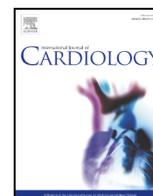




Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Poorer cardiovascular health is associated with psychiatric comorbidity: results from the ELSA-Brasil Study[☆]



Claudia Szlejf^{a,*,1}, Claudia K. Suemoto^{a,b,2}, Itamar S. Santos^{a,c,3}, Andre R. Brunoni^{d,2}, Maria Angélica Nunes^{e,4}, Maria Carmen Viana^{f,4}, Sandhi Maria Barreto^{g,4}, Paulo A. Lotufo^{a,c,4}, Isabela M. Benseñor^{a,c,3}

^a Center for Clinical and Epidemiological Research, Hospital Universitario, University of Sao Paulo, Sao Paulo, Brazil

^b Division of Geriatrics, University of Sao Paulo Medical School, Sao Paulo, Brazil

^c Department of Internal Medicine, University of Sao Paulo Medical School, Sao Paulo, Brazil

^d Service of Interdisciplinary Neuromodulation, Laboratory of Neuroscience and National Institute of Biomarkers in Psychiatry, Department and Institute of Psychiatry, Hospital das Clinicas, University of Sao Paulo Medical School, Sao Paulo, Brazil

^e Universidade Federal do Rio Grande do Sul, Rio Grande do Sul, Brazil

^f Center of Psychiatric Epidemiology (CEPEP), Department of Social Medicine, Postgraduate Program in Public Health, Federal University of Espírito Santo, Vitória, Brazil

^g Faculty of Medicine, Universidade Federal de Minas Gerais, Minas Gerais, Brazil

ARTICLE INFO

Article history:

Received 6 February 2018

Received in revised form 5 June 2018

Accepted 11 June 2018

Available online 12 June 2018

Keywords:

Ideal cardiovascular health

Depression

Anxiety

Psychiatric diagnosis

Lifestyle

ABSTRACT

Background: Common psychiatric symptoms may hinder achieving ideal cardiovascular health (ICH). We aimed to investigate the association between the ICH score and psychiatric disorders in Brazilian adults.

Methods: In this cross-sectional analysis, 13,743 participants free of cardiovascular disease from the ELSA-Brasil study were assessed using the American Heart Association ICH score. Cardiovascular health was classified as poor (0–2 ideal metrics), intermediate (3–4 ideal metrics), and optimal (5–7 ideal metrics). We used the Clinical Interview Scheduled Revised (CIS-R) to assess psychiatric disorders and investigate their association with the ICH score and each non-ICH metric.

Results: The frequency of poor, intermediate, and optimal cardiovascular health were 54.1%, 38.1%, and 7.8%, respectively. Depressive and anxiety disorders were associated with poor cardiovascular health (depressive disorder: OR = 2.49, 95% CI = 1.62–3.80, $p < 0.001$; anxiety disorder: OR = 1.47, 95% CI = 1.22–1.78, $p < 0.001$), and intermediate cardiovascular health (depressive disorder: OR = 1.94, 95% CI = 1.26–2.98, $p = 0.002$; anxiety disorder: OR = 1.22, 95% CI = 1.01–1.47, $p = 0.043$). In the analysis stratified by sex, these associations were significant only among women. The disorders were also associated with the following non-ICH metrics: body mass index, physical activity, healthy diet score, and smoking. Participants with depressive disorder and anxiety disorder had expected lower global and lifestyle ICH score than participants without these conditions, with significant results among women in the stratified analysis.

Conclusion: Psychiatric comorbidity was associated with poorer cardiovascular health. These conditions may compromise the adoption of healthy cardiovascular risk reduction behaviors.

© 2018 Elsevier B.V. All rights reserved.

[☆] Szlejf, Nunes, Viana, Barreto, and Lotufo report no relationships that could be construed as a conflict of interest. Brunoni is recipient of a CAPES/Alexander von Humboldt fellowship award for experienced researchers and a consultant of the Neurocare group GmbH (Munich, Germany). Lotufo, Benseñor and Santos are recipients of a scholarship from CNPq. Suemoto was supported by CAPES. None of these bodies had a further role in study design; in the collection, analysis and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication.

* Corresponding author at: Centro de pesquisa Clínica e Epidemiológica, Hospital Universitário, Av. Lineu Prestes 2565, 3° andar, CEP 05508-000, São Paulo, SP, Brazil.

E-mail address: claujeru@gmail.com (C. Szlejf).

¹ This author contributed to data analysis and interpretation, wrote the manuscript, and takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

² This author contributed to data analysis and interpretation, and manuscript revision, adding substantial intellectual content to the article.

³ This author contributed to study design, data analysis and interpretation, and manuscript revision, adding substantial intellectual content to the article.

⁴ This author contributed to study design and manuscript revision, adding substantial intellectual content to the article.

1. Introduction

In 2010 the American Heart Association (AHA) defined the 2020 Strategic Impact Goals to reduce aged-adjusted mortality due to cardiovascular diseases by 20%, and to improve cardiovascular health by 20% in the United States. A score to measure and monitor cardiovascular health was developed based on ideal levels of 7 cardiovascular health and lifestyle metrics, which are targets of cardiovascular disease primary prevention [1]. Since then, the Ideal Cardiovascular Health (ICH) score has been applied in studies worldwide, showing that higher scores were associated with lower risk of all-cause mortality, cardiovascular mortality, clinical and sub-clinical cardiovascular disease [2–5]. Moreover, studies demonstrated that the ICH score may also be used to predict other health outcomes, such as self-rated health status in middle-aged adults [6], and functional status and frailty in older adults [7, 8].

Unfortunately, the frequency of individuals with 7 ICH metrics remains low, ranging from 0.3% to 12% around the world [9]. The understanding of potentially modifiable obstacles to the achievement of ICH could help reverse this distressing picture. Psychiatric comorbidity, such as depression and anxiety disorders, are frequent in individuals with cardiovascular disease and are related to cardiovascular health outcomes [10]. Individuals with these common psychiatric disorders may have lower ICH scores due to low adherence to a healthy lifestyle and lack of motivation to change unhealthy lifestyle. Cross-sectional studies demonstrated that depression was associated with worse cardiovascular health in different populations, mainly due to its association with poorer lifestyle ICH metrics [11–15]. On the other hand, a prospective study showed that individuals with higher ICH scores had lower odds of developing depressive symptoms [16]. However, there is less evidence on the relation between anxiety and cardiovascular health. ICH scores were negatively correlated with symptoms of anxiety and stress in Chinese adults [11], although it was not associated with anxiety symptoms in Finnish women [15].

Although the AHA metrics can be applied worldwide, not many studies have used them to assess cardiovascular health and its associated factors in different populations. The investigation of cardiovascular health determinants and the quantification of their influence on population health is relevant to reduce the cardiovascular burden. Studies exploring the relationship between psychiatric comorbidity and ICH scores were not conducted in Latin American countries, where these scores are typically low [17–19]. Therefore, the aim of this study is to investigate the baseline association of ICH and psychiatric comorbidity in Brazilian adults from the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil).

2. Methods

2.1. Study population and design

The present study is a cross-sectional analysis of the ELSA-Brasil baseline evaluation. The study design and cohort profile have been published elsewhere [20, 21]. Briefly, it is a cohort of 15,105 active and retired employees from public institutions located in different Brazilian cities, aged between 35 and 74 years at baseline. Information on socio-demographics, clinical history, family history of diseases, lifestyle factors, mental health, cognitive status, and occupational exposure were assessed from August 2008 to December 2010. Anthropometric measurements, and laboratory and imaging tests were also obtained. The study was conducted in accordance with the Declaration of Helsinki and was approved by the local institutional review boards. All participants signed the informed consent prior to enrollment. For this analysis, we excluded (1) participants with previous history of cardiovascular disease (including stroke, myocardial infarction and myocardial revascularization) because the ICH score was developed to assess cardiovascular health as a primary prevention tool, and (2) participants with incomplete data for exposure, outcomes, or covariates.

2.2. Sociodemographic, clinical, and laboratory profile

Questionnaires addressed age, sex, self-reported race (white, black, brown, Asian, and indigenous, dichotomized as whites and non-whites for analytic purposes), schooling (middle school or lower vs high school or higher), smoking status, leisure physical activity using the International Physical Activity Questionnaire long form [22], current alcohol use,

and diet patterns using the Food Frequency Questionnaire [23]. Anthropometric measurements were assessed using standard techniques and body mass index was obtained dividing weight per height squared (kg/m^2). Blood pressure was measured in a seated position, after 5 min of rest, with a validated oscillometric device (Omron HEM 705CPINT, Tokyo, Japan). Three measurements were performed with 1-min intervals and the mean of the latest two readings was considered. Venous blood samples were obtained following an overnight fast. Enzymatic assays in the centrifugated serum – colorimetric and Hexokinase method (ADVIA 1200, Siemens®, Germany) – determined total cholesterol and fasting plasma glucose, respectively. Participant's medications were classified according to the Anatomical Therapeutic Chemical Classification System Codes [24]. The use of antihypertensive medication was defined as the use of medications under the codes C02, C03, C07, C08, and C09, hypoglycemic medication as the use of medications under the code A10, and lipid-lowering medications as the use of medications under the code C10.

2.3. Ideal cardiovascular health profile

The ICH score is composed by 4 lifestyle-factors (body mass index, smoking, physical activity, and healthy diet score) and 3 health-factors (blood pressure, fasting plasma glucose, total cholesterol), summing up to 7 health metrics [1]. In the present study, each metric was categorized as ideal according to the following criteria: (1) systolic blood pressure < 120 mmHg and diastolic blood pressure < 80 mmHg in the absence of antihypertensive medication; (2) fasting plasma glucose < 100 mg/dL in the absence of hypoglycemic medication; (3) total cholesterol < 200 mg/dL in the absence of lipid-lowering medication; (4) no smoking history or quit smoking > 2 years; (5) body mass index < 25 kg/m^2 ; (6) ideal physical activity defined as ≥ 75 min/week of vigorous physical activity, or ≥ 150 min/week of moderate physical activity, or a combination of both; and (7) a healthy diet score: 4 to 5 adequate components according to the AHA recommendation criteria [19]. We made some adaptations for smoking and the healthy diet score: (1) participants with ideal smoking profiles were those who had never smoked or whose age at quitting smoking was ≥ 2 years less than their current age because, in the ELSA-Brasil questionnaire, past smokers stated the age (in years) at which they had quit smoking. Therefore, a minimum period of one-year since the participant quit smoking would be warranted; (2) the following were considered as healthy food intake: ≥ 4 servings of fruit and vegetables per day, ≥ 7 oz. of fish per week, ≥ 2 servings of fiber-rich whole grains per day, and ≤ 450 kcal of sugar-sweetened beverages per week. Sodium consumption was corrected for total energy intake [25] and the consumption < 1500 mg/day was considered adequate [19]. The global ICH score was calculated by summing the number of ideal metrics for each participant, ranging from 0 to 7. Participants with 0–2, 3–4, and 5–7 ideal metrics were classified as having poor, intermediate, and optimal cardiovascular health, respectively [14]. We also calculated the lifestyle ICH score as the sum of lifestyle ICH metrics, ranging from 0 to 4; and the health ICH score as the sum of health ICH metrics, ranging from 0 to 3.

2.4. Assessment of mental symptoms

An adapted Brazilian version of the Clinical Interview Scheduled Revised (CIS-R) was used to assess mental symptoms and psychiatric disorders [26]. This questionnaire is reliable when applied by trained lay interviewers and it is composed by 14 sections: somatic symptoms, fatigue, concentration and forgetfulness, sleep problems, irritability, worry about physical health, depression, depressive ideas, worry, anxiety, phobias, panic, compulsions, and obsessions. Each section presents two introductory questions that confirm the presence of the specific symptom in the last month. Afterwards, frequency, duration, and severity of the positive symptom in the last 7 days are assessed. Scores for each section range from 0 to 4 (except the score for depressive ideas that range from 0 to 5), therefore the total score ranges from 0 to 57. Each symptom is considered clinically relevant if the corresponding section score is ≥ 2 . A score ≥ 12 indicate current common mental disorder [27]. The CIS-R also yields diagnoses of current psychiatric disorders according to the International Classification of Diseases, 10th Revision (ICD-10): depressive disorder (mild, moderate, and severe), and anxiety disorder (generalized anxiety disorder, panic disorder, all phobias, and obsessive-compulsive disorder).

2.5. Statistical analysis

Data were analyzed using Stata version 14.2 (StataCorp LP, College Station, TX, USA) and R software version 3.2.0 (R Core Team, Vienna, Austria). Continuous variables with normal distribution are presented as mean and standard deviation (SD), non-normally distributed continuous variables as median and interquartile range (IQR), and categorical variables as absolute and relative frequencies. Characteristics of participants according to ICH score classification were compared using one-way ANOVA, Kruskal-Wallis test, and Chi-square test for continuous variables with normal distribution, non-normally distributed continuous variables, and categorical variables, respectively.

To investigate the association between categorized ICH metrics (poor, intermediate and optimal) with psychiatric disorders (depressive disorder, anxiety disorder, and common mental disorder) we used simple and adjusted multinomial logistic regression models. Optimal cardiovascular health was considered as the reference level. Hierarchical multiple models were built as follows: model 1 adjusted by age and sex, and model 2 adjusted by age, sex, race, education, and current alcohol consumption. We tested for interactions of older age (≥ 65 years-old) and sex with depressive and anxiety disorder, and common mental disorder, stratifying the analysis when the interaction term p -value was < 0.10. Also, simple and adjusted binary logistic regression models were used to

explore the association between each non-ideal cardiovascular health metric and the psychiatric conditions, using the same variables for adjustment of the multinomial models. An OR > 1 means that the explanatory psychiatric condition increases the odds of having a non-ideal cardiovascular health metric.

Finally, to explore the association of the global, lifestyle, and health ICH scores with depressive and anxiety disorder, and common mental disorder, we fitted simple and adjusted (for the same possible confounders aforementioned) quasi-Poisson regression models. Quasi-Poisson models are derivatives of the classic Poisson model, appropriate for dependent variables that assume only non-negative integer numbers (usually counts). However, differently than the classic Poisson model, the quasi-Poisson does not assume that the conditional variance equals the conditional mean, compensating the over or under-dispersion of the data by calculating a dispersion parameter to be included in the model. We found significant under-dispersion in all models, with dispersion parameters between 0.40 and 0.84 and z-scores from -106.3 to -19.2 , justifying the use of quasi-Poisson models. Results are presented as relative predicted score differences (rPSD) and their 95% CI. rPSD can be interpreted as the change in the predicted value of the dependent variable attributable to the presence of the psychiatric disorder (main independent variable), holding constant other covariates. Therefore, a percentage of -10% indicates that participants with a given psychiatric disorder present a predicted 10% lower ICH score than individuals without that psychiatric disorder. We also tested for interactions between older age (≥ 65 years-old) or sex and depressive and anxiety disorders, or common mental disorder, stratifying the analysis when the interaction term p -value was < 0.10 .

3. Results

Among the 15,105 ELSA-Brasil participants, we excluded 575 individuals with self-reported previous stroke, myocardial infarction, and/or myocardial revascularization, and 787 with incomplete data for the CIS-R score, ICH score, and covariates. Therefore, 13,743 participants [mean age (SD): 51.8 (9.0) years, 45.3% men] were included in this analysis. Included participants were younger, had lower BMI, lower fasting plasma glucose levels, higher total cholesterol levels, lower systolic blood pressure, had lower frequency of males, higher frequencies of high-school diploma, moderate or intense leisure physical activity, current smokers, and current alcohol consumption than the excluded individuals. The frequency of poor, intermediate, and optimal cardiovascular health were 54.1%, 38.1%, and 7.8%, respectively. Depressive disorder was present in 4.1% of the total sample, 5.6% among women, and 2.3% among men. The frequency of anxiety disorder was 16.2%, 20.4%, and 11.0% in the total sample, among women, and among men, respectively. Common mental disorder (CIS-R score ≥ 12) was identified in 26.7% of the total sample, 33.6% among women, and 18.4% among men. Table 1 shows the participants characteristics according to cardiovascular health classification. Depressive disorder and common mental disorder were less frequent among participants with optimal cardiovascular health. These participants were also younger, with higher education, and with higher proportion of women and whites.

Table 2 shows the ORs and 95% CI for the association of poor and intermediate cardiovascular health with depressive disorder, anxiety disorder, and common mental disorder, considering optimal cardiovascular health as the reference for the total sample and stratified by sex. We found that sex was an effect modifier on the association of cardiovascular health with depressive disorder (interaction term p -value = 0.043 for poor cardiovascular health and 0.036 for intermediate cardiovascular health), anxiety disorder (interaction term p -value = 0.056 for poor cardiovascular health and 0.067 for intermediate cardiovascular health), and common mental disorder (interaction term p -value = 0.068 for poor cardiovascular health and 0.048 for intermediate cardiovascular health). After adjustment for sociodemographic characteristics and alcohol consumption, depressive disorder, anxiety disorder, and common mental disorder were associated with higher odds of intermediate and poor cardiovascular health in the total sample and among women, but not in men. There were no interactions between older age and depressive disorder, anxiety disorder, or common mental disorder (interaction term p -values > 0.10).

When we investigated the association between each non-ideal cardiovascular health metric and current psychiatric disorders, we found that depressive disorder, anxiety disorder, and common mental

disorder increased the odds of non-ideal cardiovascular health body mass index, non-ideal cardiovascular health practice of physical activity, and non-ideal cardiovascular health smoking status, after adjustment for possible confounders. Also, the presence of depressive disorder and common mental disorder increased the odds of non-ideal cardiovascular health fasting plasma glucose levels (Table 3).

Finally, after adjustment for covariates, participants with depressive disorder, anxiety disorder, and common mental disorder showed expected lower global and lifestyle ICH scores than participants without these psychiatric comorbidities. However, health ICH score was not associated with any of the psychiatric conditions (see Fig. 1 and Appendix A, Table A.1). Sex also was an effect modifier on the associations of global ICH score with depressive disorder (interaction term p -value = 0.043), anxiety disorder (interaction term p -value = 0.086), and common mental disorder (interaction term p -value = 0.021), and of lifestyle ICH score with depressive disorder (interaction term p -value = 0.003), anxiety disorder (interaction term p -value = 0.061), and common mental disorder (interaction term p -value = 0.010). After adjustment for confounders, women with current depressive disorder, anxiety disorder, and common mental disorder showed lower predicted global and lifestyle ICH scores than women without these psychiatric conditions, but there was no difference in the health ICH score among women with or without psychiatric comorbidity. On the other hand, among men anxiety disorder was associated with lower predicted lifestyle ICH score, and common mental disorder with lower predicted global and lifestyle ICH score (see Appendix A, Table A.2).

4. Discussion

The present study demonstrates that adults with depressive disorder, anxiety disorder, and common mental disorder have higher odds of poor and intermediate cardiovascular health, higher odds of some non-ideal cardiovascular health metrics, and lower global and lifestyle ICH scores, after adjustment for sociodemographic characteristics and alcohol consumption. Also, sex was an effect modifier on the association between ICH and the psychiatric comorbidities, with higher odds of poor/intermediate cardiovascular health and lower global and lifestyle ICH scores among women with psychiatric disorders. To the extent of our knowledge, this is the first large study to explore the association of ICH and psychiatric comorbidity in a Latin American country, where the ICH scores were previously reported to be low [19], and has high prevalence of common mental disorders and racial diversity.

Studies that investigated the association between depression and ICH found similar results. Three large cross-sectional studies determined that depression or depressive symptoms were associated with lower global and lifestyle ICH scores [12–14]. A Chinese cross-sectional study demonstrated that mean scores for depressive symptoms were lower in individuals with all 7 ICH metrics compared to those with at least one non-ideal metric [11]. The prevalence of depressive symptoms in Finnish women employees decreased with higher ICH scores [15], and in a prospective study with adults free of depression at baseline, lower ICH scores were associated with higher risk of subsequent depressive symptoms [16]. In our study, depressive disorder was not associated with health ICH score. However, Kronish et al. found that participants with depressive symptoms had lower health ICH scores, although the difference in scores between participants with and without depression was lower on the health ICH score than on the lifestyle ICH score [12]. Given that the prevalence of depressive disorder in this cohort is lower than previously described in other Brazilian studies [28], we believe that the association between depressive disorder and lower ICH scores in Brazil may be even stronger than the present findings.

Fewer studies investigated the association between anxiety and ICH score. Similarly, a cross-sectional study of Chinese adults found that ICH scores were negatively correlated with anxiety and stress scores on the 21-item Depression Anxiety Stress Scales [11]. On the other hand,

Table 1
Characteristics of participants according to cardiovascular health classification (n = 13,743).

	Poor CVH n = 7435	Intermediate CVH n = 5231	Optimal CVH n = 1077	p
CIS-R score, median (IQR)	6 (2–12)	6 (2–11)	5 (2–11)	0.005 ^a
Depressive disorder, n (%)	334 (4.5)	210 (4.0)	25 (2.3)	0.003 ^b
Anxiety disorder, n (%)	1241 (16.7)	822 (15.7)	156 (14.5)	0.103 ^b
Common mental disorder (CIS-R score ≥ 12), n (%)	2064 (27.8)	1343 (25.7)	265 (24.6)	0.009 ^b
Age (years), mean (SD)	53.8 (8.6)	50.1 (8.8)	46.0 (7.5)	<0.001 ^c
Male, n (%)	3718 (50.0)	2150 (41.1)	351 (32.6)	<0.001 ^b
Race, n (%)				<0.001 ^b
White	3604 (48.5)	2872 (54.9)	667 (61.9)	
Black	1367 (18.4)	746 (14.3)	101 (9.4)	
Brown	2197 (29.6)	1434 (27.4)	267 (25.0)	
Asian	165 (2.2)	141 (2.7)	36 (3.6)	
Indigenous	102 (1.4)	38 (0.7)	6 (0.6)	
High school or more, n (%)	6207 (83.5)	4798 (91.7)	1048 (97.3)	<0.001 ^b
Current alcohol use, n (%)	5121 (68.9)	3643 (69.6)	812 (75.4)	<0.001 ^b
Current smoker, n (%)	2417 (32.5)	1373 (26.3)	209 (19.4)	<0.001 ^b
BMI (kg/m ²), mean (SD)	28.9 (4.6)	25.2 (4.0)	22.8 (2.4)	<0.001 ^c
Moderate or intense leisure-time physical activity	1120 (15.1)	1495 (28.6)	525 (48.8)	<0.001 ^b
Healthy diet score > 1, n (%)	2829 (38.0)	2026 (38.7)	472 (43.8)	0.001 ^b
Fasting plasma glucose (mg/dL), mean (SD)	118.9 (35.7)	103.8 (18.3)	96.2 (8.5)	<0.001 ^c
Systolic blood pressure (mmHg), mean (SD)	127.1 (17.0)	115.3 (14.6)	106.8 (9.6)	<0.001 ^c
Diastolic blood pressure (mmHg), mean (SD)	80.0 (10.4)	72.7 (9.4)	67.6 (7.0)	<0.001 ^c
Total cholesterol (mg/dL), mean (SD)	225.1 (42.3)	207.4 (39.2)	185.9 (30.3)	<0.001 ^c

BMI: body mass index; CIS-R: Clinical Interview Scheduled Revised; IQR: interquartile range; SD: standard deviation.

^a Kruskal-Wallis test.

^b Chi-square test.

^c One-way ANOVA.

anxiety symptoms were not associated with ICH scores in Finnish women [15]. Our finding of high frequency of anxiety disorders is in agreement with data from the Global Burden of Disease, that showed that anxiety disorders are especially common in Brazil, representing the eighth highest cause of disability-adjusted life-years, which is higher than in most other countries [29]. To the extent of our knowledge, the relationship between ICH and common mental disorder, defined as CIS-R score ≥ 12, has not been addressed in the literature and future studies are needed to confirm our findings.

In our study, several interaction term *p*-values between psychiatric disorders and sex were significant, suggesting a different intensity on the association of psychiatric disorders and cardiovascular health among men and women, that seems to be stronger in women. This finding is in accordance with existing evidence that depression and anxiety may be stronger predictors of cardiovascular disease in

women [30, 31], although in a recent meta-analysis the association between depression and coronary heart disease or myocardial infarction was similar between men and women [32]. Other works on the association of depression and ICH had results that differ from ours. Gaye et al. found that the prevalence of intermediate and ideal lifestyle cardiovascular health was systematically higher in women compared to men, independent of depressive symptoms [14]. Li et al. showed that depressive symptoms lower the odds of higher ICH scores in men, although the authors do not mention whether the interaction between depressive symptoms and sex was statistically significant [13]. We believe that this is the first study to evaluate the effect modification of sex on the association between ICH and anxiety disorder.

Evidence points to the role of depression and anxiety as predictors of cardiovascular diseases and mortality, although studies on anxiety show conflicting results. [10, 33–36]. Different pathways could explain

Table 2
Association between ICH score classification and psychiatric disorders in the total sample and stratified by sex.

	Total sample (n = 13,743)				Men (n = 6219)				Women (n = 7524)			
	Poor		Intermediate		Poor		Intermediate		Poor		Intermediate	
	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>
Depressive disorder												
Crude	1.98 (1.31–2.99)	0.001	1.76 (1.16–2.68)	0.008	1.11 (0.54–2.31)	0.776	0.88 (0.41–1.88)	0.732	2.88 (1.75–4.74)	<0.001	2.39 (1.44–3.96)	0.001
Model 1 ^a	2.66 (1.74–4.05)	<0.001	2.01 (1.31–3.08)	0.001	1.27 (0.62–2.62)	0.514	0.95 (0.44–2.02)	0.883	3.40 (2.04–5.68)	<0.001	2.54 (1.52–4.24)	<0.001
Model 2 ^b	2.49 (1.62–3.80)	<0.001	1.94 (1.26–2.98)	0.002	1.24 (0.60–2.58)	0.558	0.93 (0.43–1.99)	0.851	3.12 (1.86–5.23)	<0.001	2.43 (1.45–4.07)	0.001
Anxiety disorder												
Crude	1.18 (0.99–1.42)	0.068	1.10 (0.92–1.33)	0.310	1.04 (0.73–1.47)	0.834	0.89 (0.62–1.28)	0.541	1.46 (1.18–1.81)	<0.001	1.27 (1.03–1.58)	0.028
Model 1 ^a	1.57 (1.30–1.89)	<0.001	1.26 (1.04–1.52)	0.018	1.14 (0.80–1.62)	0.473	0.94 (0.65–1.35)	0.729	1.78 (1.43–2.21)	<0.001	1.38 (1.11–1.72)	0.004
Model 2 ^b	1.47 (1.22–1.78)	<0.001	1.22 (1.01–1.47)	0.043	1.10 (0.77–1.58)	0.588	0.93 (0.64–1.33)	0.675	1.65 (1.32–2.06)	<0.001	1.33 (1.07–1.66)	0.010
Common mental disorder												
Crude	1.18 (1.02–1.37)	0.030	1.06 (0.91–1.23)	0.464	1.09 (0.82–1.45)	0.543	0.88 (0.66–1.19)	0.411	1.47 (1.23–1.75)	<0.001	1.24 (1.03–1.48)	0.021
Model 1 ^a	1.70 (1.45–1.99)	<0.001	1.26 (1.08–1.48)	0.004	1.27 (0.95–1.69)	0.110	0.96 (0.71–1.29)	0.776	1.94 (1.61–2.32)	<0.001	1.39 (1.16–1.67)	<0.001
Model 2 ^b	1.57 (1.34–1.84)	<0.001	1.21 (1.04–1.42)	0.017	1.24 (0.93–1.65)	0.149	0.95 (0.71–1.28)	0.733	1.73 (1.44–2.08)	<0.001	1.31 (1.10–1.58)	0.003

Optimal cardiovascular health as the reference.

ICH: ideal cardiovascular health.

^a Multinomial regression adjusted for age and sex for the total sample, and for age in the stratified analysis.

^b Multinomial regression adjusted for age, sex, race, education, and alcohol consumption in the total sample. Adjusted for age, race, education, and alcohol consumption in the stratified analysis.

Table 3
Association between each non-ICH metric and psychiatric disorders.

	BMI		Physical activity		Healthy diet score		Smoking		Fasting plasma glucose		Blood pressure		Total cholesterol	
	OR (95%CI)	p	OR (95%CI)	p	OR (95%CI)	p	OR (95%CI)	p	OR (95%CI)	p	OR (95%CI)	p	OR (95%CI)	p
Depressive disorder														
Crude	1.46 (1.21–1.75)	<0.001	1.90 (1.51–2.39)	<0.001	1.26 (0.56–2.86)	0.576	1.52 (1.24–1.88)	<0.001	1.02 (0.84–1.22)	0.878	0.78 (0.66–0.92)	0.003	0.96 (0.80–1.15)	0.663
Model 1 ^a	1.56 (1.30–1.88)	<0.001	1.75 (1.39–2.21)	<0.001	1.36 (0.60–3.08)	0.467	1.60 (1.30–1.97)	<0.001	1.31 (1.08–1.59)	0.006	0.97 (0.82–1.16)	0.772	0.98 (0.82–1.18)	0.848
Model 2 ^b	1.52 (1.27–1.84)	<0.001	1.65 (1.30–2.08)	<0.001	1.26 (0.56–2.87)	0.579	1.63 (1.31–2.01)	<0.001	1.29 (1.06–1.56)	0.011	0.92 (0.77–1.11)	0.391	1.01 (0.84–1.22)	0.888
Anxiety disorder														
Crude	1.18 (1.07–1.30)	0.001	1.59 (1.42–1.78)	<0.001	1.10 (0.73–1.66)	0.651	1.39 (1.23–1.56)	<0.001	0.81 (0.74–0.89)	<0.001	0.90 (0.82–0.98)	0.018	0.93 (0.84–1.02)	0.125
Model 1 ^a	1.26 (1.14–1.38)	<0.001	1.49 (1.33–1.68)	<0.001	1.15 (0.76–1.74)	0.517	1.45 (1.28–1.63)	<0.001	1.01 (0.91–1.12)	0.809	1.13 (1.02–1.25)	0.016	0.96 (0.87–1.06)	0.415
Model 2 ^b	1.23 (1.11–1.35)	<0.001	1.43 (1.27–1.61)	<0.001	1.09 (0.72–1.65)	0.697	1.44 (1.28–1.63)	<0.001	0.99 (0.90–1.01)	0.903	1.08 (0.98–1.19)	0.142	0.98 (0.89–1.08)	0.677
Common mental disorder														
Crude	1.23 (1.14–1.37)	<0.001	1.82 (1.65–2.00)	<0.001	1.43 (0.99–2.05)	0.056	1.41 (1.27–1.56)	<0.001	0.85 (0.79–0.93)	<0.001	0.84 (0.78–0.91)	<0.001	0.90 (0.83–0.98)	0.013
Model 1 ^a	1.34 (1.24–1.46)	<0.001	1.72 (1.56–1.90)	<0.001	1.49 (1.03–2.16)	0.033	1.48 (1.34–1.65)	<0.001	1.13 (1.03–1.23)	0.007	1.11 (1.02–1.21)	0.013	0.96 (0.88–1.04)	0.291
Model 2 ^b	1.30 (1.20–1.41)	<0.001	1.64 (1.49–1.81)	<0.001	1.39 (0.96–2.02)	0.081	1.49 (1.34–1.65)	<0.001	1.11 (1.01–1.21)	0.026	1.04 (0.96–1.13)	0.327	0.98 (0.90–1.06)	0.571

BMI: body mass index; ICH: ideal cardiovascular health.

^a Logistic regression adjusted for age and sex.

^b Logistic regression adjusted for age, sex, race, schooling, and alcohol consumption.

the effect of depression, anxiety, and psychiatric symptoms on cardiovascular health. Biological mechanisms, such as inflammatory processes, endothelial dysfunction, and autonomic nervous system dysfunction have been postulated and are supported by many studies [37–40]. In fact, previous works with the ELSA-Brasil data found a positive association of carotid intima-media thickness and coronary artery calcium with higher CIS-R scores, indicating that non-psychotic psychiatric symptoms may be associated with subclinical cardiovascular

disease [41, 42]. Other possible mechanism is that individuals with psychiatric comorbidity may adopt behaviors that compromise cardiovascular risk reduction. Studies have shown that depression and anxiety were associated with lower medication adherence, physical activity, and smoking cessation [43–45]. In our study, all psychiatric disorders were associated with non-ideal cardiovascular health body mass index, non-ideal cardiovascular health practice of physical activity, and non-ideal cardiovascular health smoking, suggesting a trend of

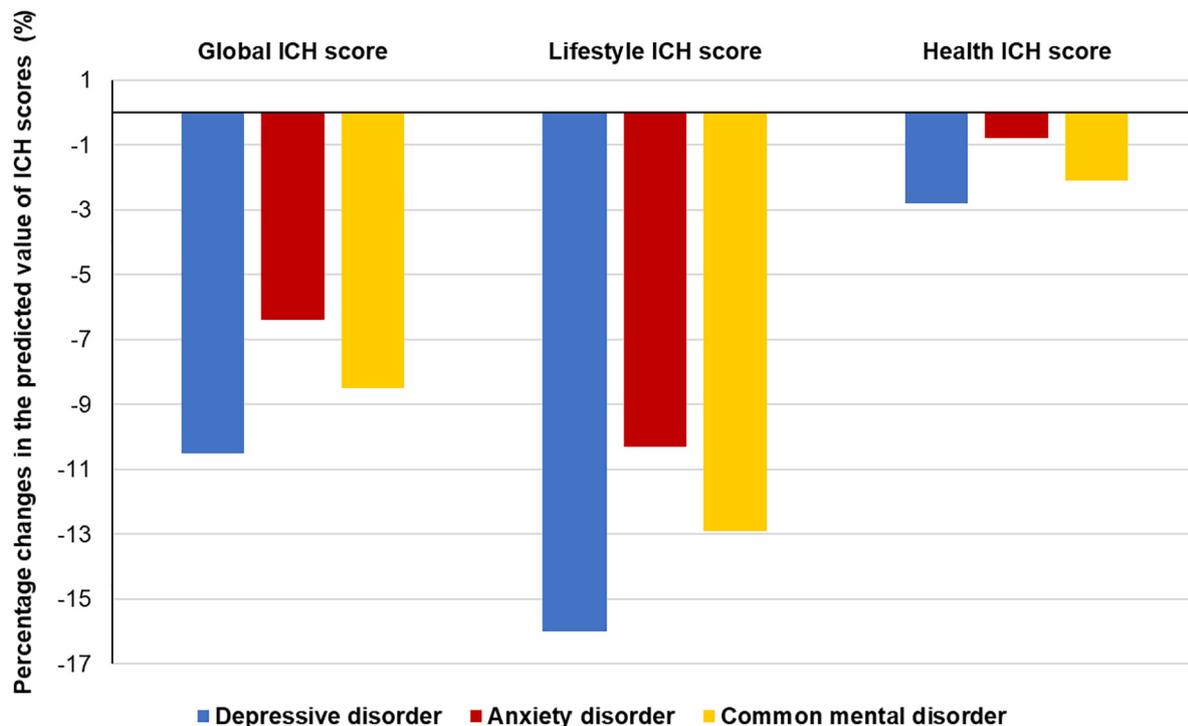


Fig. 1. Percentage changes in the predicted value of ICH scores attributable to the presence of psychiatric disorders, obtained by quasi-Poisson regression models adjusted for age, sex, race, education, and alcohol consumption.

low adherence to healthy lifestyle. Besides, adverse psychosocial factors may play a negative role in cardiovascular health, corroborating the behavioral pathway. In a prospective study that followed Finnish youth aged 3 to 18 years, favorable psychosocial factors in youth predicted ICH in adulthood [46].

Our study has several strengths: (1) it is one of the largest studies in the field, including a wide range of psychiatric symptoms; (2) the study explores the association between cardiovascular health and psychiatric disorders in a Latin American sample, while previous studies were conducted in Asia, North America, or Europe; (3) the CIS-R questionnaire enables the assessment of current mental symptoms and the identification of psychiatric morbidity according to the ICD-10 criteria; (4) we used different statistical analysis strategies, with consistent results; and (5) the large sample allowed us to test for interactions of the psychiatric comorbidities with sex and age. Nevertheless, the study has some limitations: the cross-sectional design prevents establishing a causal and temporal relationship between ICH and the psychiatric conditions, an association that may be bilateral. Further longitudinal analysis of upcoming examinations of the ELSA-Brasil may assess the evolution of cardiovascular health metrics in participants with depressive, anxiety, and common mental disorders at baseline, or the incidence of psychiatric disorders in individuals with baseline lower ICH scores. Also, the CIS-R does not assess lifetime psychiatric morbidity, only the presence of current symptoms, and therefore, false negative cases are counted among those without a psychiatric diagnosis. This is especially important considering the insidious time dependent nature of the outcomes assessed. Additionally, the CIS-R is applied by lay interviewers and the lack of insight into mental illness may affect responses to questions and mislead the interpretation of results [27]. Another relevant point is that the ELSA-Brasil is not a population-based study. Participants have higher education level and higher income status than the Brazilian population. Although recognizing that the choice of the ELSA-Brasil sampling strategy limits investigation in the domains of the

extremely poor and the unemployed, the racial, social, and regional diversity captured in the cohort will permit in-depth investigation of important health inequalities in Brazil. The applicability of the estimates from ELSA-Brasil to Brazilian adults is supported by the similarities in prevalence of behavioral risk factors and chronic conditions evaluated by ELSA-Brasil and by VIGITEL, a telephone-based behavioral risk factor survey, which has representative data for adults living in 27 Brazilian state capitals and Federal District [47]. Finally, we adjusted the analysis for relevant confounders on the association between ICH and psychiatric conditions, however residual confounding cannot be ruled out.

The knowledge that common psychiatric disorders, such as depression, anxiety, and non-psychotic psychiatric symptoms were associated with poorer cardiovascular health suggests that these conditions may compromise the adoption of a healthy cardiovascular profile. Pharmacological and non-pharmacological interventions to minimize the impact of psychiatric disorders on cardiovascular health are targets for future studies. Although there may be some concern that antidepressants may increase the risk of cardiovascular outcomes, a recent large observational study demonstrated a secure risk profile for most of them [48]. In a large randomized clinical trial, anti-depressants reduced the hazard of major adverse cardiovascular events in individuals with moderate to severe depressive symptoms [49]. On the other hand, there is some evidence that non-pharmacological interventions for mental health may benefit cardiovascular disease, although studies have reported mixed results [50]. Randomized clinical trials are needed to assess the effects of these interventions on the cardiovascular health profile of depressed and anxious individuals.

Funding

The ELSA-Brasil study was supported by the Brazilian Ministry of Health and CNPq (grants 01060010.00RS, 01060212.00BA, 01060300.00ES, 01060278.00MG, 01060115.00SP, 01060071.00RJ).

Appendix A

Table A.1

Crude and adjusted relative predicted score differences for the association between ICH scores and psychiatric disorders ($n = 13,743$).

	Global ICH score		Lifestyle ICH score		Health ICH score	
	rPSD (95% CI)	<i>p</i>	rPSD (95% CI)	<i>p</i>	rPSD (95% CI)	<i>p</i>
Depressive disorder						
Crude	-7.3% (-11.5%; -3.0%)	0.001	-16.7% (-20.6%; -12.6%)	<0.001	6.8% (-0.9%; 15.0%)	0.084
Model 1 ^a	-11.4% (-15.2%; -7.5%)	<0.001	-17.1% (-21.0%; -13.0%)	<0.001	-3.6% (-10.1%; 3.4%)	0.307
Model 2 ^b	-10.5% (-14.3%; -6.5%)	<0.001	-16.0% (-19.9%; -11.9%)	<0.001	-2.8% (-9.4%; 4.2%)	0.422
Anxiety disorder						
Crude	-3.1% (-5.4%; -0.7%)	0.012	-10.8% (-13.0%; -8.6%)	<0.001	8.8% (4.5%; 13.3%)	<0.001
Model 1 ^a	-7.4% (-9.5%; -5.2%)	<0.001	-11.3% (-13.5%; -9.1%)	<0.001	-1.7% (-5.4%; 2.1%)	0.376
Model 2 ^b	-6.4% (-8.5%; -4.2%)	<0.001	-10.3% (-12.5%; -8.1%)	<0.001	-0.8% (-4.5%; 3.1%)	0.688
Common mental disorder						
Crude	-4.2% (-6.1%; -2.2%)	<0.001	-13.2% (-14.9%; -11.4%)	<0.001	9.9% (6.3%; 13.7%)	<0.001
Model 1 ^a	-9.6% (-11.4%; -7.9%)	<0.001	-14.0% (-15.8%; -12.2%)	<0.001	-3.3% (-6.4%; -0.1%)	0.042
Model 2 ^b	-8.5% (-10.2%; -6.7%)	<0.001	-12.9% (-14.7%; -11.1%)	<0.001	-2.1% (-5.2%; 1.1%)	0.202

ICH: ideal cardiovascular health; rPSD: relative predicted score differences (the change in the predicted value of the ICH score attributable to the presence of the psychiatric disorder, holding covariates values constant).

^a Quasi-Poisson regression model, adjusted for age and sex.

^b Quasi-Poisson regression model, adjusted for age, sex, race, education, and alcohol consumption.

Table A.2

Crude and adjusted relative predicted score differences for the association between ICH scores and psychiatric disorders stratified by sex.

	Global ICH score		Lifestyle ICH score		Health ICH score	
	rPSD (95% CI)	<i>p</i>	rPSD (95% CI)	<i>p</i>	rPSD (95% CI)	<i>p</i>
Women ($n = 7524$)						
Depressive disorder						
Crude	-12.2% (-16.7%; -7.4%)	<0.001	-20.3% (-24.7%; -15.6%)	<0.001	-1.7% (-9.4%; 6.6%)	0.674

(continued on next page)

Table A.2 (continued)

	Global ICH score		Lifestyle ICH score		Health ICH score	
	rPSD (95% CI)	p	rPSD (95% CI)	p	rPSD (95% CI)	p
Model 1 ^a	-13.9% (-18.1%; -9.5%)	<0.001	-20.5% (-24.9%; -15.9%)	<0.001	-5.2% (-12.1%; 2.3%)	0.169
Model 2 ^b	-12.5% (-16.7%; -8.0%)	<0.001	-19.1% (-23.5%; -14.4%)	<0.001	-3.7% (-10.7%; 3.8%)	0.325
Anxiety disorder						
Crude	-6.4% (-9.0%; -3.6%)	<0.001	-12.3% (-15.0%; -9.6%)	<0.001	1.5% (-3.0; 6.3%)	0.518
Model 1 ^a	-9.0% (-11.4%; -6.4%)	<0.001	-12.7% (-15.3%; -10.0%)	<0.001	-3.9% (-7.9%; 0.3%)	0.067
Model 2 ^b	-7.7% (-10.1%; -5.1%)	<0.001	-11.4% (-14.0%; -8.6%)	<0.001	-2.7% (-6.7%; 1.6%)	0.216
Common mental disorder						
Crude	-7.5% (-9.7%; -5.2%)	<0.001	-15.2% (-17.4%; -13.0%)	<0.001	3.1% (-0.9%; 7.2%)	0.128
Model 1 ^a	-11.1% (-13.1%; -9.0%)	<0.001	-15.8% (-18.0%; -13.6%)	<0.001	-4.7% (-8.1%; -1.1%)	0.010
Model 2 ^b	-9.4% (-11.4%; -7.2%)	<0.001	-14.2% (-16.3%; -11.9%)	<0.001	-2.9% (-6.4%; 0.7%)	0.118
Men (n = 6219)						
Depressive disorder						
Crude	-1.9% (-10.3%; 7.4%)	0.680	-6.7% (-14.7%; 2.0%)	0.128	6.9% (-9.0%; 25.7%)	0.416
Model 1 ^a	-3.6% (-11.7%; 5.2%)	0.410	-7.2% (-15.1%; 1.5%)	0.103	2.6% (-12.4%; 20.1%)	0.751
Model 2 ^b	-3.5% (-11.6%; 5.3%)	0.420	-6.4% (-14.4%; 2.3%)	0.146	1.2% (-13.5%; 18.5%)	0.881
Anxiety disorder						
Crude	-2.8% (-6.9%; 1.6%)	0.206	-8.1% (-12.0%; -4.0%)	<0.001	7.0% (-1.0%; 15.8%)	0.089
Model 1 ^a	-4.1% (-8.1%; 0.0%)	0.051	-8.5% (-12.4%; -4.4%)	<0.001	3.7% (-3.9%; 12.0%)	0.346
Model 2 ^b	-3.7% (-7.7%; 0.5%)	0.080	-7.8% (-11.7%; -3.7%)	<0.001	3.6% (-4.0%; 11.9%)	0.360
Common mental disorder						
Crude	-5.1% (-8.3%; -1.7%)	0.004	-10.1% (-13.2%; -6.9%)	<0.001	4.2% (-2.2%; 11.1%)	0.205
Model 1 ^a	-7.1% (-10.2%; -3.8%)	<0.001	-10.6% (-13.7%; -7.5%)	<0.001	-0.6% (-6.7%; 5.8%)	0.842
Model 2 ^b	-6.7% (-9.9%; -3.5%)	<0.001	-10.1% (-13.2%; -7.0%)	<0.001	-0.6% (-6.6%; 5.9%)	0.859

ICH: ideal cardiovascular health; rPSD: relative predicted score differences (the change in the predicted value of the ICH score attributable to the presence of the psychiatric disorder, holding covariates values constant).

^a Quasi-Poisson regression model, adjusted for age.

^b Quasi-Poisson regression model, adjusted for age, race, education, and alcohol consumption.

References

- D.M. Lloyd-Jones, Y. Hong, D. Labarthe, D. Mozaffarian, L.J. Appel, L. Van Horn, K. Greenlund, S. Daniels, G. Nichol, G.F. Tomaselli, D.K. Arnett, G.C. Fonarow, P.M. Ho, M.S. Lauer, F.A. Masoudi, R.M. Robertson, V. Roger, L.H. Schwamm, P. Sorlie, C.W. Yancy, W.D. Rosamond, Defining and setting national goals for cardiovascular health promotion and disease reduction: the American heart association's strategic impact goal through 2020 and beyond, *Circulation* 121 (2010) 586–613.
- N. Fang, M. Jiang, Y. Fan, Ideal cardiovascular health metrics and risk of cardiovascular disease or mortality: a meta-analysis, *Int. J. Cardiol.* 214 (2016) 279–283.
- I.S. Santos, A.C. Goulart, A.C. Pereira, P.A. Lotufo, I.M. Benseñor, Association between cardiovascular health score and carotid intima-media thickness: cross-sectional analysis of the Brazilian longitudinal study of adult health (ELSA-Brasil) baseline assessment, *J. Am. Soc. Echocardiogr.* 29 (2016) 1207–1216.e4.
- I.M. Benseñor, A.C. Goulart, I.S. Santos, M.S. Bittencourt, A.C. Pereira, R.D. Santos, K. Nasir, R. Blankstein, P.A. Lotufo, Association between a healthy cardiovascular risk factor profile and coronary artery calcium score: results from the Brazilian longitudinal study of adult health (ELSA-Brasil), *Am. Heart J.* 174 (2016) 51–59.
- L. Guo, S. Zhang, Association between ideal cardiovascular health metrics and risk of cardiovascular events or mortality: a meta-analysis of prospective studies, *Clin. Cardiol.* (2017) 1–8.
- M. Manczuk, G. Vaidean, M. Dehghan, R. Vedanthan, P. Boffetta, W.A. Zatonski, Ideal cardiovascular health is associated with self-rated health status. The Polish Norwegian Study (PONS), *Int. J. Cardiol.* 230 (2017) 549–555.
- M.S. Dharmoon, C. Dong, M.S.V. Elkind, R.L. Sacco, Ideal cardiovascular health predicts functional status independently of vascular events: the Northern Manhattan Study, *J. Am. Heart Assoc.* 4 (2015) <https://doi.org/10.1161/JAHA.114.001322>.
- A. Graciani, E. García-Esquinas, E. López-García, J.R. Banegas, F. Rodríguez-Artalejo, Ideal cardiovascular health and risk of frailty in older adults, *Circ. Cardiovasc. Qual. Outcomes* 9 (2016) 239–245.
- A. Younus, E.C. Aneni, E.S. Spatz, C.U. Osondu, L. Roberson, O. Ogunmoroti, R. Malik, S.S. Ali, M. Aziz, T. Feldman, S.S. Virani, W. Maziak, A.S. Agatston, E. Veledar, K. Nasir, A systematic review of the prevalence and outcomes of ideal cardiovascular health in US and non-US populations, *Mayo Clin. Proc.* 91 (2016) 649–670.
- B.E. Cohen, D. Edmondson, I.M. Kronish, State of the art review: depression, stress, anxiety, and cardiovascular disease, *Am. J. Hypertens.* 28 (2015) 1295–1302.
- Q. Zeng, S.-Y. Dong, Z.-Y. Song, Y.-S. Zheng, H.-Y. Wu, L.-N. Mao, Ideal cardiovascular health in Chinese urban population, *Int. J. Cardiol.* 167 (2013) 2311–2317.
- I.M. Kronish, A.P. Carson, K.W. Davidson, P. Muntner, M.M. Safford, Depressive symptoms and cardiovascular health by the American Heart Association's definition in the reasons for geographic and racial differences in stroke (REGARDS) study, *PLoS One* 7 (2012) 1–8.
- Z. Li, X. Yang, A. Wang, J. Qiu, W. Wang, Q. Song, X. Wang, Association between ideal cardiovascular health metrics and depression in Chinese population: a cross-sectional study, *Sci. Rep.* 5 (2015) 1–7.
- B. Gaye, C. Prugger, M.C. Perier, F. Thomas, M. Plichart, C. Guibout, C. Lemogne, B. Pannier, P. Boutouyrie, X. Jouven, J.P. Empana, High level of depressive symptoms as a barrier to reach an ideal cardiovascular health. The Paris Prospective Study III, *Sci. Rep.* 6 (2016) 1–10.
- V. Veromaa, H. Kautiainen, U. Saxen, K. Malmberg-Ceder, E. Bergman, P.E. Korhonen, Ideal cardiovascular health and psychosocial risk factors among Finnish female municipal workers, *Scand. J. Public Health* 45 (2017) 50–56.
- V. España-Romero, E.G. Artero, D. Chul Lee, X. Sui, M. Baruth, J.R. Ruiz, R.R. Pate, S.N. Blair, A prospective study of ideal cardiovascular health and depressive symptoms, *Psychosomatics* 54 (2013) 525–535.
- G. Velasquez-Melendez, M.S. Felisbino-Mendes, F.P. Matozinhos, R. Claro, C.S. Gomes, D.C. Malta, Prevalência de saúde cardiovascular ideal na população brasileira - Pesquisa Nacional de Saúde (2013), *Rev. Bras. Epidemiol.* 18 (2015) 97–108.
- A. García-Hermoso, R. Ramírez-Vélez, R. Ramírez-Campillo, M. Izquierdo, Prevalence of ideal cardiovascular health and its association with cognitive function in older adults: the Chilean National Health Survey (2009–2010), *Rejuvenation Res.* 21 (2018) 333–340.
- L.B.M. Machado, B.L.S. Silva, A.P. Garcia, R.A.M. Oliveira, S.M. Barreto, M.J.M. de Fonseca, P.A. Lotufo, I.M. Benseñor, I.S. Santos, Ideal cardiovascular health score at the ELSA-Brasil baseline and its association with sociodemographic characteristics, *Int. J. Cardiol.* 254 (2018) 333–337.
- E.M.L. Aquino, S.M. Barreto, I.M. Benseñor, M.S. Carvalho, D. Chor, B.B. Duncan, P.A. Lotufo, J.G. Mill, M.D.C. Molina, E.L.A. Mota, V.M.A. Passos, M.I. Schmidt, M. Szklo, Brazilian longitudinal study of adult health (ELSA-Brasil): objectives and design, *Am. J. Epidemiol.* 175 (2012) 315–324.
- M.I. Schmidt, B.B. Duncan, J.G. Mill, P.A. Lotufo, D. Chor, S.M. Barreto, E.M.L. Aquino, V.M.A. Passos, S.M.A. Matos, M. del C.B. Molina, M.S. Carvalho, I.M. Benseñor, Cohort profile: longitudinal study of adult health (ELSA-Brasil), *Int. J. Epidemiol.* 44 (2015) 68–75.
- C.L. Craig, A.L. Marshall, M. Sjöström, A.E. Bauman, M.L. Booth, B.E. Ainsworth, M. Pratt, U. Ekelund, A. Ngve, J.F. Sallis, P. Oja, International physical activity questionnaire: 12-country reliability and validity, *Med. Sci. Sports Exerc.* 35 (2003) 1381–1395.
- R. Sichert, J.E. Everhart, Validity of a Brazilian food frequency questionnaire against dietary recalls and estimated energy intake, *Nutr. Res.* 18 (1998) 1649–1659.
- WHO, Guidelines for ATC Classification and DDD Assignment, 2017 <https://doi.org/10.1021/la902623c>.
- W. Willet, G. Howe, L. Kushi, Adjustment for total energy intake in epidemiologic studies, *Am. J. Clin. Nutr.* 65 (1997) 1220S–1228S.
- M.A. Nunes, M.G.M. de Alves, D. Chor, M.I. Schmidt, Adaptação transcultural do CIS-R (Clinical Interview Schedule- Revised Version) para o português no Estudo Longitudinal De Saúde Do Adulto (ELSA) Cross-cultural adaptation of CIS-R (Clinical Interview Schedule-Revised Version) for the portuguese in Longit, 31, *Rev HCPA*, 2011 487–490.

- [27] G. Lewis, A.J. Pelosi, R. Araya, G. Dunn, Measuring psychiatric disorder in the community: a standardized assessment for use by lay interviewers, *Psychol. Med.* 22 (1992) 465.
- [28] M.T. Silva, T.F. Galvao, S.S. Martins, M.G. Pereira, Prevalence of depression morbidity among Brazilian adults: a systematic review and meta-analysis, *Rev. Bras. Psiquiatr.* 36 (2014) 262–270.
- [29] GBD 2013 DALYs and HALE Collaborators, Global, regional, and national disability-adjusted life years (DALYs) for 306 diseases and injuries and healthy life expectancy (HALE) for 188 countries, 1990–2013: quantifying the epidemiological transition, *Lancet* 386 (2015) 2145–2191.
- [30] A.J. Shah, N. Ghasemzadeh, E. Zaragoza-Macias, R. Patel, D.J. Eapen, I.J. Neeland, P.M. Pimple, A.M. Zafari, A.A. Quyyumi, V. Vaccarino, Sex and age differences in the association of depression with obstructive coronary artery disease and adverse cardiovascular events, *J. Am. Heart Assoc.* 3 (2014) e000741.
- [31] S. Wassertheil-Smoller, E.M. Arredondo, J.W. Cai, S.F. Castaneda, J.P. Choca, L.C. Gallo, M. Jung, L.M. Lavange, E.T. Lee-Rey, T. Mosley, F.J. Penedo, D.A. Santistaban, P.C. Zee, Depression, anxiety, antidepressant use, and cardiovascular disease among Hispanic men and women of different national backgrounds: results from the Hispanic community health study/study of Latinos, *Ann. Epidemiol.* 24 (2014) 822–830.
- [32] Y. Gan, Y. Gong, X. Tong, H. Sun, Y. Cong, X. Dong, Y. Wang, X. Xu, X. Yin, J. Deng, L. Li, S. Cao, Z. Lu, Depression and the risk of coronary heart disease: a meta-analysis of prospective cohort studies, *BMC Psychiatry* 14 (2014) 371.
- [33] A. Pan, Q. Sun, O.I. Okereke, K.M. Rexrode, F.B. Hu, Depression and risk of stroke morbidity and mortality: a meta-analysis and systematic review, *JAMA* 306 (2011) 1241–1249.
- [34] A. Nicholson, H. Kuper, H. Hemingway, Depression as an aetiological and prognostic factor in coronary heart disease: a meta-analysis of 6362 events among 146 538 participants in 54 observational studies, *Eur. Heart J.* 27 (2006) 2763–2774.
- [35] C.A. Emdin, A. Oduyayo, C.X. Wong, J. Tran, A.J. Hsiao, B.H.M. Hunn, Meta-analysis of anxiety as a risk factor for cardiovascular disease, *Am. J. Cardiol.* 118 (2016) 511–519.
- [36] A.M. Roest, E.J. Martens, P. de Jonge, J. Denollet, Anxiety and risk of incident coronary heart disease. A meta-analysis, *J. Am. Coll. Cardiol.* 56 (2010) 38–46.
- [37] C. Pitsavos, D.B. Panagiotakos, C. Papageorgiou, E. Tsetsekou, C. Soldatos, C. Stefanadis, Anxiety in relation to inflammation and coagulation markers, among healthy adults: the ATTICA study, *Atherosclerosis* 185 (2006) 320–326.
- [38] K. Narita, T. Murata, T. Hamada, T. Takahashi, M. Omori, N. Suganuma, H. Yoshida, Y. Wada, Interactions among higher trait anxiety, sympathetic activity, and endothelial function in the elderly, *J. Psychiatr. Res.* 41 (2007) 418–427.
- [39] F.E.P. van Dooren, M.T. Schram, C.G. Schalkwijk, C.D.A. Stehouwer, R.M.A. Henry, P.C. Dagnelie, N.C. Schaper, C.J.H. van der Kallen, A. Koster, S.J.S. Sep, J. Denollet, F.R.J. Verhey, F. Pouwer, Associations of low grade inflammation and endothelial dysfunction with depression – the Maastricht study, *Brain Behav. Immun.* 56 (2016) 390–396.
- [40] A. Sgoifo, L. Carnevali, M. de L.A. Pico Alfonso, M. Amore, Autonomic dysfunction and heart rate variability in depression, *Stress* 3890 (2015) 1–10.
- [41] I.S. Santos, A.C. Goulart, A.R. Brunoni, A.H. Kemp, P.A. Lotufo, I.M. Bensenor, Anxiety and depressive symptoms are associated with higher carotid intima-media thickness. Cross-sectional analysis from ELSA-Brasil baseline data, *Atherosclerosis* 240 (2015) 529–534.
- [42] I.S. Santos, M.S. Bittencourt, P.T. Rocco, A.C. Pereira, S.M. Barreto, A.R. Brunoni, A.C. Goulart, M.J. Blaha, P.A. Lotufo, I.M. Bensenor, Relation of anxiety and depressive symptoms to coronary artery calcium (from the ELSA-Brasil baseline data), *Am. J. Cardiol.* 118 (2016) 183–187.
- [43] I.M. Kronish, N. Rieckmann, E.A. Halm, D. Shimbo, D. Vorchheimer, D.C. Haas, K.W. Davidson, Persistent depression affects adherence to secondary prevention behaviors after acute coronary syndromes, *J. Gen. Intern. Med.* 21 (2006) 1178–1183.
- [44] M.A. Whooley, P. de Jonge, E. Vittinghoff, C. Otte, R. Moos, R.M. Carney, S. Ali, S. Dowray, B. Na, M.D. Feldman, N.B. Schiller, W.S. Browner, Depressive symptoms, health behaviors, and risk of cardiovascular events in patients with coronary heart disease, *JAMA* 300 (2008) 2379–2388.
- [45] E.A. Kuhl, J.A. Fauerbach, D.E. Bush, R.C. Ziegelstein, Relation of anxiety and adherence to risk-reducing recommendations following myocardial infarction, *Am. J. Cardiol.* 103 (2009) 1629–1634.
- [46] L. Pulkki-Råback, M. Elovainio, C. Hakulinen, J. Lipsanen, M. Hintsanen, M. Jokela, L.D. Kubzansky, T. Hintsala, A. Serlachius, T. Laitinen, K. Pahlkala, V. Mikkilä, J. Nevalainen, N. Hutri-Kähönen, M. Juonala, J. Viikari, O.T. Raitakari, L. Keltikangas-Järvinen, Cumulative effect of psychosocial factors in youth on ideal cardiovascular health in adulthood the cardiovascular risk in young Finns study, *Circulation* 131 (2015) 245–253.
- [47] Brasil, VIGITEL BRASIL 2010, Vigilância de fatores de risco e proteção para doenças crônicas por inquérito telefônico, Ministério Da Saúde, 2011.
- [48] C. Coupland, T. Hill, R. Morriss, M. Moore, A. Arthur, J. Hippisley-Cox, Antidepressant use and risk of cardiovascular outcomes in people aged 20 to 64: cohort study using primary care database, *BMJ* 352 (2016) i1350.
- [49] H.T. May, T.L. Bair, B. Reiss-Brennan, S. Knight, J.L. Anderson, B.D. Horne, K.D. Brunisholz, J.B. Muhlestein, The association of antidepressant and statin use with death and incident cardiovascular disease varies by depression severity, *Psychol. Health Med.* 22 (2017) 919–931.
- [50] M.P. Tan, K. Morgan, Psychological interventions in cardiovascular disease: an update, *Curr. Opin. Psychiatry* 28 (2015) 371–377.