

## Research Article

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**Abbreviations:**

AHA, American Heart Association; CAC, coronary artery calcification; CHDI, Cardiovascular Health Diet Index; cIMT, carotid intima-media thickness; ELSA-Brasil, Brazilian Longitudinal Study of Adult Health; HEI-2015, Healthy Eating Index 2015; SSB, sugar-sweetened beverages

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# Prospective association between the Cardiovascular Health Diet Index and subclinical atherosclerosis: the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil) cohort study

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**Abstract**

The Cardiovascular Health Diet Index (CHDI) is a diet quality score based on the dietary guidelines of the American Heart Association for cardiovascular health but with some adaptations, such as red meat, dairy products, beans and ultra-processed foods in its components. The CHDI has shown good relative validity parameters; however, its association with health outcomes is still unclear. Thus, our aim was to investigate the association between the CHDI score with subclinical atherosclerosis. Data from the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil) cohort were used. Subclinical atherosclerosis was assessed by measuring coronary artery calcification at baseline (2008–2010) and second wave (2012–2014) and carotid intima-media thickness at baseline and at the third wave (2017–2019). The CHDI score (ranges from 0 to 110 points) was applied to dietary data obtained from an FFQ at baseline. Poisson regression with robust variance, linear regression and linear mixed-effects models were used to evaluate the association of the CHDI score with coronary artery calcification incidence ( $n$  2224), coronary artery calcification progression ( $n$  725) and changes in carotid intima-media thickness ( $n$  7341) over time, respectively. After a median 8-year follow-up period, a 10-point increase in the CHDI score was associated with a decrease in carotid intima-media thickness of 0.002 mm (95 % CI –0.005, –0.001). No association was observed between the CHDI score and coronary artery calcification incidence and progression after a 4-year follow-up period. Higher scores in the CHDI were prospectively associated with decreased subclinical atherosclerosis after an 8-year follow-up period.

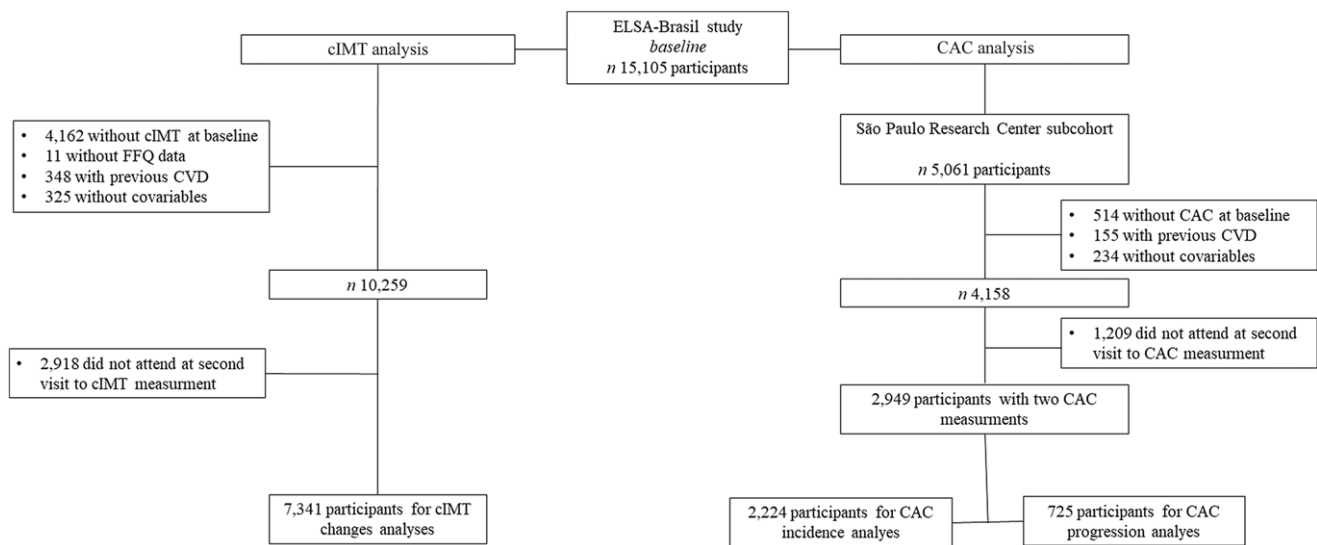
CVD remains a major cause of death worldwide, and its prevalence is still increasing globally<sup>(1)</sup>. Early detection of subclinical atherosclerosis is an opportunity to allow optimal prevention and control of risk factors<sup>(2–4)</sup>. Carotid intima-media thickness (cIMT) and coronary artery calcification (CAC) score are non-invasive measurements and established surrogate markers of subclinical atherosclerosis<sup>(5,6)</sup>. cIMT is obtained through an ultrasound examination of carotid arteries that identifies and quantifies the distance between the lumen intima and media adventitia interfaces<sup>(7,8)</sup>, which is altered from the initial phases of atherosclerotic disease<sup>(9)</sup>, while CAC is conducted via non-contrast cardiac computed tomography and is the most common method applied to evaluate and identify subclinical atherosclerosis<sup>(5)</sup>. However, both cIMT and CAC are useful tools to predict CVD events<sup>(2,10)</sup>.

Lifestyle factors such as regular physical activity, non-smoking, non-alcoholic consumption and a healthy dietary pattern are pointed as modifiable risk factors for CVD<sup>(11)</sup>, including subclinical atherosclerosis. The relationship between specific dietary components and nutrients and CVD has been well explored in the scientific literature<sup>(12–14)</sup>. However, overall diet should be considered to interpret the diet-health-related effects<sup>(15)</sup>. Diet quality scores or indices are useful for this purpose, as they are tools to assess nutrient adequacy, the analysis of geographic disparities and temporal fluctuations in dietary patterns and the evaluation of adherence to established dietary recommendations<sup>(16,17)</sup>.

Diet quality scores can be developed and tailored for a given population<sup>(18)</sup>. The Cardiovascular Health Diet Index (CHDI) was proposed<sup>(19)</sup>, based on the dietary recommendations for a healthy diet to prevent CVD and promote cardiovascular health advocated by the American Heart Association (AHA)<sup>(20)</sup>, and includes other food groups

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**Figure 1.** Flow chart presenting the study population from the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil) who were eligible for statistical analyses in this present study according to coronary artery calcification (CAC) incidence, CAC progression and carotid intima-media thickness (cIMT) changes over time.

relevant to cardiovascular health, such as legumes and dairy products, and food groups related to risk for CVD, such as red meat and ultra-processed foods. In this manner, the CHDI incorporates the most recent scientific findings pertaining to CVD prevention, aligning itself with the latest dietary recommendations from both the Dietary Guidelines for the Brazilian Population<sup>(21)</sup> and the recommendations of the AHA recommendations<sup>(22)</sup>.

Although the CHDI score has demonstrated good relative validity and reliability parameters, its predictive criteria validity remains unexplored. Therefore, the primary objective of this study is to assess the association between the CHDI score and subclinical atherosclerosis, as determined by CAC over a 4-year period and cIMT over an 8-year period. Additionally, we aim to compare these associations with those obtained using the Healthy Eating Index-2015 (HEI-2015)<sup>(23)</sup>, a well-established diet quality score.

## Material and methods

### Study design and population

The Brazilian Longitudinal Study of Adult Health (ELSA-Brasil) is a multicentre ongoing cohort of 15 105 male and female civil servants, who were active and retired workers from six institutions (five public universities and one public research institute) located in six different Brazilian cities from three major Brazilian regions (Northeast, Southeast and South). Briefly, the ELSA-Brasil study aimed to investigate the incidence and risk factors for CVD and diabetes in Brasil. All active or retired employees from the aforementioned institutions, aged between 34 and 74 years, were eligible for the study. The exclusion criteria were those with cognitive or communication disabilities, current or recent (< 4 months prior to the first interview) pregnancy and intention to quit work at the institution in the near future for reasons not related to retirement and if retired with the residence outside the corresponding metropolitan area of a study centre. Baseline data from ELSA-Brasil were collected by trained and certified personnel under strict quality control between August 2008 and December 2010 (*n* 15 105). The second visit of interviews and exams was

between 2012 and 2014 (*n* 14 104), and the third wave took place between 2017 and 2019 (*n* 12 636). More details of the sample and data collection methods of this cohort study have been previously published<sup>(24)</sup>.

For the present study, two main outcomes were evaluated to define subclinical atherosclerosis: CAC and cIMT. For the analysis with CAC as the outcome, participants from the baseline and second wave were eligible. In brief, from the 15 105 participants in the baseline, only a sub-sample (*n* 5061) from the São Paulo Research Center underwent non-contrast computed tomography for CAC measurement at two different periods throughout the study. Individuals with no CAC measure at the baseline and follow-up, a history of CVD (myocardial infarction, stroke or coronary revascularization), no dietary data and no information on covariates (sociodemographic and lifestyle factors) were excluded. For the analysis with cIMT as the outcome, participants from the baseline and third wave were eligible. The same exclusion criteria described above for CAC analysis were also applied. The flow chart of the included participants is described in Fig. 1.

The ELSA-Brasil study was conducted according to the guidelines laid down in the Declaration of Helsinki, and all procedures were approved by the research ethics committees of all research centres. All participants volunteered and signed an informed consent form. In addition, the present study was also approved by the research ethics committee of the School of Public Health of the University of São Paulo (no. 3.970.703).

### Coronary artery calcification measurement

The CAC measurements were performed using a 64-slice multidetector computed tomography scanner (Brilliance 64, Phillips Healthcare) with a standard technique for CAC scoring, including prospective acquisition in mid-diastole, 120 kVp tube voltage and variable current based on BMI<sup>(25)</sup>. The CAC was expressed in Agatston units<sup>(26)</sup>, and the percentile was evaluated in a blinded fashion by an experienced cardiologist using semi-automatic software (Calcium Scoring, Philip Workstation). CAC incidence was defined as a CAC of zero (CAC = 0) at the baseline

followed by a CAC greater than zero ( $CAC > 0$ ) at the follow-up. To compute the CAC incidence, 2224 individuals with  $CAC = 0$  at the baseline were considered. CAC progression was defined according to the Hokanson method for those individuals who had a  $CAC > 0$  at the baseline. To compute CAC progression, we considered 725 individuals with  $CAC > 0$  at baseline. The difference between the follow-up square root transformed CAC measure and the baseline square root transformed CAC measure was calculated for each individual, and those who presented a change greater than 2.5 were classified with CAC progression<sup>(27)</sup> (Fig. 1).

### Carotid intima-media thickness measurement

The cIMT measurement protocol was previously described<sup>(28)</sup>. Briefly, the ELSA-Brasil study acquired cIMT images in accordance with guidelines from the American and Brazilian Societies of Echocardiography. Images were captured using Toshiba Aplio XG ultrasound machines equipped with a 7.5 MHz linear transducer and then sent to the centralised reading centre in São Paulo for analysis. The ELSA-Brasil study used MIA software (Medical Imaging Applications) to standardise the reading and interpretation of carotid scans as previously described. For cIMT measurement, the common carotid artery was identified along its longitudinal axis with standard brightness and contrast settings. Measurements focused on the proximal far wall of the common carotid artery, specifically 1 cm proximal to the carotid bifurcation over a 1 cm segment, and both mean and maximum values were recorded for each common carotid artery.

Images were considered valid when clearly visualised left on the and right sides: (1) the anatomical guides for the common carotid artery, (2) interfaces between the lumen and the distant vessel wall and (3) interfaces between the media and the adventitious layers of the vessel wall. All patients were examined by technicians and/or physicians who had previously been trained and certified for this protocol. The intra- and interobserver variations were previously evaluated in the ELSA-Brasil study, and the results show excellent intra- and interobserver reproducibility for the mean cIMT measurements in the ELSA-Brasil study.

In this paper, we defined cIMT as the average between the mean left and the mean right cIMT values. The average values in millimetres (mm) from the measurements of left and right cIMT at baseline and 8-year follow-up were considered for analysis (Fig. 1).

### Dietary assessment

Food consumption was assessed using a previously developed and validated semi-quantitative FFQ with 114 food items<sup>(29,30)</sup>. This FFQ comprises the past 12 months, and the questions are structured into three sections: (1) food products/food preparations, (2) measures of consumed products and (3) consumption frequencies with eight response options (more than 3 times/d, 2–3 times/d, once a day, 5–6 times a week, 2–4 times a week, once a week, 1–3 times a month and never/almost never). The daily consumption of each FFQ item (in g/d) was obtained by multiplying the portion size by the corresponding frequency.

### Cardiovascular Health Diet Index computation

The CHDI was developed based on the AHA's guidelines for a cardiovascular-healthy diet<sup>(19)</sup>. In summary, the AHA recommends the regular consumption of fruits and vegetables, fish and seafood, whole-grain cereals, nuts and legumes, while advising a

**Table 1.** Cardiovascular Health Diet Index (CHDI): components, cut-off points and scoring system

| Components            | Scores | Maximum score | Minimum score |
|-----------------------|--------|---------------|---------------|
| Fruits                | 0–10   | ≥ 340 g/d     | 0 g/d         |
| Vegetables            | 0–10   | ≥ 180 g/d     | 0 g/d         |
| Nuts                  | 0–10   | ≥ 12.9 g/d    | 0 g/d         |
| Whole-grain cereals   | 0–10   | ≥ 90 g/d      | 0 g/d         |
| Beans                 | 0–10   | ≥ 80 g/d      | 0 g/d         |
| Fish and seafoods     | 0–10   | ≥ 28.6 g/d    | 0 g/d         |
| Dairy products        | 0–10   | ≥ 250 g/d     | 0 g/d         |
| Red meat              | 0–10   | 0 g/d         | > 28.6 g/d    |
| Processed meat        | 0–10   | 0 g/d         | > 12.9 g/d    |
| SSB                   | 0–10   | 0 g/d         | > 142.9 ml/d  |
| Ultra-processed foods | 0–10   | ≤ 4 points    | > 23 points   |
| CHDI total score      | 0–110  |               |               |

SSB, sugar-sweetened beverages.

reduced intake of sodium, sugar-sweetened beverages (SSB), processed meats and saturated fats. In creating the CHDI, the emphasis was placed on dietary patterns, focusing on food groups rather than specific nutrients. Additionally, other food groups were included in the CHDI, such as dairy products, due to their association with a lower risk of CVD<sup>(31)</sup>. Red meat was incorporated due to its connection with CVD<sup>(32)</sup>, and ultra-processed foods were added because of their strong links to CVD, diabetes, hypertension and overall mortality<sup>(33)</sup>. Thus, the CHDI recommends the consumption of fruits, vegetables, nuts, whole grains, legumes, fish, seafood and dairy products, while advising the reduction or avoidance of processed meats, SSB, red meat and ultra-processed foods for better cardiovascular health. In this study, ultra-processed foods were classified according to the Nova food classification system<sup>(34)</sup>. More detail regarding the development and validation of the CHDI process, including the components, cut-off points and validity results, is described elsewhere<sup>(19)</sup>.

For components such as fruits, vegetables, fish and seafood, whole grains, nuts, beans and dairy products, participants received a maximum score of 10 points if their consumption met or exceeded the recommended levels and a minimum score of 0 points if there was no consumption. Intermediate scores were assigned proportionally. Conversely, for components like SSB, red meat, processed meat and ultra-processed foods, the scoring process was reversed, with a minimum score of 0 points given for consumption meeting or exceeding the recommended values and a maximum score of 10 points awarded when there was no consumption. Intermediate scores were applied proportionally. The final score ranges from zero to 110 points, and the higher the score, the better the diet quality. Table 1 describes the components, cut-off points and score system. Online Supplementary Table S1 describes examples of foods components. More details on the development and validation process of the CHDI score can be found elsewhere<sup>(19)</sup>.

### Covariates

The sociodemographic characteristics and lifestyle habits were used as covariates. All the covariates included in this analysis were self-reported through standardised questionnaires performed by

trained personnel under strict quality control at ELSA-Brasil assessment<sup>(35)</sup>. Participants were classified according to sex (male and female) and according to age as adults (34–59 years) and elderly ( $\geq 60$  years). Self-reported race was classified into white, brown, black or Asian and Indigenous. Per capita family income, also based on self-report, was calculated as the total family monthly income divided by the number of family members and then divided in tertiles. Smoking was stratified as non-smokers (including ex-smokers) and current smokers. Alcohol consumption was obtained according to the amount ingested per week (male  $\geq 210$  g; female  $\geq 140$  g) and then dichotomised into high alcohol consumption (yes or no). Physical activity level during leisure time was classified as low (no or less than moderate category), moderate ( $> 150$  min/week of moderate activity) or vigorous ( $\geq 75$  min/week of vigorous activity) according to the International Physical Activity Questionnaire<sup>(36)</sup>.

### Statistical analyses

Descriptive analysis was performed using proportions and means with standard deviation (SD) for categorical and continuous variables, respectively.

Poisson's regression models with robust variance were performed to estimate the association between the CHDI score and CAC incidence ( $CAC_{\text{baseline}} = 0$  v.  $CAC_{\text{follow-up}} > 0$ ) and CAC progression dichotomous (CAC square root method  $> 2.5$ ). In these models, the time between two measures (years) was considered using the option *exposure* on Stata. Linear regression models were fitted to evaluate the association between CHDI score with CAC progression as a continuous variable (square root method).

Linear mixed-effects regression was fitted to estimate the association between the CHDI score with longitudinal changes in the cIMT in the follow-up period. To explore whether an annual change in cIMT related to the CHDI score existed, that is, whether the association between the CHDI score with cIMT differed across the follow-up time, a CHDI score  $\times$  time interaction term was added.

Crude models were fitted with the CHDI score as exposure and the cIMT or CAC as outcomes. All models (i.e. linear mixed and Poisson) were adjusted for potential confounders, including sex (male, female), age group (adults, elderly), self-reported race (white, brown, black or Asian and Indigenous), per capita income (tertiles), smoking status (non-smokers, current smokers), sporadic alcohol consumption (yes, no), physical activity level (low, moderate or vigorous) and total energy intake (kcal). In the analyses with cIMT, the statin and dyslipidaemia presence were included in the models, as they can influence the reduction of cIMT.

While the main analyses treated the CHDI score as a 10-point increase, additional analyses categorised it into tertiles. In addition, as the CHDI score is a diet quality score based on specific recommendations for cardiovascular health, we built regression models using the HEI-2015 as an alternative index of overall diet quality as an additional analysis. HEI-2015 is a diet quality score with thirteen components (total fruits, whole fruits, total vegetables, greens and beans, whole grains, dairy products, total protein foods, seafood and plant proteins, fatty acids, refined grains, sodium, added sugars and saturated fats) that can range from 0 to 100 points<sup>(23)</sup>. The same models were built (i.e. linear mixed models and Poisson model), with the same adjustment variables.

**Table 2.** Poisson regression models of the association between each 10-point increase in the Cardiovascular Health Diet Index score with longitudinal coronary artery calcification (CAC) score. ELSA-Brasil, 2008–2010 to 2012–2014

|   | CAC incidence<br>(n 2224) |            |       |
|---|---------------------------|------------|-------|
|   | IRR                       | 95% CI     | P     |
| Cardiovascular Health Diet Index score* |                           |            |       |
| Unadjusted model                        | 1.03                      | 0.94, 1.11 | 0.505 |
| Model 1                                 | 0.96                      | 0.89, 1.04 | 0.322 |
| Model 2                                 | 0.97                      | 0.90, 1.06 | 0.567 |

IRR, incidence risk ratio.

\*As each 10-point increase. Model 1 adjusted by age, sex, self-reported race and per capita income. Model 2 adjusted by Model 1 plus smoking status, alcohol consumption, physical activity level and total energy intake.

All statistical analyses were performed using Stata (StataCorp), version 14.2, and the *P*-value  $< 0.05$  was considered statistically significant.

## Results

### Descriptive results

Among the individuals with no presence of CAC at the baseline (*n* 2224), 331 exhibited CAC greater than zero during follow-up (14.9%). The baseline CHDI scores for those included in the CAC incidence analyses ranged from 18.5 to 105.8 points, with a mean score of 54.6 points. Conversely, among those with CAC greater than zero at baseline (*n* 725), 442 displayed CAC progression during follow-up (61.0%). For participants included in the CAC progression analyses, the baseline CHDI scores varied from 18.6 to 97.3 points, with a mean score of 57.4 points. Online Supplementary Tables S2 and S3 present the baseline characteristics of individuals in relation to CAC incidence and progression.

At baseline, the average cIMT measurement was 0.600 mm, while the baseline CHDI scores for participants included in the cIMT changes analyses ranged from 12.0 to 106.5 points, with an average score of 56.6 points. Detailed baseline characteristics related to cIMT can be found in online Supplementary Table S4.

### Diet quality and coronary artery calcification incidence and progression

The mean follow-up period was 4.2 years. Table 2 presents the incidence risk ratio with their respective 95% CI of the association between CAC incidence and each 10-point increase in the CHDI score. No association was observed after a 4-year follow-up, neither in the unadjusted nor in the fully adjusted model, indicating that higher scores in the CHDI had no effect on the CAC incidence. Accordingly, no association was observed between a 10-point increase in the CHDI score with CAC progression (Table 3). Furthermore, there was no observed significant association when evaluating the CHDI components in relation to either CAC incidence or progression or when the CHDI was evaluated in tertiles (data not presented).

### Diet quality and carotid intima-media thickness changes

After multivariate adjustments, each 10-point increase in the CHDI score was associated with  $-0.002$  mm (95% CI  $-0.005$ ,  $-$

**Table 3.** Poisson regression models of the association between each 10-point increase in the Cardiovascular Health Diet Index score with CAC progression. ELSA-Brasil, 2008–2010 to 2012–2014

| Cardiovascular Health Diet Index score* | CAC progression<br>(n 725) |            | P     |
|---|----------------------------|------------|-------|
|   | IRR                        | 95 % CI    |       |
| Unadjusted model                        | 1.01                       | 0.96, 1.05 | 0.745 |
| Model 1                                 | 1.03                       | 0.98, 1.08 | 0.285 |
| Model 2                                 | 1.03                       | 0.98, 1.09 | 0.199 |

CAC, coronary artery calcification; IRR, incidence risk ratio.

\*As each 10-point increase. Model 1 adjusted by age, sex, self-reported race and per capita income. Model 2 adjusted by Model 1 plus smoking status, alcohol consumption, physical activity level and total energy intake.

**Table 4.** Linear mixed-effects regressions between each 10-point increase in the Cardiovascular Health Diet Index score with longitudinal carotid intima-media thickness (cIMT). ELSA-Brasil, 2008–2010 to 2017–2019

| Cardiovascular Health Diet Index* | cIMT mm (n 7341) |                | P       |
|-----------------------------------|------------------|----------------|---------|
|                                   | $\beta$          | 95 % CI        |         |
| Unadjusted model                  |                  |                |         |
| CHDI score                        | -0.005           | -0.007, -0.003 | < 0.001 |
| CHDI score $\times$ time          | -0.000           | -0.001, -0.000 | < 0.001 |
| Model 1                           |                  |                |         |
| CHDI score                        | -0.003           | -0.005, -0.001 | 0.008   |
| CHDI score $\times$ time          | -0.001           | -0.001, -0.000 | < 0.001 |
| Model 2                           |                  |                |         |
| CHDI score                        | -0.002           | -0.005, -0.001 | 0.035   |
| CHDI score $\times$ time          | -0.000           | -0.001, -0.000 | < 0.001 |

CHDI, Cardiovascular Health Diet Index.

\*As each 10-point increase. Values are regression coefficients ( $\beta$ ) 95 % CI based on linear mixed models and reflect differences in cIMT averaged across a median follow-up of 8.2 years per 10 points higher score in the diet quality scores. cIMT, carotid intima-media thickness. Model 1: unadjusted. Model 1: age, sex, self-reported race and per capita income. Model 2: model 1 plus smoking status, alcohol consumption, physical activity level, total energy intake and presence of dyslipidaemia and statin use.

0.001) in the cIMT over the median follow-up time of 8.0 years (Table 4). Notably, we observed an inverse association in the interaction terms between the CHDI score and time, suggesting that the diet's impact on cIMT diminishes each year throughout the follow-up period. When evaluating the association between each CHDI component with cIMT across the follow-up period, we observed that higher scores in the whole-grain cereals and nuts components (indicating higher consumption of these foods) were inversely associated with cIMT over time. Conversely, higher scores in the SSB, processed meat and ultra-processed foods (indicating lower consumption of these foods) were inversely associated with cIMT over time (online Supplementary Table S5). Online Supplementary Fig. S1 demonstrates that individuals in the third tertile of the CHDI had a smaller increase in cIMT compared with those in the first tertile, as they showed a reduced increase of -0.013 mm (95 % CI -0.019, -0.007) in cIMT over the follow-up period in the adjusted models.

### Additional analyses

For the HEI-2015, the baseline score ranged from 25.8 to 96.5, with a mean score of 60.2 points for the entire population, and ranged from 26.4 to 94.6 for the sub-cohort sample with a mean score of 59.2 points. The HEI-2015 was correlated with the CHDI score ( $r$  0.66,  $P$  < 0.001). No associations were observed when using the HEI-2015 score with CAC incidence or progression either in the unadjusted or in the fully adjusted models (online Supplementary Tables S6 and S7). In the unadjusted model, a 10-point increase in the HEI-2015 score was associated with -0.005 mm (95 % CI -0.008, -0.002) in the cIMT over the median follow-up time of 8.0 years. However, these results did not persist after adjusting for the covariables (online Supplementary Table S8).

### Discussion

In this large Brazilian cohort study with middle-aged individuals without overt CVD, higher diet quality – evaluated through the CHDI – was prospectively associated with a slight decrease in cIMT values. Furthermore, higher consumption of whole-grain cereals and nuts led to a reduction in cIMT, while lower consumption of processed meat, SSB and ultra-processed foods also contributed to a reduction in this outcome after an 8-year follow-up period. However, no association was observed between the diet quality score and CAC incidence and progression after 4 years of follow-up.

The prospective association between diet quality scores and subclinical atherosclerosis evaluated throughout cIMT and CAC score has been hardly studied. Maddock *et al.*<sup>(37)</sup> observed that long-term adherence (24–28-year period for each individual) to the Dietary Approaches to Stop Hypertension score was associated with decreasing cIMT in participants from a British birth cohort study. Petersen *et al.*<sup>(38)</sup> observed that higher scores in the adapted Healthy Eating Index were inversely associated with cIMT values after 2 years of follow-up period in eighty-seven individuals diagnosed with diabetes. These results, in alignment with our findings, suggest that higher diet quality might slow down the increase in cIMT over time.

Consistent with our lack of association between the diet quality scores and CAC, Richardson *et al.*<sup>(39)</sup> observed that a Mediterranean-style dietary pattern score was not associated with CAC in a case-control study with individuals from the USA with and without type 1 diabetes. In alignment, the same authors found no association in a prospective analysis between the MedDiet score and Dietary Approaches to Stop Hypertension score with CAC progression<sup>(40)</sup>. However, Gao *et al.*<sup>(41)</sup>, using data from the CARDIA study, observed that individuals with animal-based low-carbohydrate diet score was associated with higher risk of CAC progression after a follow-up period of 8.3 years.

In previous cross-sectional studies, no association was observed between diet quality scores and cIMT or CAC. Recio-Rodriguez *et al.*<sup>(42)</sup> found no association between higher scores in the diet quality score – a diet score that includes eighteen food groups and can range from 18 to 54 points – with cIMT in middle-aged Spanish adults with intermediate cardiovascular risk. Furthermore, Hoebeek *et al.*<sup>(43)</sup> found no statistical significance between an overall dietary score (composed of the sum of the dietary quality score, dietary diversity score and dietary equilibrium score) with cIMT and plaques in Belgian individuals aged 35–55 years. In the same direction, Gardener *et al.*<sup>(44)</sup> found no association between adherence to the Mediterranean diet assessed through the

Mediterranean-style diet score with cIMT, in individuals from New York, USA, although they observed a slight decrease in the carotid plaque. In a cross-sectional analysis with data from the Multi-Ethnic Study of Atherosclerosis (MESA) study, Nettleton *et al.*<sup>(45)</sup> found an inverse association between higher scores in the Healthy Dietary Pattern score and cIMT, but the association did not withstand after adjustments for waist circumference. According to Nettleton *et al.*<sup>(45)</sup>, no association was observed between the Healthy Dietary Pattern and CAC in participants from the MESA study. However, in a study with 172 individuals from Canada diagnosed with hypercholesterolaemia, lower adapted Healthy Eating Index scores were associated with CAC presence, after controlling for multiple factors<sup>(46)</sup>.

Notably, in our study, the consumption of whole grains and nuts emerged as influential factors in reducing cIMT. Plant-based diets are posited as pathways to prevent and reduce CVD<sup>(47,48)</sup>. According to Mellen *et al.*<sup>(49)</sup>, higher whole-grain intake was prospectively associated with lower cIMT values in 1178 individuals from the Insulin Resistance Atherosclerosis Study (IRAS), after 5 years of follow-up. Accordingly, Steffen *et al.*<sup>(50)</sup> observed that higher intake of whole grain was associated with a lower risk of incidence of coronary artery disease and total mortality after an 11-year follow-up among 11 940 middle-aged participants from the Atherosclerosis Risk in Communities (ARIC) Study. In a randomised clinical trial with 175 subjects from the PREDIMED study (*Prevención con Dieta Mediterránea*), Sala-Vila *et al.*<sup>(51)</sup> observed that those group who followed a Mediterranean diet supplemented with 30 g/d of mixed nuts (15 g walnuts, 7.5 g hazelnuts and 7.5 g almonds) had a regression in intima-media thickness and delayed the progression of intima-media thickness and carotid plaque, after a mean of 2.4 years, as compared with those who followed a low-fat diet for the same period.

On the other hand, the adoption of dietary patterns characterised by higher intakes of processed meat, SSB and ultra-processed foods contributed to an unfavourable increase in cIMT over time as observed in our study. The negative effects of ultra-processed foods on cardiovascular health have been widely debated, and systematic reviews with meta-analyses suggest that ultra-processed food intake is associated with risk for CVD<sup>(52,53)</sup>. Riccardi *et al.*<sup>(54)</sup> in a recent review reported that meta-analyses of prospective observational studies observed that higher intake of processed meat and SSB has been associated with increasing risk of carotid heart disease incidence.

Several factors may contribute to the differences observed in studies utilising various diet quality scores. Many of the mentioned studies employed general and non-specific diet quality scores when assessing their association with subclinical atherosclerosis, and a majority of them limited their analysis to cross-sectional designs. In our study, we adopted a diet quality score specifically tailored for the Brazilian population, which is rooted in the recommendations for a heart-healthy diet as endorsed by the AHA. This diet quality score incorporates foods that hold significance in the Brazilian food culture, such as red meat and beans. We also integrated ultra-processed foods as a component of this index, recognising their link to CVD risk<sup>(52,55)</sup>. Our findings revealed a prospective association between the CHDI score and subclinical atherosclerosis, as assessed by cIMT. However, when we examined the relationship between the HEI-2015 and the same outcome, we did not identify a statistically significant association. Hence, it appears that a diet quality score specifically designed to target cardiovascular health may offer more valuable insights when evaluating cardiovascular outcomes.

Despite this, we were unable to identify a significant relationship between diet quality scores and CAC. However, it's worth noting that our findings align with existing literature<sup>(39,40,45)</sup>. While CAC and cIMT are widely recognised tools for detecting subclinical atherosclerosis and assessing CVD risk, some important points should be addressed. For instance, the correlation between these two diagnostic tools appears to be weak and one possible explanation is that CAC may represent a more advanced stage of vascular alterations<sup>(56)</sup>. Lester *et al.*<sup>(57)</sup> have shown that individuals without clinically apparent atherosclerosis, but with a CAC score of zero, still exhibit atherosclerotic changes as revealed by cIMT assessments. This suggests that cIMT might be more sensitive than CAC in detecting subclinical atherosclerosis, particularly among middle-aged adults. Nonetheless, the lack of association with CAC in our study may be partly attributed to the relatively short follow-up period, which was limited to 4 years, in contrast to the average 8-year follow-up period for cIMT assessments. Future research efforts should explore the relationship between CHDI and CAC using longer follow-up periods to provide a more comprehensive understanding of these associations.

Our study addressed the prospective association between a diet quality score and subclinical atherosclerosis – assessed using the CAC score and cIMT – in a large sample of Brazilian individuals without overt CVD. Besides that, the ELSA-Brasil followed a strict protocol when measuring the cIMT and the CAC score. We used a validated diet quality score that considers the Brazilian food culture context and included ultra-processed foods metric in its components to evaluate diet quality among the participants of the ELSA-Brasil study. In addition, the follow-up period can be considered a strength since the ELSA-Brasil is one the largest cohort studies in Brazil.

However, some limitations may be pointed out as well. Food consumption was assessed using an FFQ, an instrument that, despite being one of the most commonly used methods in nutritional epidemiological studies, still features some limitations, such as the finitude of its food list and dietary misreporting bias. Although the ELSA-Brasil is a multicentre cohort study, it is not representative of the entire Brazilian population. However, the ELSA-Brasil sample and design allowed the inclusion of an ethnic and social diversity that is observed in populations who live in Brazilian large cities. Thus, our results can be extended to urban centres with similar characteristics.

## Conclusion

In conclusion, this study conducted in a large Brazilian cohort of middle-aged individuals, free of apparent CVD, underscores the correlation between diet quality – assessed throughout the CHDI score – and a prospective decrease in the rate of increase in cIMT values. Notably, consumption of whole grains and nuts emerged as influential factors in reducing cIMT, while the adoption of dietary patterns characterised by higher intakes of processed meat, SSB and ultra-processed foods contributed to a favourable increase in cIMT over time. Nonetheless, no discernible link was seen between the diet quality and the incidence of CAC after a 4-year follow-up period. More prospective studies with large period designs are needed to explore the nuanced interactions between diet quality and markers of subclinical atherosclerosis.

**Supplementary material.** For supplementary material/s referred to in this article, please visit <https://doi.org/10.1017/S0007114524002836>.

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## References

- Roth GA, Mensah GA, Johnson CO, *et al.* (2020) Global burden of cardiovascular diseases and risk factors, 1990–2019. *J Am Coll Cardiol* **76**, 2982–3021.
- Faggiano P, Dasseni N, Gaibazzi N, *et al.* (2019) Cardiac calcification as a marker of subclinical atherosclerosis and predictor of cardiovascular events: a review of the evidence. *Eur J Prev Cardiol* **26**, 1191–1204.
- Polak JF, Pencina MJ, Meisner A, *et al.* (2010) Associations of carotid artery Intima-Media Thickness (IMT) with risk factors and prevalent cardiovascular disease. *J Ultrasound Med* **29**, 1759–1768.
- Stein JH, Korcarz CE, Hurst RT, *et al.* (2008) Use of carotid ultrasound to identify subclinical vascular disease and evaluate cardiovascular disease risk: a consensus statement from the American Society of Echocardiography Carotid Intima-Media Thickness Task Force Endorsed by the Society for Vascular Medicine. *J Am Soc Echocardiogr* **21**, 93–111.
- Hoffmann U, Massaro JM, D'Agostino RB, *et al.* (2016) Cardiovascular event prediction and risk reclassification by coronary, aortic, and valvular calcification in the Framingham Heart Study. *J Am Heart Assoc* **5**, e003144.
- Nezu T, Hosomi N, Aoki S, *et al.* (2016) Carotid intima-media thickness for atherosclerosis. *J Atheroscler Thromb* **23**, 18–31.
- Pignoli P, Tremoli E, Poli A, *et al.* (1986) Intimal plus medial thickness of the arterial wall: a direct measurement with ultrasound imaging. *Circulation* **74**, 1399–1406.
- Bots ML, Hoes AW, Koudstaal PJ, *et al.* (1997) Common carotid intima-media thickness and risk of stroke and myocardial infarction. *Circulation* **96**, 1432–1437.
- Kanters SDJM, Algra A, van Leeuwen MS, *et al.* (1997) Reproducibility of *in vivo* carotid intima-media thickness measurements. *Stroke* **28**, 665–671.
- Lorenz MW, Markus HS, Bots ML, *et al.* (2007) Prediction of clinical cardiovascular events with carotid intima-media thickness. *Circulation* **115**, 459–467.
- Joseph P, Leong D, McKee M, *et al.* (2017) Reducing the global burden of cardiovascular disease, part 1. *Cir Res* **121**, 677–694.
- Zong G, Gao A, Hu FB, *et al.* (2016) Whole grain intake and mortality from all causes, cardiovascular disease, and cancer. *Circulation* **133**, 2370–2380.
- AlEsa HB, Cohen R, Malik VS, *et al.* (2018) Carbohydrate quality and quantity and risk of coronary heart disease among US women and men. *Am J Clin Nutr* **107**, 257–267.
- Micha R & Mozaffarian D (2010) Saturated fat and cardiometabolic risk factors, coronary heart disease, stroke, and diabetes: a fresh look at the evidence. *Lipids* **45**, 893–905.
- Hu FB (2002) Dietary pattern analysis: a new direction in nutritional epidemiology. *Curr Opin Lipidol* **13**, 3–9.
- Fransen HP & Ocké MC (2008) Indices of diet quality. *Curr Opin Clin Nutr Metab Care* **11**, 559–565.
- Ocké MC (2013) Evaluation of methodologies for assessing the overall diet: dietary quality scores and dietary pattern analysis. *Proc Nutr Soc* **72**, 191–199.
- Waijers PMCM, Feskens EJM & Ocké MC (2007) A critical review of predefined diet quality scores. *Br J Nutr* **97**, 219–231.
- Cacau LT, Marcadenti A, Bersch-Ferreira AC, *et al.* (2022) The AHA recommendations for a healthy diet and ultra-processed foods: building a new diet quality index. *Front Nutr* **9**, 804121.
- Benjamin EJ, Virani SS, Callaway CW, *et al.* (2018) Heart disease and stroke statistics—2018 update: a report from the American Heart Association. *Circulation* **137**, e67–e492.
- Ministério da Saúde (2014) Guia Alimentar para a População Brasileira, 2nd ed. Brasília: Ministério da Saúde.
- Lichtenstein AH, Appel LJ, Vadiveloo M, *et al.* (2021) 2021 dietary guidance to improve cardiovascular health: a scientific statement from the American Heart Association. *Circulation* **144**, e472–e487.
- Krebs-Smith SM, Pannucci TE, Subar AF, *et al.* (2018) Update of the Healthy Eating Index: HEI-2015. *J Acad Nutr Diet* **118**, 1591–1602.
- Schmidt MI, Duncan BB, Mill JG, *et al.* (2015) Cohort profile: longitudinal study of adult health (ELSA-Brasil). *Int J Epidemiol* **44**, 68–75.
- Bensenor IM, Goulart AC, Santos IS, *et al.* (2016) 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**, 51–59.
- Agatston AS, Janowitz WR, Hildner FJ, *et al.* (1990) Quantification of coronary artery calcium using ultrafast computed tomography. *J Am Coll Cardiol* **15**, 827–832.
- Hokanson JE, MacKenzie T, Kinney G, *et al.* (2004) Evaluating changes in coronary artery calcium: an analytic method that accounts for interscan variability. *AJR Am J Roentgenol* **182**, 1327–1332.
- Santos IS, Bittencourt MS, Oliveira IRS, *et al.* (2014) Carotid intima-media thickness value distributions in The Brazilian Longitudinal Study of Adult Health (ELSA-Brasil). *Atherosclerosis* **237**, 227–235.
- Molina MD, Faria CP, Cardoso LD, *et al.* (2013) Diet assessment in the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil): development of a food frequency questionnaire. *Rev Nutr* **26**, 167–176.
- Molina MD, Benseñor IM, Cardoso LD, *et al.* (2013) Reproducibility and relative validity of the Food Frequency Questionnaire used in the ELSA-Brasil. *Cad Saúde Pública* **29**, 379–389.
- Dehghan M, Mente A, Rangarajan S, *et al.* (2018) Association of dairy intake with cardiovascular disease and mortality in 21 countries from five continents (PURE): a prospective cohort study. *Lancet* **392**, 2288–2297.
- Micha R, Michas G & Mozaffarian D (2012) Unprocessed red and processed meats and risk of coronary artery disease and type 2 diabetes – an updated review of the evidence. *Curr Atheroscler Rep* **14**, 515–524.
- Lane MM, Gamage E, Du S, *et al.* (2024) Ultra-processed food exposure and adverse health outcomes: umbrella review of epidemiological meta-analyses. *BMJ* **384**, e077310.
- Monteiro CA, Cannon G, Levy RB, *et al.* (2019) Ultra-processed foods: what they are and how to identify them. *Public Health Nutr* **22**, 936–941.
- Bensenor IM, Griep RH, Pinto KA, *et al.* (2013) Rotinas de organizacao de exames e entrevistas no centro de investigacao ELSA-Brasil (Routines of organization of clinical tests and interviews in the ELSA-Brasil investigation center). *Rev Saúde Pública* **47**, 37–47.
- Craig CL, Marshall AL, Sjöström M, *et al.* (2003) International physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc* **35**, 1381–1395.
- Maddock J, Ziauddeen N, Ambrosini GL, *et al.* (2018) Adherence to a Dietary Approaches to Stop Hypertension (DASH)-type diet over the life course and associated vascular function: a study based on the MRC 1946 British birth cohort. *Br J Nutr* **119**, 581–589.
- Petersen KS, Keogh JB, Lister NB, *et al.* (2018) Dietary quality and carotid intima media thickness in type 1 and type 2 diabetes: Follow-up of a randomised controlled trial. *Nutr Metab Cardiovasc Dis* **28**, 830–838.
- Richardson LA, Basu A, Chien L-C, *et al.* (2022) Associations of the Mediterranean-style dietary pattern score with coronary artery calcification and pericardial adiposity in a sample of US adults. *Nutrients* **14**, 3385.
- Richardson LA, Basu A, Chien L-C, *et al.* (2023) Longitudinal associations of healthy dietary pattern scores with coronary artery calcification and

- pericardial adiposity in United States adults with and without type 1 diabetes. *J Nutr* **153**, 2085–2093.
41. Gao J-W, Hao Q-Y, Zhang H-F, *et al.* (2021) Low-carbohydrate diet score and coronary artery calcium progression. *Arterioscler Thromb Vasc Biol* **41**, 491–500.
  42. Recio-Rodriguez JI, Garcia-Yu IA, Alonso-Dominguez R, *et al.* (2017) Diet quality and carotid atherosclerosis in intermediate cardiovascular risk individuals. *Nutr J* **16**, 40.
  43. Hoebeek LI, Rietzschel ER, Langlois M, *et al.* (2011) The relationship between diet and subclinical atherosclerosis: results from the Asklepios Study. *Eur J Clin Nutr* **65**, 606–613.
  44. Gardener H, Wright CB, Cabral D, *et al.* (2014) Mediterranean diet and carotid atherosclerosis in the Northern Manhattan Study. *Atherosclerosis* **234**, 303–310.
  45. Nettleton JA, Schulze MB, Jiang R, *et al.* (2008) A priori-defined dietary patterns and markers of cardiovascular disease risk in the Multi-Ethnic Study of Atherosclerosis (MESA). *Am J Clin Nutr* **88**, 185–194.
  46. Drouin-Chartier J-P, Tremblay AJ, Godbout D, *et al.* (2021) Correlates of coronary artery calcification prevalence and severity in patients with heterozygous familial hypercholesterolemia. *CJC Open* **3**, 62–70.
  47. Martínez-González MA, Gea A & Ruiz-Canela M (2019) The Mediterranean Diet and cardiovascular health. *Circ Res* **124**, 779–798.
  48. Cacao LT, Benseñor IM, Goulart AC, *et al.* (2023) Adherence to the EAT-Lancet sustainable reference diet and cardiometabolic risk profile: cross-sectional results from the ELSA-Brasil cohort study. *Eur J Nutr* **62**, 807–817.
  49. Mellen PB, Liese AD, Toozé JA, *et al.* (2007) Whole-grain intake and carotid artery atherosclerosis in a multiethnic cohort: the Insulin Resistance Atherosclerosis Study. *Am J Clin Nutr* **85**, 1495–1502.
  50. Steffen LM, Jacobs DR, Stevens J, *et al.* (2003) Associations of whole-grain, refined-grain, and fruit and vegetable consumption with risks of all-cause mortality and incident coronary artery disease and ischemic stroke: the Atherosclerosis Risk in Communities (ARIC) Study. *Am J Clin Nutr* **78**, 383–390.
  51. Sala-Vila A, Romero-Mamani E-S, Gilabert R, *et al.* (2014) Changes in ultrasound-assessed carotid intima-media thickness and plaque with a Mediterranean Diet. *Arterioscler Thromb Vasc Biol* **34**, 439–445.
  52. Pagliai G, Dinu M, Madarena MP, *et al.* (2021) Consumption of ultra-processed foods and health status: a systematic review and meta-analysis. *Br J Nutr* **125**, 308–318.
  53. Lane MM, Davis JA, Beattie S, *et al.* (2021) Ultraprocessed food and chronic noncommunicable diseases: a systematic review and meta-analysis of 43 observational studies. *Obes Rev* **22**, e13146.
  54. Riccardi G, Giosuè A, Calabrese I, *et al.* (2022) Dietary recommendations for prevention of atherosclerosis. *Cardiovasc Res* **118**, 1188–1204.
  55. Nilson EAF, Ferrari G, Louzada ML, *et al.* (2022) The estimated burden of ultra-processed foods on cardiovascular disease outcomes in Brazil: a modeling study. *Front Nutr* **9**, 1043620.
  56. Oei H-HS, Vliegenthart R, Hak AE, *et al.* (2021) The association between coronary calcification assessed by electron beam computed tomography and measures of extracoronary atherosclerosis. *J Am Coll Cardiol* **39**, 1745–1751.
  57. Lester SJ, Eleid MF, Khandheria BK, *et al.* (2009) Carotid intima-media thickness and coronary artery calcium score as indications of subclinical atherosclerosis. *Mayo Clin Proc* **84**, 229–233.