Leisure Time Physical Activity and Cardio-Metabolic Health: Results From the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil)

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Background—Although increasing effort has been devoted to the promotion of a healthy lifestyle such as leisure time physical activity for cardio-metabolic health, specific evidence supporting health policy remains sparse, particularly in those ethnically diverse populations where cardio-metabolic diseases are reaching epidemic proportion and yet are grossly understudied.

Methods and Results—We conducted a cross-sectional analysis of the baseline data from 10 585 participants aged 35 to 74 free of cardiovascular diseases in the Brazilian Longitudinal Study of Adult Health. Leisure time physical activity status was defined by the American Heart Association and the World Health Organization recommendations (≥150 min/week moderate activities or 75 min/week vigorous activities). In total, 1183 (21%) women and 1387 (29%) men were active. After accounting for covariates, the favorable effects of leisure time physical activity on cardio-metabolic parameters were evident. Specifically, the average blood pressure, heart rate, and Framingham Risk Score for cardiovascular diseases of the active were significantly lower within each sex. The ORs comparing the active versus the inactive women were 0.78 (95% CI: 0.66–0.92) for hypertension and 0.78 (95% CI: 0.65–0.93) for cardiovascular diseases in 10 years. Among men, the ORs were 0.75 (95% CI: 0.65–0.87) for hypertension and 0.73 (95% CI: 0.61–0.87) for diabetes. The 10-year risk of cardiovascular diseases was significantly lower among the active men with a 33% reduction (OR=0.67, 95% CI: 0.57–0.78).

Conclusions—We observed beneficial effects of leisure time physical activity on cardio-metabolic health in this large Brazilian population that are consistent with studies in North America and Europe. **(*J Am Heart Assoc*. 2016;5:e003337 doi: 10.1161/JAHA.116.003337)**

Key Words: Brazil • cardio-metabolic health • physical exercise

Cardio-metabolic diseases are the epidemics of our time, and they inflict individual suffering on a global scale. Just 2 diseases alone—cardiovascular diseases (CVD) and diabetes—are responsible for 19 million deaths each year, with more than 80% of these disorders occurring in low- and middle-income countries.[1] As the largest democratic, middle-income country in the world, Brazil has, over the past several decades, undergone one of the world's most rapid demographic and economic transitions. More than 85% of Brazilians currently live in urban areas,[2] and have acquired the risks of chronic diseases typical of an urbanized culture. Also, population aging has resulted in an increased cardio-metabolic disease burden, currently with a rapid lifestyle transition characterized by a significant decrease in physical activity and increase in overweight and obesity.

A survey conducted in Brazil reported around 87% of the population not engaging in leisure time physical activity

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(LTPA), which is much higher than the prevalence in the United States.[3,4] According to the National Health Survey, the prevalence of practice of the recommended level of LTPA was 22.5%.[5] Because cardio-metabolic diseases are more prevalent among the poor, their rising burden threatens to widen the already large gap in health care between the poor and affluent. It has been estimated that the identification of risk factors and subsequent reduction explain ≈44% to 76% of the decline in mortality from CVD alone in high-income countries.[6] Evidence from high-income settings suggests that it is possible to use lifestyle interventions to curb the epidemic of chronic diseases and promote cardio-metabolic health in other settings. For example, Brazil, as a large middle-income country, has shown a significant decrease in noncommunicable diseases mortality, related to successful smoking and hypertension control policies.[7] However, the rising prevalence of obesity and physical inactivity may threaten the achievements already made.

To ensure the health benefits of the population and the cost-effectiveness of preventive interventions, the current focus of cardio-metabolic health care should be expanded to include essential lifestyle interventions. Despite the fact that the Brazilian government has already implemented an integrated policy plan to address the problem of physical inactivity, few resources are available to comprehensively evaluate the impact of the high and ever-increasing prevalence of physical inactivity on the burden of cardio-metabolic diseases. Although increasing attention has been given to the promotion of healthy lifestyles,[8,9] more well-designed prevention studies in Brazilian populations are still needed.

Therefore, we conducted a comprehensive assessment of the evidence about the effects of LTPA on cardio-metabolic parameters in the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil), the first multicenter cohort study of Brazilians focusing on cardio-metabolic diseases. The aims of our study were (1) to comprehensively evaluate the association of LTPA with intermediate cardio-metabolic biomarkers, and (2) to investigate the benefits of LTPA relating to cardio-metabolic outcomes, including the risk of hypertension and diabetes and the predicted 10-year risk of CVD.

Methods

Study Population

The design and methodology of the ELSA-Brasil have been detailed elsewhere.[10,11] Briefly, 15 105 civil servants (6887 men and 8218 women) aged 35 to 74 years were enrolled at 6 sites from August 2008 to December 2010 for baseline data collection. Of the 15 105 participants enrolled, ≈52% of the participants were white, 16% black, 28% mixed, 2% Asian, and 1% indigenous. The large sample size and wide variety of well-characterized variables of the ELSA-Brasil make it a unique resource for comprehensive and systematic investigations of the determinants and distribution of cardio-metabolic diseases in Brazilian adults. Furthermore, the availability of data on CVD intermediaries and cardio-metabolic diseases allows for the comprehensive assessment of the biological mechanisms by which physical inactivity may affect CVD risk. Participants with self-reported coronary heart disease, CVDs, or peripheral artery disease at baseline were excluded. Participants without information on total physical activity were additionally excluded from the 11 547 participants free of coronary heart disease, CVD, and peripheral artery disease, and the current study consists of 10 585 participants in total. The ELSA-Brasil was approved by the Institutional Review Boards (IRB) in Hospital Universitário da Universidade de São Paulo IRB (Universidade de São Paulo), Fundação Oswaldo Cruz IRB (Fundação Oswaldo Cruz), Instituto de Saúde Coletiva da Universidade Federal da Bahia IRB (Universidade Federal da Bahia), Universidade Federal de Minas Gerais IRB (Universidade Federal de Minas Gerais), Centro de Ciências da Saúde da Universidade Federal do Espírito Santo IRB (Universidade Federal do Espírito Santo), and Hospital de Clínicas de Porto Alegre IRB (Universidade Federal do Rio Grande do Sul). All individuals who participated in the study provided written informed consent.

Measurement of Physical Activity

Questionnaires and interviews were used to collect the information, with an emphasis on the social and racial inequalities and health-related living conditions that are distinctive in Brazil. In particular, the International Physical Activity Questionnaire (IPAQ) was used to ascertain various types of activities in the domains of LTPA and transport. The detailed protocol of the IPAQ can be found elsewhere.[12] In brief, IPAQ is an instrument designed primarily for adult physical activity surveillance. Frequency and duration for walking, moderate-intensity activities, and vigorous-intensity activities were collected for each type of activity using the IPAQ.

Measurement of Cardio-Metabolic Outcomes

Medical assessments and measurements of clinical and subclinical parameters were conducted at baseline visit.[13] The body mass index (BMI) was weight in kilograms divided by height in meters, squared. Blood pressure (BP) was taken using a validated oscillometric device (Omron HEM 705CPINT) after a 5-minute rest with the subject in a sitting position in a quiet, temperature-controlled room (20–24°C). Three measurements were taken at 1-minute intervals. The mean of the 2 latest BP measurements was calculated and used for our analyses. Conventional 12-lead ECGs were performed using a digital device (Atria 6100; Burdick, Cardiac Science Corporation, Bothell, WA, USA) and were analyzed according to the Minnesota Code.[14] The Framingham Risk Score was calculated for the participants of the ELSA-Brasil, and the detailed scoring scheme has been reported elsewhere.[15] Based on the recent American College of Cardiology/American Heart Association (ACC/AHA) Guideline on the Assessment of Cardiovascular Risk, an arteriosclerotic cardiovascular disease (ASCVD) Risk Score was also computed.[16]

Diabetes status used in the current study was classified by using laboratory measurements. A 12-hour fasting blood sample was drawn by venipuncture soon after each participant arrived at the baseline clinic visit. A 2-hour 75-g oral glucose tolerance test was then administered to participants without known diabetes. Glucose was measured centrally by the hexokinase method (ADVIA Chemistry; Siemens, Deerfield, IL). Percent glycosylated hemoglobin (HbA1c) was measured using high-pressure liquid chromatography (Bio-Rad Laboratories, Hercules, CA). Participants were classified as having diabetes if they reached the threshold for fasting plasma glucose (7.0 mmol/L), 2-hour postload plasma glucose (11.1 mmol/L), or HbA1c (6.5%).[17,18] A participant was classified to have hypertension if systolic blood pressure (SBP) was ≥140 mm Hg, diastolic blood pressure (DBP) was ≥90 mm Hg, or she/he had taken any medication to treat hypertension in the past 2 weeks. According to Framingham Risk Score, participants were classified as with low, intermediate, or high 10-year risk of CVD if they have 6% or less, 6% to 20%, or 20% or more CVD risk in 10 years.[15] According to the ACC/AHA ASCVD Risk Score, participants were classified as with low, intermediate, or high 10-year risk of ASCVD if they have 5% or less, 5% to 7.5%, or 7.5% or more ASCVD risk in 10 years.[16]

Statistical Analysis

Based on current recommendations from the American College of Sports Medicine and the AHA, participants who had at least 150 minutes of moderate activities per week or at least 75 minutes of vigorous activities per week during their leisure time were categorized as active.[19] Participants who did not meet the recommendations were considered inactive. Baseline characteristics and LTPA-related traits are summarized below for the active and the inactive women and men. The χ^2 test and the t test were used to evaluate the difference between the active and the inactive participants.

The cardio-metabolic outcomes for the sex-specific analyses include SBP, DBP, heart rate, the Framingham Risk Score for CVD, the ACC/AHA ASCVD Risk Score, hypertension, diabetes, and the predicted 10-year risk of CVD. To ensure the robustness of our results, different sets of covariates were considered for adjustment: (1) age (continuous), race, and research centers; (2) covariates in (1), along with BMI; and (3) covariates in (2), along with smoking and alcohol consumption. Generalized linear regression was used for continuous outcome variables, and regular logistic and ordered logistic regression models were used for categorical variables with the inactive category treated as the reference. The coefficients or ORs with 95% CIs were computed from the generalized linear regression models or logistic regression models, respectively.

To evaluate the robustness of primary findings, we also conducted 3 sets of sensitivity analyses using (1) the additional adjustment for education and income, (2) the alternative definition of being active versus inactive (≥1000 kcal/week versus <1000 kcal/week following criteria recommended by the Centers for Disease Control and Prevention, the American College of Sports Medicine, and the US Surgeon General[20,21]), and (3) mixed-effect models with the effects of study centers treated as random effects. Standard metabolic equivalents were assigned to different activity categories, and we converted them into the total LTPA-related energy expenditure in kilocalories per week by multiplying metabolic equivalents by the frequency and the duration of each activity category and body weight.[22,23] Generalized linear mixed models and cumulative link mixed models were used for categorical outcomes, and linear mixed models were used for continuous outcomes.

To explore the potential mediation, a preliminary mediation analysis was conducted to quantify the direct effects of LTPA on the risk of hypertension, diabetes, and CVD, along with the mediated effects through SBP, DBP, heart rate, the Framingham Risk Score, and the ACC/AHA ASCVD Risk Score.[24,25] The proportions of effects mediated were also computed for each mediator–outcome combination.

Statistical analyses were conducted using R statistical package, version 3.2.2 (R Foundation for Statistical Computing, Vienna, Austria). Two-sided inference with $P<0.05$ was considered statistically significant.

Results

Study Population

In total, there were 5752 (54%) women and 4833 (46%) men. The mean age was 51.64 (SD=8.71) years for women and 51.54 (SD=9.02) for men. Among women, 51% identified themselves as white, 18% as black, 27% as mixed, 4% as Asian and indigenous; among men, 52% identified themselves as white, 14% as black, 30% as mixed, 3% as Asian and indigenous. Around 12% of the women and 14% of the men were current smokers, and 25% of the women and 34% of the men were former smokers. Current drinkers and former drinkers constitute 65% and 20% of the women and 77% and 19% of the men, respectively. Other baseline characteristics are also summarized in Table 1. All demographic characteristics and LTPA-related traits significantly differ between the active men and the inactive men (all $P<0.05$). The active women and the inactive women are significantly different in terms of all characteristics except for age ($P=0.92$ for continuous age variable and 0.64 for age strata).

Association Between Physical Activity Status and Cardio-Metabolic Outcomes

Physical activity status was directly associated with each measure for cardio-metabolic health at baseline among both women and men who participated in the ELSA-Brasil (all $P<0.05$) (Table 2). The active participants, compared to the inactive, tended to have lower BMI, SBP and DBP, heart rate, and Framingham Risk Score for CVD. Also, the prevalence of hypertension and diabetes, along with the predicted 10-year risk of CVD, appeared to be lower among the active participants (Table 2).

After taking into account age, race, study sites, BMI, smoking status, and alcohol consumption (Model 3), the sex-specific relation between physical activity status and the measures of cardio-metabolic health at baseline remained evident. Specifically, the average SBP of the active women was 1.33 (95% CI: −2.30 to −0.37, $P=0.01$) mm Hg lower than the inactive women; the average SBP of the active men was 1.08 (95% CI: −2.05 to −0.11, $P=0.03$) mm Hg lower than the inactive men (Table 3). The average DBP was 0.79 (95% CI: −1.41 to −0.17, $P=0.01$) mm Hg lower among the active women and 1.71 (95% CI: −2.35 to −1.07, $P<0.0001$) mm Hg lower among the active men, compared with their inactive counterparts. The active women had an average heart rate 1.96 (95% CI: −2.59 to −1.33, $P<0.0001$) bpm slower than that of the inactive women; the average heart rate of the active men was 4.32 (95% CI: −4.98 to −3.66, $P<0.0001$) bpm slower. Framingham Risk Scores for CVD were favorable among the active (women: $\beta=-0.37$, 95% CI: −0.66 to −0.08, $P=0.01$; men: $\beta=-0.83$, 95% CI: −1.16 to −0.50, $P<0.0001$). The estimated ORs comparing the active versus the inactive women were 0.78 (95% CI: 0.66–0.92, $P=0.003$) for hypertension and 0.78 for the predicted 10-year risk of CVD (95% CI: 0.65–0.93, $P=0.005$). Among men, the estimated ORs comparing the active versus the inactive were 0.75 (95% CI: 0.65–0.87, $P=0.0002$) for hypertension and 0.73 (95% CI: 0.61–0.87, $P=0.0006$) for diabetes. The predicted 10-year risk of CVD based on Framingham Risk Scores was significantly lower among the active men with a 33% reduction in risk (OR=0.67 comparing the high-risk category versus the low-risk category, 95% CI: 0.57–0.78, $P<0.0001$). The predicted 10-year risk of ASCVD based on the 2013 ACC/AHA Guideline on the Assessment of Cardiovascular Risk was significantly lower among the active men with a 29% reduction in risk (OR=0.71 comparing the high-risk category versus the low-risk category, 95% CI: 0.59–0.85, $P<0.0003$).

Sensitivity Analysis

To evaluate the robustness of primary findings, we also conducted 3 sets of sensitivity analyses using (1) the additional adjustment for education and income, (2) the alternative definition of being active versus inactive (≥1000 kcal/week versus <1000 kcal/week following criteria recommended by the Centers for Disease Control and Prevention, the American College of Sports Medicine, and the US Surgeon General[20,21]), and (3) mixed-effect models with the effects of study centers treated as random effects. The associations discovered in the primary analysis did not change appreciably when we further adjusted for the socioeconomic variables (Table 4). Similar to the results from the primary analysis with the adjustment for the final set of covariates, the energy expenditure from LTPA ≥1000 kcal/week was associated with improved cardio-metabolic health (Table 5). The findings from the sensitivity analyses for the risk of hypertension, diabetes, and the predicted 10-year risk of CVD were consistent with those from the primary analysis, although the significance of the associations for intermediaries was attenuated. Results from the sensitivity analysis based on mixed-effect models were almost identical to those from the primary analysis based on fixed-effect models (Table 6).

Mediation Analysis

We estimated that ≈32% (95% CI: 25–43), 32% (95% CI: 24–46), 33% (95% CI: 26–48), and 32% (95% CI: 25–51) of the total physical activity effects on hypertension, diabetes, the Framingham predicted 10-year risk of CVD, and the ACC/AHA 2013 Guideline predicted 10-year risk of ASCVD appeared to be mediated by BMI, respectively (Table 7). Systolic blood pressure levels mediated ≈28% (95% CI: 15–40) of the total effects of LTPA on hypertension risk, 7% (95% CI: 3–12) on diabetes risk, 26% (95% CI: 16–44) on the Framingham predicted 10-year risk of CVD, and 23% (95% CI: 12–54) on the ACC/AHA 2013 Guideline predicted 10-year risk of ASCVD. Diastolic blood pressure levels mediated 49% (95% CI: 31–66) of the total effects on hypertension, 10% (95% CI: 4–15) on diabetes risk, 40% (95% CI: 27–68) on the Framingham predicted 10-year risk of CVD, and 31% (95% CI: 20–71) on the ACC/AHA 2013 Guideline predicted 10-year risk of ASCVD. Sixteen percent (95% CI: 10–30) and 17% (95% CI:

Table 1. Baseline Characteristics of Leisure Time Physically Inactive Versus Active (AHA Recommendations)* Women (N=5752) and Men (N=4833) of the ELSA-Brasil

	Women							Men						
	Overall (N=5752)		Inactive (N=4569)		Active (N=1183)			Overall (N=4833)		Inactive (N=3446)		Active (N=1387)		
	N/ Mean	%/ SD	N/ Mean	%/ SD	N/ Mean	%/ SD	*P* Value	N/ Mean	%/ SD	N/ Mean	%/ SD	N/ Mean	%/ SD	*P* Value
Demographic characteristics														
Age, y	51.64	8.71	51.64	8.65	51.62	8.97	0.92	51.54	9.02	52.12	8.95	50.10	9.06	<0.0001
Race							<0.0001							0.008
White	2945	51	2220	49	725	61		2496	52	1737	50	759	55	
Mixed	1534	27	1276	28	258	22		1459	30	1050	30	409	29	
Black	1007	18	870	19	137	12		658	14	495	14	163	12	
Other	204	4	152	3	52	4		156	3	121	4	35	3	
Age strata							0.64							<0.0001
35 to 44	1296	23	1020	22	276	23		1150	24	733	21	417	30	
45 to 54	2319	40	1861	41	458	39		1972	41	1393	40	579	42	
55 to 64	1638	28	1292	28	346	29		1250	26	984	29	266	19	
65 to 74	499	9	396	9	103	9		461	10	336	10	125	9	
Smoking							<0.0001							<0.0001
Current smokers	697	12	606	13	91	8		665	14	543	16	122	9	
Former smokers	1415	25	1104	24	311	26		1643	34	1216	35	427	31	
Never smokers	3640	63	2859	63	781	66		2524	52	1686	49	838	60	
Alcohol consumption							<0.0001							<0.0001
Current drinkers	3738	65	2855	62	883	75		3718	77	2572	75	1146	83	
Former drinkers	1126	20	959	21	167	14		895	19	706	20	189	14	
Never drinkers	878	15	747	16	131	11		218	5	166	5	52	4	
Education							<0.0001							<0.0001
Without college degree	2554	44	2255	49	299	25		2319	48	1822	53	497	36	
With college degree	3198	56	2314	51	884	75		2514	52	1624	47	890	64	
Per capita family income, US dollars	1825	1501	1681	1406	2378	1712	<0.0001	1670	1354	1556	1287	1953	1469	<0.0001
PA-related traits														
Total days/wk of PA	2.09	2.82	1.17	1.94	5.65	2.83	<0.0001	2.63	3.01	1.44	2.07	5.58	2.94	<0.0001
Walking, min/wk	57.16	96.30	49.36	91.85	87.31	106.65	<0.0001	71.67	115.26	63.60	107.32	91.72	130.87	<0.0001

Continued

Table 1. Continued

	Women							Men						
	Overall (N=5752)		Inactive (N=4569)		Active (N=1183)			Overall (N=4833)		Inactive (N=3446)		Active (N=1387)		
	N/ Mean	%/ SD	N/ Mean	%/ SD	N/ Mean	%/ SD	*P* Value	N/ Mean	%/ SD	N/ Mean	%/ SD	N/ Mean	%/ SD	*P* Value
Light PA, min/wk	17.93	60.78	6.63	25.47	66.29	117.69	<0.0001	19.43	63.62	7.10	24.55	55.59	111.38	<0.0001
Vigorous PA, min/wk	38.91	101.59	1.14	7.79	184.78	152.20	<0.0001	62.04	126.04	3.24	12.79	208.13	158.17	<0.0001
Total MET-h/wk	9.50	16.51	3.31	5.87	33.42	21.72	<0.0001	13.45	19.59	4.40	6.77	35.93	22.69	<0.0001

AHA indicates American Heart Association; ELSA-Brazil, Brazilian Longitudinal Study of Adult Health; MET, metabolic equivalents; PA, physical activity.
*American Heart Association guidelines recommend at least 150 min/wk moderate exercise or 75 min/wk vigorous exercise.

10–43) of the total effects on the Framingham predicted 10-year risk of CVD and the ACC/AHA 2013 Guideline predicted 10-year risk of ASCVD were mediated by heart rate; 10% and 36% of the total effects on hypertension and diabetes were mediated by heart rate.

Discussion

The current study presents the results based on detailed data carefully collected from more than 15 000 women and men who participated in the ELSA-Brasil, which is the largest cohort of the Brazilian population to date. Ours is the first large-scale multiethnic study to directly examine the role of LTPA in relation to cardio-metabolic health in Brazilians. We observed significantly favorable profiles of cardio-metabolic health among the physically active women and men, which provides direct evidence of demonstrable benefits of being active, characterized by a comprehensive set of CVD intermediate biomarkers and cardio-metabolic diseases, for the Brazilian adult population. Physical activity was associated with improved profiles of blood pressure, heart rate, and the Framingham Risk Score for CVD in both women and men. Among women, physical activity was significantly associated with the reduced risk of hypertension and the reduced predicted 10-year risk of CVD; among men, the risk of hypertension, diabetes, and the predicted 10-year risk of CVD were significantly lower for the active, compared to the inactive.

According to the World Health Organization Non-communicable Diseases Country Profiles 2011, the age-standardized death rate per 100 000 due to CVD and diabetes alone were 304 for men and 226 for women in Brazil.[26] The large proportion of physically inactive people in Brazil appears to play a significant role in the high morbidity and mortality for cardio-metabolic diseases and highly prevalent cardio-metabolic risk factors.[26] In the current study, the prevalence of physical inactivity defined based on the AHA recommendation on leisure time physical activity is 75.72%, which corroborates the previous findings from the ELSA-Brasil and Brazil's 2008 national surveillance system for risk and protective factors for chronic diseases (VIGITEL) survey.[11,27] The Brazilian government used results from the evaluations of LTPA intervention carried out by Project Guide for Useful Interventions for Physical Activity in Brazil and Latin America (GUIA), particularly the evaluation of the Academia da Cidade Program of the city of Recife (ACP),[28–33] to support statewide expansion of ACP by the government of the state of Pernambuco in 2010. In April 2011, the Brazilian Ministry of Health supported the expansion to over 4000 cities in Brazil of the Academia da Saúde (AS), a national program modeled after ACP. The AS is one of the few and possibly the largest physical activity and healthy lifestyle–promoting programs in the world.[28] In 2005, Brazil published their first official dietary recommendation for

Table 2. Comparison of Cardio-Metabolic Measures at Baseline Between Leisure Time Physically Inactive Versus Active Women (N=5752) and Men (N=4833) (AHA Recommendations)*

	Women							Men						
	Overall (N=5752)		Inactive (N=4569)		Active (N=1183)			Overall (N=4833)		Inactive (N=3446)		Active (N=1387)		
Cardio-Metabolic Variables	N/ Mean	%/ SD	N/ Mean	%/ SD	N/ Mean	%/ SD	*P* Value	N/ Mean	%/ SD	N/ Mean	%/ SD	N/ Mean	%/ SD	*P* Value
BMI, kg/m^2	26.79	4.89	27.13	4.96	25.48	4.36	<0.0001	26.79	4.14	26.99	4.32	26.28	3.58	<0.0001
SBP, mm Hg	117.14	16.48	117.81	16.78	114.55	14.97	<0.0001	125.15	16.24	125.94	16.85	123.18	14.42	<0.0001
DBP, mm Hg	73.87	10.11	74.30	10.26	72.18	9.31	<0.0001	78.87	10.64	79.56	10.85	77.15	9.88	<0.0001
Heart rate, bpm	71.00	9.70	71.38	9.73	69.55	9.44	<0.0001	69.15	10.51	70.45	10.33	65.93	10.26	<0.0001
FHS CVD score	6.43	6.07	6.69	6.24	5.46	5.26	<0.0001	13.49	8.90	14.43	9.01	11.16	8.16	<0.0001
ASCVD score	0.03	0.05	0.03	0.05	0.03	0.04	<0.0001	0.08	0.09	0.09	0.09	0.07	0.08	<0.0001
Hypertension							<0.0001							<0.0001
No	4026	70	3115	68	911	77		3071	64	2085	61	986	71	
Yes	1722	30	1450	32	272	23		1757	36	1358	39	399	29	
Diabetes (ADA)							<0.0001							<0.0001
No	4888	85	3837	84	1051	89		3787	78	2605	76	1182	85	
Yes	863	15	731	16	132	11		1044	22	839	24	205	15	
FHS 10-yr risk of CVD							<0.0001							<0.0001
<6	3676	64	2841	62	835	71		1177	24	701	20	476	34	
≤6 and <20	1781	31	1468	32	313	26		2483	51	1792	52	691	50	
≥20	290	5	255	6	35	3		1161	24	942	27	219	16	
10-yr risk of ASCVD							0.001							<0.0001
<5	4691	82	3682	81	1009	85		2318	48	1482	43	836	60	
≤5 and <7.5	418	7	350	8	68	6		657	14	490	14	167	12	
≥7.5	638	11	532	12	106	9		1846	38	1463	42	383	28	

ADA indicates American Diabetes Association; ASCVD, arteriosclerotic cardiovascular disease; BMI, body mass index; CVD, cardiovascular disease; DBP, diastolic blood pressure; FHS, Framingham Heart Study; SBP, systolic blood pressure.
*American Heart Association guidelines recommend at least 150 min/wk moderate exercise or 75 min/wk vigorous exercise.

the adult Brazilian population. Recently, a revised version based on food types rather than nutrients was launched.[34] Brazil has adopted the World Health Organization Global Strategy on Diet, Physical Activity and Health, and much effort has been made to define healthy diet and physical activity policies and action. Although numerous initiatives have been taken by the Brazilian Ministry of Health,[35,36] there remains a need for more evidence about the effects of LTPA on cardio-metabolic parameters directly from the adults in Brazil.

Results from the current study are also in line with those comprehensive findings from Brazil and the US population despite many significant differences in health systems, lifestyles, and socioeconomic factors between Brazil and the United States. A recent study using data from VIGITEL, Brazil's 2008 national surveillance system for risk and protective factors for chronic diseases, found that LTPA may be protective against hypertension in Brazilian men.[37] However, no association was found between LTPA and hypertension for women in the same study. The authors suggested a possible explanation that women tended to report a lower level of LTPA and total amount of energy expenditure than men.[38] In the current study, significant associations between LTPA and hypertension were found for both women and men after adjusting for a comprehensive set of covariates. The different findings for women from the current study may be due to the use of IPAQ-based self-reported physical activity levels. The validity of IPAQ in Brazilian populations has been evaluated previously.[39] Results from the validation study indicated that IPAQ-based measures can correctly classify individual levels of LTPA and are valid for the purpose of studying relations between LTPA and chronic diseases. According to the 2008 Physical Activity Guidelines Advisory Committee Report issued by the US Department of Health and Human Services, the median risk ratios of having coronary heart disease and CVD among men summarized from studies published since 1996 were 0.65 and 0.65, respectively; the median risk ratios

Table 3. Associations of Cardio-Metabolic Measures With LTPA Status (AHA Recommendations)* at Baseline Among Women (N=1183 Active and 4569 Inactive) and Men (N=1387 Active and 3446 Inactive) in the ELSA-Brasil

Cardio-Metabolic Variables	Model 1†			Model 2			Model 3		
	OR/β‡	95% CI	*P* Value	OR/β	95% CI	*P* Value	OR/β	95% CI	*P* Value
Women									
SBP, mm Hg	−2.24	−3.21 to −1.28	<0.0001	−1.36	−2.32 to −0.41	0.01	−1.33	−2.30 to −0.37	0.01
DBP, mm Hg	−1.67	−2.31 to −1.04	<0.0001	−0.77	−1.38 to −0.16	0.01	−0.79	−1.41 to −0.17	0.01
Heart rate, bpm	−2.09	−2.71 to −1.47	<0.0001	−2.03	−2.65 to −1.40	<0.0001	−1.96	−2.59 to −1.33	<0.0001
FHS CVD score	−0.99	−1.30 to −0.69	<0.0001	−0.67	−0.97 to −0.37	<0.0001	−0.37	−0.66 to −0.08	0.01
ASCVD score	−0.53	−0.75 to −0.30	<0.0001	−0.41	−0.64 to −0.18	0.0004	−0.16	−0.38 to 0.06	0.14
Hypertension	0.67	0.57 to 0.78	<0.0001	0.77	0.65 to 0.91	0.002	0.78	0.66 to 0.92	0.003
Diabetes§	0.69	0.56 to 0.84	0.0003	0.81	0.65 to 0.99	0.04	0.83	0.67 to 1.03	0.09
FHS 10-yr risk of CVD	0.60	0.50 to 0.70	<0.0001	0.68	0.57 to 0.81	<0.0001	0.78	0.65 to 0.93	0.005
10-yr risk of ASCVD	0.57	0.46 to 0.72	<0.0001	0.64	0.51 to 0.81	0.0002	0.78	0.61 to 1.01	0.06
Men									
SBP, mm Hg	−1.49	−2.47 to −0.52	0.003	−1.02	−1.98 to −0.06	0.04	−1.08	−2.05 to −0.11	0.03
DBP, mm Hg	−2.23	−2.89 to −1.57	<0.0001	−1.72	−2.35 to −1.09	<0.0001	−1.71	−2.35 to −1.07	<0.0001
Heart rate, bpm	−4.63	−5.29 to −3.98	<0.0001	−4.47	−5.13 to −3.82	<0.0001	−4.32	−4.98 to −3.66	<0.0001
FHS CVD score	−1.75	−2.12 to −1.37	<0.0001	−1.47	−1.84 to −1.10	<0.0001	−0.83	−1.16 to −0.50	<0.0001
ASCVD score	−0.85	−1.22 to −0.48	<0.0001	−0.68	−1.05 to −0.32	0.0003	−0.25	−0.60 to 0.10	0.16
Hypertension	0.69	0.60 to 0.80	<0.0001	0.76	0.66 to 0.88	0.0003	0.75	0.65 to 0.87	0.0002
Diabetes	0.62	0.52 to 0.74	<0.0001	0.68	0.57 to 0.82	<0.0001	0.73	0.61 to 0.87	0.0006
FHS 10-yr risk of CVD	0.52	0.45 to 0.60	<0.0001	0.56	0.48 to 0.65	<0.0001	0.67	0.57 to 0.78	<0.0001
10-yr risk of ASCVD	0.52	0.44 to 0.62	<0.0001	0.57	0.48 to 0.67	<0.0001	0.71	0.59 to 0.85	0.0003

AHA indicates American Heart Association; ASCVD, arteriosclerotic cardiovascular disease; BMI, body mass index; CVD, cardiovascular disease; DBP, diastolic blood pressure; ELSA-Brazil, Brazilian Longitudinal Study of Adult Health; FHS, Framingham Heart Study; LTPA, leisure time physical activity; SBP, systolic blood pressure.
*AHA guidelines recommend at least 150 min/wk moderate exercise or 75 min/wk vigorous exercise.
†Estimates and 95% CIs were from regular logistic regression or ordered logistic regression or generalized linear regression models. Model 1 was adjusted for age, race, and study centers; Model 2 was adjusted for age, race, study centers, and BMI; Model 3 was adjusted for age, race, study centers, BMI, smoking status, and alcohol consumption.
‡Mean differences (βs) estimated from the generalized linear regression models were reported for continuous outcomes; ORs estimated from the logistic regression models are reported for discrete outcomes. For CVD risk scores, ORs comparing the high-risk category vs the low-risk category were obtained from ordered logistic regression models.
§Diabetes was defined using self-reported information and laboratory measurements (fasting plasma glucose level ≥7.0 mmol/L, 2-hour postload plasma glucose ≥11.1 mmol/L, or HbA1c ≥6.5%).

for women were 0.62 and 0.89.[40] The most inclusive meta-analysis to date for the US population suggests that mean reductions in resting BP ranged from 2 to 5 mm Hg for SBP and 2 to 3 mm Hg for DBP across all categories.[41] In the United States, large prospective cohort and cross-sectional observational studies that assessed physical activity all show that increased levels of physical activity, both vigorous and moderate, are associated with a reduced risk for developing type 2 diabetes regardless of how these studies were conducted.[42–44] The current findings for intermediate cardio-metabolic biomarkers are also consistent with those from randomized controlled trials conducted in the United States. In a meta-analysis of randomized controlled trials of 4 weeks or longer, the investigators found that aerobic exercise reduced SB by 4.7 mm Hg (95% CI: 4.4–5.0) and diastolic BP by 3.1 mm Hg (95% CI: 3.0–3.3) as compared to a nonexercising control group.[45] A more recent meta-analysis of randomized controlled trials showed consistent findings: a reduction of 6 (95% CI: 3–8) mm Hg in SBP and 5 (95% CI: 3–7) mm Hg in DBP was observed among hypertensive subjects; among normotensive subjects, the reduction was 2 (95% CI: 1–3) mm Hg for SBP and 1 (95% CI: 1–2) mm Hg for DBP.[46] In addition, a most inclusive meta-analysis of 160 randomized controlled trials suggested that physical activity significantly improved cardiorespiratory fitness and CVD biomarkers of lipid and lipoprotein metabolism, glucose intolerance and insulin resistance, systemic inflammation, and hemostasis, which may mediate the effects of physical activity on the risk of cardio-metabolic diseases.[47]

There are several aspects of our study that merit further discussion. One limitation of the current study is the cross-sectional design, which cannot establish temporality for

Table 4. Robustness of the Sex-Specific Associations Between LTPA Status* and Cardio-Metabolic Measures With Respect to Education and Income†

Cardio-Metabolic Variables	Women (N=1183 Active and 4569 Inactive)			Men (N=1387 Active and 3446 Inactive)		
	OR/β‡	95% CI	*P* Value	OR/β	95% CI	*P* Value
SBP, mm Hg	−0.72	−1.69 to 0.25	0.15	−0.41	−1.37 to 0.56	0.41
DBP, mm Hg	−0.53	−1.15 to 0.09	0.10	−1.35	−2.00 to −0.71	<0.0001
Heart rate, bpm	−2.08	−2.22 to −1.44	<0.0001	−4.25	−4.91 to −3.58	<0.0001
FHS CVD score	−0.20	−0.50 to 0.10	0.19	−0.68	−1.01 to −0.35	<0.0001
ASCVD score	−0.11	−0.34 to 0.11	0.32	−0.19	−0.54 to 0.16	0.29
Hypertension	0.83	0.70 to 0.98	0.03	0.79	0.68 to 0.92	0.002
Diabetes§	0.89	0.72 to 1.11	0.31	0.77	0.64 to 0.93	0.005
FHS 10-yr risk of CVD	0.84	0.70 to 1.00	0.06	0.71	0.61 to 0.83	<0.0001
10-yr risk of ASCVD	0.87	0.67 to 1.12	0.27	0.77	0.64 to 0.93	0.007

AHA indicates American Heart Association; ASCVD, arteriosclerotic cardiovascular disease; BMI, body mass index; CVD, cardiovascular disease; DBP, diastolic blood pressure; FHS, Framingham Heart Study; LTPA, leisure time physical activity; SBP, systolic blood pressure.
*AHA guidelines recommend at least 150 min/wk moderate exercise or 75 min/wk vigorous exercise.
†Estimates and 95% CIs were from regular logistic regression or ordered logistic regression or generalized linear regression models adjusting for age, race, study centers, BMI, smoking status, alcohol consumption, education, and income.
‡ORs are reported to discrete outcomes, and mean differences (βs) were reported for continuous outcomes. For CVD risk scores, ORs comparing the high-risk category vs the low-risk category were obtained from ordered logistic regression models.
§Diabetes was defined using self-reported information and laboratory measurements (fasting plasma glucose level ≥7.0 mmol/L, 2-hour postload plasma glucose ≥11.1 mmol/L, or HbA1c ≥6.5%).

potential causal relation. Although the exploratory mediation analysis may provide some insight into the potential causal pathways, the results are preliminary due to the lack of clear temporality and need to be confirmed by further investigations. We are in the process of completing the second wave of data collection for physical activity and cardio-metabolic outcomes in the ELSA-Brasil. These prospective data linking physical activity and incident cardio-metabolic diseases will be utilized to improve the longitudinal understanding of the physical activity–CVD relation. Secondly, the ELSA-Brasil specifically targeted Brazilian adults, who have been understudied with respect

Table 5. Robustness of the Sex-Specific Associations Between LTPA Status* and Cardio-Metabolic Measures With Respect to an Alternative Definition of Physical Inactivity (LTPA-Related EE ≥1000 kcal/wk)†

Cardio-Metabolic Variables	Women (N=1183 Active and 4569 Inactive)			Men (N=1387 Active and 3446 Inactive)		
	OR/β‡	95% CI	*P* Value	OR/β	95% CI	*P* Value
SBP, mm Hg	−0.70	−1.61 to 0.22	0.14	−0.70	−1.59 to 0.19	0.12
DBP, mm Hg	−0.50	−1.08 to 0.09	0.10	−1.54	−2.13 to −0.95	<0.0001
Heart rate, bpm	−1.54	−2.13 to −0.94	<0.0001	−3.67	−4.28 to −3.06	<0.0001
FHS CVD score	−0.17	−0.45 to 0.11	0.23	−0.53	−0.83 to −0.23	0.001
ASCVD score	−0.04	−0.25 to 0.17	0.71	−0.27	−0.59 to 0.05	0.10
Hypertension	0.85	0.73 to 0.99	0.03	0.85	0.74 to 0.97	0.01
Diabetes§	0.92	0.75 to 1.11	0.38	0.86	0.74 to 1.01	0.07
FHS 10-yr risk of CVD	0.87	0.74 to 1.02	0.09	0.87	0.78 to 0.98	0.02
10-yr risk of ASCVD	0.90	0.71 to 1.13	0.35	0.82	0.69 to 0.98	0.02

AHA indicates American Heart Association; ASCVD, arteriosclerotic cardiovascular disease; BMI, body mass index; CVD, cardiovascular disease; DBP, diastolic blood pressure; FHS, Framingham Heart Study; LTPA, leisure time physical activity; SBP, systolic blood pressure.
*LTPA-related energy expenditure (LTPA-EE) ≥1000 kcal/wk vs <1000 kcal/wk.
†Estimates and 95% CIs were from regular logistic regression or ordered logistic regression or generalized linear regression models adjusting for age, race, study centers, BMI, smoking status, and alcohol consumption.
‡ORs are reported to discrete outcomes, and mean differences (βs) were reported for continuous outcomes. For CVD risk scores, ORs comparing the high-risk category vs the low-risk category were obtained from ordered logistic regression models.
§Diabetes was defined using self-reported information and laboratory measurements (fasting plasma glucose level ≥7.0 mmol/L, 2-hour postload plasma glucose ≥11.1 mmol/L, or HbA1c ≥6.5%).

Table 6. Robustness of the Sex-Specific Associations Between LTPA Status* and Cardio-Metabolic Measures With the Effects of Study Centers Treated as Random Effects†

Cardio-Metabolic Variables	Women (N=1183 Active and 4569 Inactive)			Men (N=1387 Active and 3446 Inactive)		
	OR/β‡	95% CI	*P* Value	OR/β	95% CI	*P* Value
SBP, mm Hg	−1.35	−2.31 to −0.39	0.006	−1.09	−2.06 to −0.12	0.03
DBP, mm Hg	−0.79	−1.41 to −0.18	0.01	−1.71	−2.35 to −1.07	<0.0001
Heart rate, bpm	−1.96	−2.58 to −1.33	<0.0001	−4.30	−4.96 to −3.64	<0.0001
FHS CVD score	−0.38	−0.67 to −0.09	0.01	−0.84	−1.17 to −0.51	<0.0001
ASCVD score	−0.17	−0.39 to 0.05	0.12	−0.26	−0.62 to 0.08	0.14
Hypertension	0.78	0.66 to 0.92	0.003	0.76	0.65 to 0.88	0.0002
Diabetes§	0.83	0.67 to 1.03	0.09	0.73	0.61 to 0.87	0.0006
FHS 10-yr risk of CVD	0.77	0.65 to 0.92	0.004	0.67	0.57 to 0.78	<0.0001
10-yr risk of ASCVD	0.78	0.61 to 1.01	0.06	0.71	0.59 to 0.85	0.0003

AHA indicates American Heart Association; ASCVD, arteriosclerotic cardiovascular disease; BMI, body mass index; CVD, cardiovascular disease; DBP, diastolic blood pressure; FHS, Framingham Heart Study; LTPA, leisure time physical activity; SBP, systolic blood pressure.

*AHA guidelines recommend at least 150 min/wk moderate exercise or 75 min/wk vigorous exercise.

†Estimates and 95% CIs were from generalized linear mixed models or cumulative link mixed models or linear mixed models with the effects of study centers treated as random effects, adjusting for age, race, BMI, smoking status, and alcohol consumption.

‡Odds ratios are reported to discrete outcomes, and mean differences (βs) were reported for continuous outcomes. For CVD risk scores, ORs comparing the high-risk category vs the low-risk category were obtained from cumulative link mixed models.

§Diabetes was defined using self-reported information and laboratory measurements (fasting plasma glucose level ≥7.0 mmol/L, 2-hour postload plasma glucose ≥11.1 mmol/L, or HbA1c ≥6.5%).

to the effects of physical activity on cardio-metabolic health. The study population comprises those who are employed and have high levels of education, which may limit its generalizability to the entire Brazilian population. Another potential limitation is the measurement error related to self-reported physical activity levels. In the current study, the relations between self-reported physical activity levels and cardio-metabolic outcomes were evaluated using IPAQ-based measures, which have been validated previously.[39] Results from the validation study indicated that IPAQ-based measures can correctly classify individual levels of LTPA and are valid for the purpose of studying relations between LTPA and chronic diseases. Although the physical activity measures are self-reported, the cardio-metabolic outcomes are objectively measured in the current study. Therefore, any measurement error in the exposure and outcome measures was less likely to be differential and dependent, which would have only led to a somewhat conservative estimate. In addition, the AHA and the World Health Organization recommendations are made for aerobic activity, while the IPAQ does not distinguish between resistance exercise and aerobic activity. However, the results from a sensitivity analysis show that our findings were robust to the use of an alternative definition of LTPA status.

Findings from our study have implications for future clinical and public health research and development of physical activity policies in Brazil. This cross-sectional study is among the very first efforts to comprehensively and systematically investigate the role of physical activity in relation to cardio-metabolic health in Brazil. The large sample size and wide variety of well-characterized variables, including directly measured CVD biomarkers, make the ELSA-Brasil a unique resource for investigators to study the determinants of cardio-metabolic diseases in an understudied population. Our analyses corroborate that being physically active is significantly correlated with favorable profiles of cardio-metabolic health in this large cohort, which is consistent with the findings from countries in North America and Europe. Findings from the current study suggest that it is possible to use lifestyle interventions to curb the epidemic of physical inactivity and cardio-metabolic diseases in Brazil. Although the effect sizes observed for intermediate biomarkers were small to modest, the reduction of cardio-metabolic risk, in terms of hypertension, diabetes, and CVD, was substantial and of clinical significance. By presenting the results for both the intermediate biomarkers and cardio-metabolic diseases, our study helps to provide a comprehensive and coherent understanding of the relation between physical activity and cardio-metabolic health. In addition, a mediation analysis was conducted to explore the potential mechanistic pathways leading from physical activity to the intermediate biomarkers and then to cardio-metabolic diseases. Specifically, we measured the extent to which each intermediate biomarker may contribute to the overall effects of LTPA on each cardio-metabolic disease of interest. Although the exact mediating mechanisms remain to be elucidated by future research using longitudinal data, preliminary findings from our exploratory

Table 7. Proportion of Mediated Effects of Physical Activity on Cardio-Metabolic Disease Risk

Mediator	Proportion Mediated		
	Estimate*	95% CI†	*P* Value
BMI			
Hypertension	0.32	0.25 to 0.43	<0.05
Diabetes	0.32	0.24 to 0.46	<0.05
10-yr risk of CVD	0.33	0.26 to 0.48	<0.05
10-yr risk of ASCVD	0.32	0.25 to 0.51	<0.05
SBP			
Hypertension	0.28	0.15 to 0.40	<0.05
Diabetes	0.07	0.03 to 0.12	<0.05
10-yr risk of CVD	0.26	0.16 to 0.44	<0.05
10-yr risk of ASCVD	0.23	0.12 to 0.54	<0.05
DBP			
Hypertension	0.49	0.31 to 0.66	<0.05
Diabetes	0.10	0.04 to 0.15	<0.05
10-yr risk of CVD	0.40	0.27 to 0.68	<0.05
10-yr risk of ASCVD	0.31	0.20 to 0.71	<0.05
Heart rate			
Hypertension	0.10	0.04 to 0.15	<0.05
Diabetes	0.36	0.21 to 0.57	<0.05
10-yr risk of CVD	0.16	0.10 to 0.30	<0.05
10-yr risk of ASCVD	0.17	0.10 to 0.43	<0.05

ASCVD indicates arteriosclerotic cardiovascular disease; BMI, body mass index; CVD, cardiovascular disease; DBP, diastolic blood pressure; SBP, systolic blood pressure.
*The mediator model adjusted for age, race, study centers, BMI, smoking status, and alcohol consumption. The explanatory variables of the outcome models include physical activity status, the mediator, and the same set of covariates adjusted in the mediator model.
†95% CIs were obtained based on 50 quasi-Bayesian simulations using robust standard errors.

mediation analysis suggest that substantial proportions of the effects of LTPA on cardio-metabolic diseases may be mediated through the intermediate biomarkers. Together with the preceding analyses, the mediation analysis provides some innovative insights into the role of lifestyle interventions in the prevention of cardio-metabolic diseases. More investigations, specifically targeting the Brazilian population, are needed to further clarify the mechanistic pathways, evaluate the effectiveness of currently ongoing interventions, inform the design of better-targeted interventions in the future, and outline the practical guidelines for physicians to use in the management of physical inactivity and related cardio-metabolic outcomes in the specific setting. Therefore, the current study results should support Brazil's ongoing efforts and that of other countries to develop interventions to increase levels of physical activity and improve cardio-metabolic health outcomes in their populations.

In summary, our findings from a cross-sectional study of 10 585 Brazilian adults point to the importance of physical activity in various aspects of cardio-metabolic health among the Brazilian population. With the growing epidemics of cardio-metabolic diseases and physical inactivity, especially in middle-income countries like Brazil, an optimal prevention strategy should emphasize the promotion of a healthy lifestyle, which should include a key component of enhanced LTPA levels. Further investigation will establish a prospective relation between physical activity and cardio-metabolic outcomes to inform public health policy and personalized interventions.

Author Contributions

The study was conceived and designed by Lin, Alvim, Liu, and Lotufo; Lotufo and Bensenor contributed to the acquisition of data; Lin conducted the statistical analyses and drafted the manuscript; all authors critically reviewed the manuscript and approved the final version.

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Disclosures

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