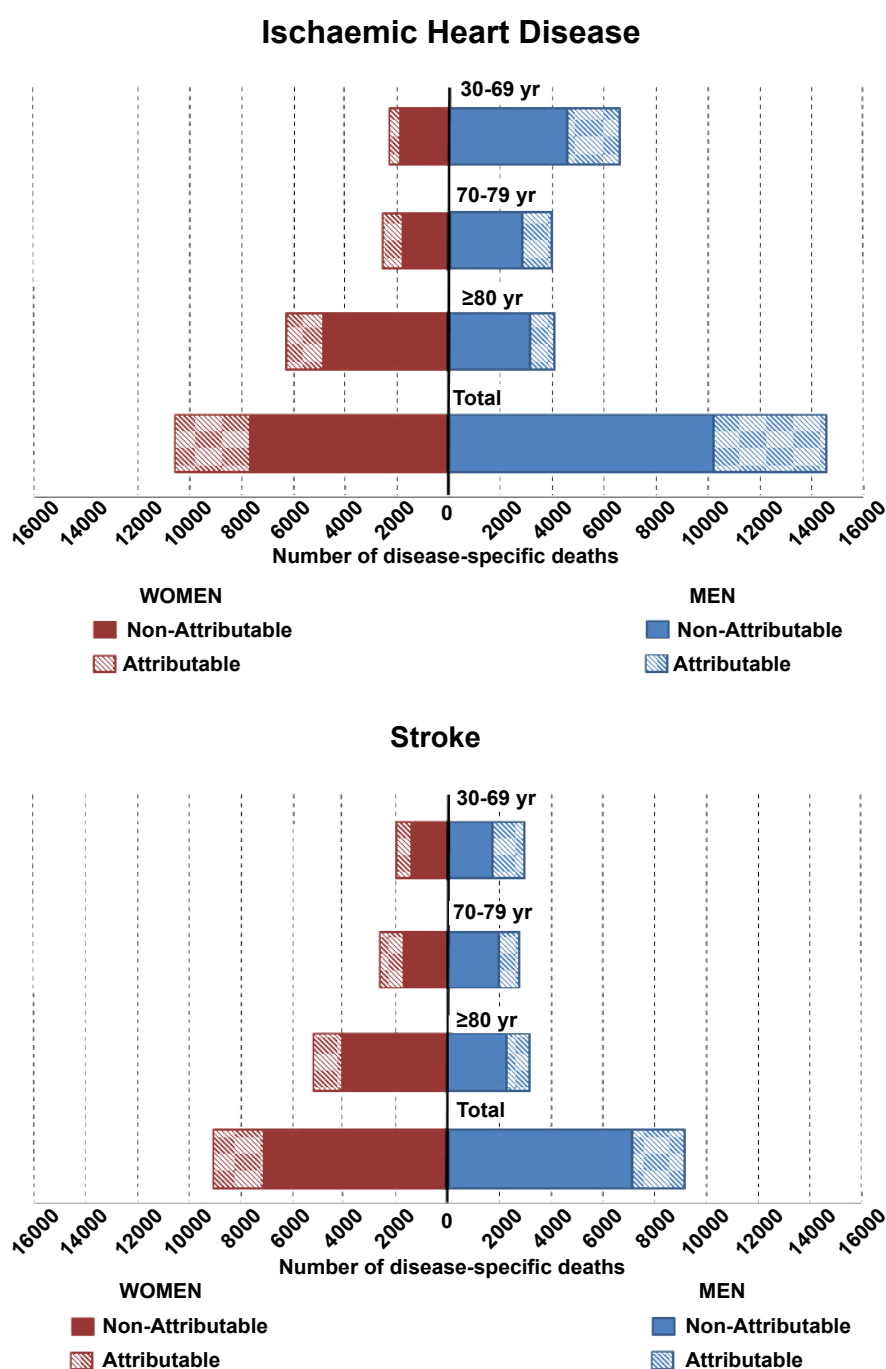


Figure 1: Cardiovascular deaths attributable to engaging in physical activity < 1600 METs.min/week by sex and age groups. Bars represent the total disease-specific deaths reported in 2010 by sex and age groups. The striped segment represents the number of the total deaths attributable to engaging in < 1600 METs.min/week.

Table 5: PAFs and deaths attributable to physical activity < 600 METs.min/week by sex and age.

| | IHD | | | Stroke | | | IHD and stroke | | |
|---------------------|----------------------|---------|---------------------|----------------------|---------|---------------------|----------------------|---------|---------------------|
| | Observed deaths [18] | PAF (%) | Attributable deaths | Observed deaths [18] | PAF (%) | Attributable deaths | Observed deaths [18] | PAF (%) | Attributable deaths |
| Both genders | | | | | | | | | |
| 30-69 | 8710 | 22 | 1923 | 5461 | 14 | 757 | 14171 | 19 | 2680 |
| 70-79 | 6416 | 20 | 1313 | 4985 | 13 | 663 | 11402 | 17 | 1976 |
| ≥ 80 | 10016 | 17 | 1670 | 10446 | 12 | 951 | 18223 | 14 | 2621 |
| All adults | 25142 | 20 | 4907 | 18654 | 13 | 2371 | 43796 | 17 | 7278 |
| Men | | | | | | | | | |
| 30-69 | 6579 | 22 | 1427 | 3423 | 14 | 469 | 10002 | 19 | 1896 |
| 70-79 | 3990 | 19 | 769 | 2688 | 12 | 329 | 6678 | 16 | 1098 |
| ≥ 80 | 4000 | 16 | 639 | 2945 | 10 | 308 | 6945 | 14 | 947 |
| All adults | 14569 | 19 | 2835 | 9056 | 12 | 1106 | 23625 | 17 | 3941 |
| Women | | | | | | | | | |
| 30-69 | 2131 | 23 | 496 | 2038 | 14 | 288 | 4169 | 19 | 784 |
| 70-79 | 2426 | 22 | 544 | 2298 | 15 | 334 | 4724 | 19 | 878 |
| ≥ 80 | 6016 | 17 | 1032 | 5262 | 12 | 643 | 11278 | 15 | 1675 |
| All adults | 10573 | 20 | 2072 | 9598 | 13 | 1265 | 20171 | 17 | 3337 |

IHD: Ischaemic heart disease; PAF: population attributable fraction

Figure 2). The largest number of attributable CVD deaths were observed between ages 30 and 69 accounting for 2,680 (19%) of CVD deaths, followed by 2,621 deaths (14%) in those aged 80 years or older.

Discussion

More than three quarters (76.8%) of adults in Argentina older than 30-years-old did not reach the optimal level of PA (< 1600 METs.min/week) and this was responsible for 29% of IHD deaths and 21% of stroke deaths in 2010. When a more feasible scenario for recommended activity levels was considered, half (52.5%) of the adult population did not reach these levels. If all adults would engage in at least the recommended level of PA (equivalent to 30 minutes of briskly walking five days a week), one fifth of IHD deaths and slightly less than one-sixth of stroke deaths would have been prevented. We found that women expended less energy than men in all age groups, mainly at expense of engaging in less intense activities. Previous research conducted in Latin America showed similar results, women were less likely to perform vigorous activities and to participate in leisure time PA and more prone to spend more time in household activities [22]. Similar patterns of PA were also described in women from developed populations [23,24].

In 2010, the global burden of disease (GBD) Study estimated that low levels of PA (< 600 METs.min/week) accounted for 3.2 million deaths and 31% of IHD DALYs worldwide representing the tenth most important contributor to the total burden of disease. Low PA ranked seventh in Southern Latin America [8].

From 1999 to 2013, prevalence of low PA has increased by 20% worldwide [25]. The impact of non-optimal PA was estimated to be larger in developed versus developing countries (3.2% vs. 1.6% of total DALYs respectively), however over the years the proportion of this contribution had changed in different directions. The share of bur-

den of disease that was attributable to non-optimal PA in developed countries declined by 9% (3.5% to 3.2% of total DALYs.) while in developing countries, its share increased by 89% (0.9% to 1.6% of total DALYs) [26]. This increase reflects the increased share of cardiovascular diseases in the total burden of disease in the developing countries which itself may be due to urbanization, changes in diet and reductions in physical activity [27].

Previous studies have estimated the impact of low PA on cardiovascular mortality in Argentina. Rubinstein, et al. estimated that low levels of PA accounted for 18.1% of CVD events in 2006 [11]. In 2013, the GBD study estimated that low PA was responsible for 12.6% of IHD deaths and 7.6% of stroke deaths in Argentina [25]. These analysis estimated a lower proportional impact of non-optimal PA (< 600 METs.min/week compared to that estimated in our study (20% for IHD and 13% for stroke deaths) mainly because the first study [11] used lower relative risks than that used in this study and the second [25] modeled the exposure data from a not representative sample of Argentina which reported a lower prevalence of non-optimal PA (26.7%) [28,29].

This study has a number of strengths: (1) It is the first population-level analysis in estimating the effects of non-optimal PA on IHD and stroke mortality using a nationally representative survey in Argentina. (2) Age-specific effect sizes were derived from meta-analysis of observational studies that had adjusted for important confounders. (3) Deaths from Stroke and IHD in 2010 were obtained from the death registry, which provides robust national-level data by age and sex for all causes of death with almost complete coverage. (4) The number of CVD deaths was adjusted using methods to enhance comparability by reducing garbage codes and underreported causes.

However, this study has some limitations; first, like many other comparative risk assessments conducted in de-

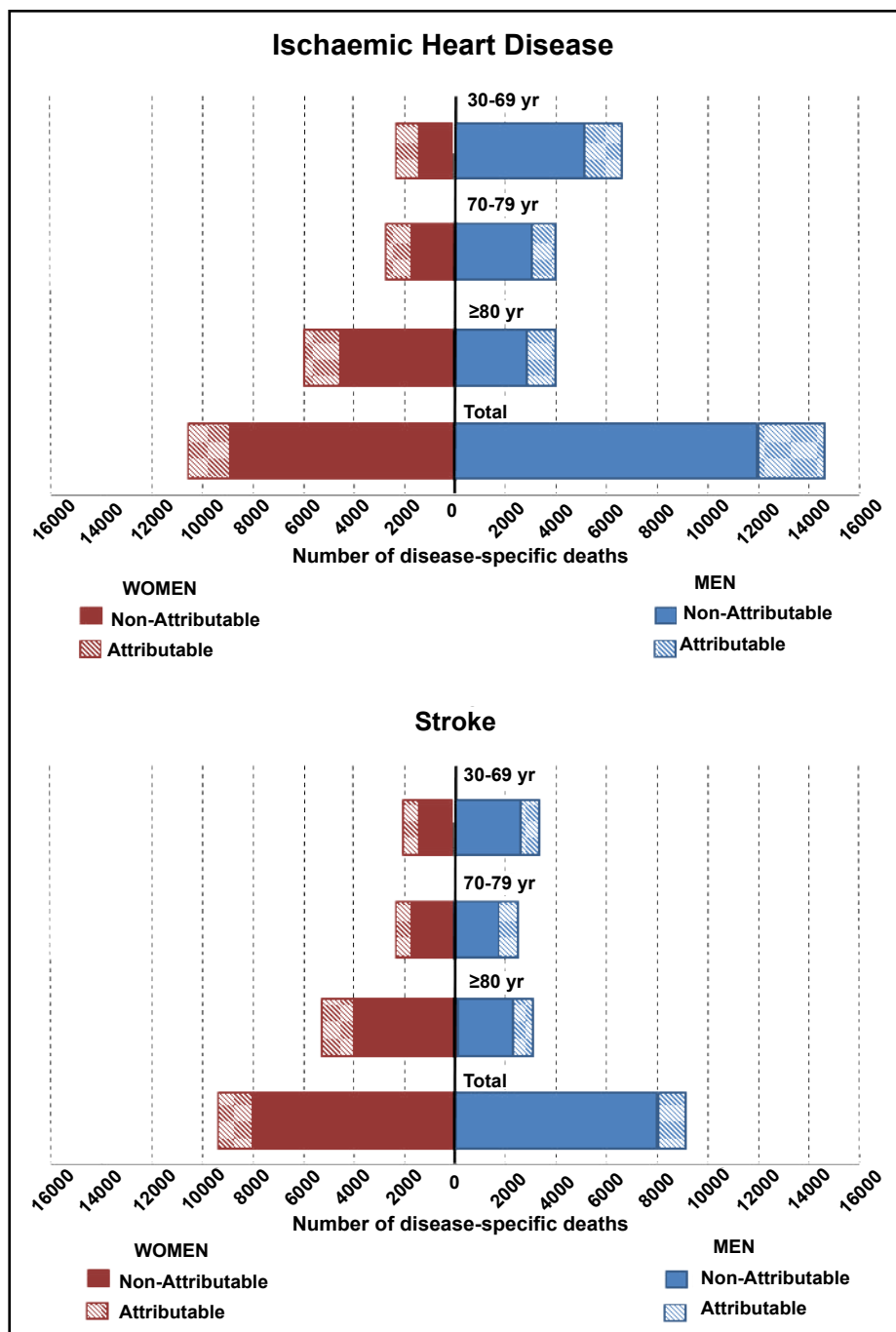


Figure 2: Cardiovascular deaths attributable to engaging in physical activity < 600 METs.min/week by sex and age groups. Bars represent the total disease-specific deaths reported in 2010 by sex and age groups. The striped segment represents the number of the total deaths attributable to engaging in < 600 METs.min/week.

veloping countries [30,31], effect sizes (here for non-optimal PA) had to be extrapolated from epidemiological studies conducted in developed countries. Second, these effect sizes were not corrected for regression dilution bias due to insufficient information on exposure measurement error and variability, which is especially important when error and variability of self-reported exposure may themselves differ across studies [9,17]. Third, the number of deaths from different stroke subtypes was not available through the vital registration system as only a small fraction of deaths from stroke are analyzed using imaging. Fourth, we did not adjust the distribution of PA for the regression dilution bias due to insufficient data from epidemiological studies on exposure mea-

surement error and variability. Fifth, we used mortality data from the year 2010 since more recent national data on causes of death were not available. Therefore, we may have overestimated the absolute number of IHD and stroke deaths that are attributable to non-optimal PA in 2013 as CVD death rates are declining in Argentina [32-35]. Finally, we did not incorporate the uncertainty of the estimates and were therefore unable to make statistical comparisons across different age groups, gender and outcomes.

In summary, non-optimal levels of PA (< 1600 METs.min/week) contribute to about a quarter of deaths from cardiovascular diseases in Argentina in the population

older than 30-years-old, showing that the impact of this modifiable risk factor is significantly higher than that previously estimated.

The principal advantage of doing a comprehensive and comparable scientific assessment of disease burden caused by non-optimal of PA is that it provides the evidence base for informing discussion about policy and interventions to increase PA. Although, the Ministry of Health has developed National Programs Against Sedentary Lifestyle [36,37], more substantial resources should be directed toward enhancing built and social environments which are essential to effectively increase PA, to improve health-related quality of life and reduce the burden of cardio-metabolic diseases in Argentina.

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References

- Sattelmair J, Pertman J, Ding EL, Kohl HW 3rd, Haskell W, et al. (2011) Dose response between physical activity and risk of coronary heart disease: a meta-analysis. *Circulation* 124: 789-795.
- Shiroma EJ, Lee IM (2010) Physical activity and cardiovascular health: lessons learned from epidemiological studies across age, gender, and race/ethnicity. *Circulation* 122: 743-752.
- Hu FB, Stampfer MJ, Colditz GA, Ascherio A, Rexrode KM, et al. (2000) Physical activity and risk of stroke in women. *JAMA* 283: 2961-2967.
- Cornelissen VA, Smart NA (2013) Exercise training for blood pressure: a systematic review and meta-analysis. *J Am Heart Assoc* 2: e004473.
- Fiuzza-Luces C, Garatachea N, Berger NA, Lucia A (2013) Exercise is the real polypill. *Physiology (Bethesda)* 28: 330-358.
- Malin SK, Gerber R, Chipkin SR, Braun B (2012) Independent and combined effects of exercise training and metformin on insulin sensitivity in individuals with prediabetes. *Diabetes Care* 35: 131-136.
- WHO (2010) Global recommendations on physical activity for health.
- Lim SS, Vos T, Flaxman AD, Danaei G, Shibuya K, et al. (2012) A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 380: 2224-2260.
- Danaei G, Ding EL, Mozaffarian D, Taylor B, Rehm J, et al. (2009) The preventable causes of death in the United States: comparative risk assessment of dietary, lifestyle, and metabolic risk factors. *PLoS Med* 6: e1000058.
- Gulsvik AK, Thelle DS, Samuelsen SO, Myrstad M, Mowé M, et al. (2012) Ageing, physical activity and mortality—a 42-year follow-up study. *Int J Epidemiol* 41: 521-530.
- Rubinstein A, Colantonio L, Bardach A, Caporale J, Martí SG, et al. (2010) Estimation of the burden of cardiovascular disease attributable to modifiable risk factors and cost-effectiveness analysis of preventative interventions to reduce this burden in Argentina. *BMC Public Health* 10: 627.
- (2013) Tercera encuesta nacional de factores de riesgo. Argentina.
- (2015) International Physical Activity Questionnaire.
- Craig CL, Marshall AL, Sjöström M, Bauman AE, Booth ML, et al. (2003) International physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc* 35: 1381-1395.
- Ainsworth BE, Haskell WL, Herrmann SD, Meckes N, Bassett DR Jr, et al. (2011) 2011 Compendium of Physical Activities: a second update of codes and MET values. *Med Sci Sports Exerc* 43: 1575-1581.
- (2013) Guidelines for Data Processing and Analysis of the International Physical Activity Questionnaire (IPAQ).
- Ezzati M, Lopez AD, Rodgers A, Murray CJL (2004) Comparative Quantification of Health Risks. Global and Regional Burden of Disease Attributable to Selected Major Risk Factors.
- (2010) Dirección de Estadísticas e Información en Salud del Ministerio de Salud de la. Argentina.
- Myerburg RJ, Juntilla MJ (2012) Sudden cardiac death caused by coronary heart disease. *Circulation* 125: 1043-1052.
- Forouzanfar MH, Moran AE, Flaxman AD, Roth G, Mensah GA, et al. (2012) Assessing the global burden of ischemic heart disease, part 2: analytic methods and estimates of the global epidemiology of ischemic heart disease in 2010. *Glob Heart* 7: 331-342.
- Naghavi M, Makela S, Foreman K, O'Brien J, Pourmalek F, et al. (2010) Algorithms for enhancing public health utility of national causes-of-death data. *Popul Health Metr* 8: 9.
- Poggio R, Seron P, Calandrelli M, Ponzo J, Mores N, et al. (2016) Prevalence, Patterns, and Correlates of Physical Activity Among the Adult Population in Latin America: Cross-Sectional Results from the CESCAS I Study. *Glob Heart* 11: 81-88.
- He XZ, Baker DW (2005) Differences in leisure-time, household, and work-related physical activity by race, ethnicity, and education. *J Gen Intern Med* 20: 259-266.
- Brownson RC, Eyster AA, King AC, Brown DR, Shyu YL, et al. (2000) Patterns and correlates of physical activity among US women 40 years and older. *Am J Public Health* 90: 264-270.
- GBD 2013 Risk Factors Collaborators, Forouzanfar MH, Alexander L, Anderson HR, Bachman VF, et al. (2015) Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks in 188 countries, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 386: 2287-2323.
- (2016) GBD visualization tool.
- Gersh BJ, Sliwa K, Mayosi BM, Yusuf S (2010) Novel therapeutic concepts: the epidemic of cardiovascular disease in the developing world: global implications. *European Heart Journal* 31: 642-648.
- GBD 2013 Risk Factors Collaborators (2015) Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks in 188 countries, 1990-2013: a systematic analysis for the Global Burden of Disease Study

2013. *Lancet*.
29. Bauman A, Bull F, Chey T, Craig CL, Ainsworth BE, et al. (2009) The International Prevalence Study on Physical Activity: results from 20 countries. *International Journal of Behavioral Nutrition and Physical Activity* 6: 21.
30. Farzadfar F, Danaei G, Namdaritabar H, Rajaratnam JK, Marcus JR, et al. (2011) National and subnational mortality effects of metabolic risk factors and smoking in Iran: a comparative risk assessment. *Popul Health Metr* 9: 55.
31. Stevens G, Dias RH, Thomas KJ, Rivera JA, Carvalho N, et al. (2008) Characterizing the epidemiological transition in Mexico: national and subnational burden of diseases, injuries, and risk factors. *PLoS Med* 5: e125.
32. Moran AE, Oliver JT, Mirzaie M, Forouzanfar MH, Chilov M, et al. (2012) Assessing the Global Burden of Ischemic Heart Disease: Part 1: Methods for a Systematic Review of the Global Epidemiology of Ischemic Heart Disease in 1990 and 2010. *Glob Heart* 7: 315-329.
33. Moran AE, Forouzanfar MH, Roth GA, Mensah GA, Ezzati M, et al. (2014) Temporal trends in ischemic heart disease mortality in 21 world regions, 1980 to 2010: the Global Burden of Disease 2010 study. *Circulation* 129: 1483-1492.
34. (2009) Evaluación De La Tendencia De Mortalidad Por Enfermedades Cardiovasculares En Argentina Entre 1987 Y 2007.
35. Rivera-Andrade A, Luna MA (2014) Trends and heterogeneity of cardiovascular disease and risk factors across Latin American and Caribbean countries. *Progress in Cardiovascular Diseases* 57: 276-285.
36. (2009) Programa Nacional de Municipios y Comunidades Saludables. Argentina.
37. (2013) Programa Nacional de Lucha contra el Sedentarismo. Argentina.