Reviewer 2:

This manuscript summarises the effects of an Atlantic diet score on a wide range of cardiovascular risk factors in a secondary data analysis from the EVIDENT 2 study. It is an interesting paper on the effects of dietary intake on CVD risk factors.

Answer:

We wish, first of all, to thank the reviewer for his comments, which we think are very valuable to improve the manuscript.

I have a few concerns that could be addressed:

Abstract:

Line 29: included in the analysis, not selected for analysis.

Answer:

We have corrected this mistake (line 29):

Line 30: without CVD is given as an exclusion here, and this does not match up with what is described in the methods.

Answer:

We have revised the paragraph relating the exclusion criteria in the methods section. We have rewording this paragraph according to the recommendations of the reviewers (line 107):

Exclusion criteria were as follows: being over 70 years of age, having cardiovascular disease, heart failure, moderate or severe chronic obstructive pulmonary disease, musculoskeletal disease which prevented walking...

Introduction:

There is no acknowledgment of the DASH diet here, and to date, it has provided the strongest evidence for prevention of heart disease. The DASH, Mediterranean and the Atlantic diet have high levels of overlap which need to be acknowledged and the differences between them need to be described clearly.

Answer:

We have revised the paragraph including references to the DASH diet and highlighting the differences between these three dietary patterns (line 60):

Among dietary patterns, the most studied has been the Mediterranean diet and the dietary approaches to stop hypertension (DASH) dietary pattern. The Mediterranean diet has shown a reduction in both the incidence and prevalence of chronic diseases like cardiovascular disease, cancer, metabolic syndrome, diabetes, neurodegenerative diseases, as well as a reduction in overall mortality [1]. This diet is considered one of the best dietary patterns in the framework of healthy lifestyle, probably due to the combination of many elements with antioxidant and anti-inflammatory properties [2], thereby constituting a useful tool for the prevention of cardiovascular disease [3-5] and making it one of the best analysed in relation to cardiovascular risk and other health outcomes [6]. The DASH dietary pattern, was originally developed to treat hypertension without medication and was associated with substantially lower risk of coronary artery disease and stroke mortality and other cardiometabolic advantages [7-9]. However, more recently, a pattern known as the Atlantic Diet (AD), representative of the traditional diet of Portugal and Galicia (Northwest Spain) has been focusing the attention. Although it has some elements in common with the Mediterranean diet (consumption of fruits and vegetables, nuts and olive oil) and with the DASH dietary pattern (fruits, vegetables nuts, legumes or moderate consumption of low fat dairy), the AD has some differentiating characteristics such as the increased intake of fish and seafood, potatoes, broths with meat and cabbage, and moderate consumption of lean meats [10]. To date, while available evidence
regarding this dietary pattern is not particularly extensive, published scientific studies have shown that it can provide important health benefits. In a case-control study conducted in 2010 in Porto by Oliveira et al. [11], an inverse association between adherence to AD and a lower probability of non-fatal myocardial infarction was reported. Guallar-Castillon et al. [12], examined the association between Southern European AD (SEAD) and various biomarkers of coronary risk, blood pressure and anthropometry. Greater adherence to the SEAD was associated with lower levels of C-reactive protein in plasma, plasma triglycerides, insulin resistance index, albumin in urine, urine albumin-creatinine ratio, and systolic blood pressure.

Materials and methods:

Line 89: baseline, not basa.

Answer:
We have corrected this mistake (line 96):

A brief description of the original study needs to be provided on line 91.

Answer:
We have included a brief description of the original study (line 97):
The results of this study are a subanalysis of the EVIDENT 2 study. This article presents the data from the baseline assessment alone. It is a cross-sectional, multi-centre design involving six participating Spanish primary care centres. The EVIDENT 2 study protocol [13], with a description of data gathering methods, has been published previously. The EVIDENT 2 was a clinical trial aiming to assess the effect of a smartphone application with brief counselling on improving the lifestyles in the general population.

Line 93: Need to describe how the participants became to be part of the original study.

Answer:
We have added this paragraph to improve the clarity on how the participants became to be part of the original study (line 101):

The EVIDENT 2 study participants were selected through random sampling from offices of general practitioners in six health centers from Spain.

Line 95: Were none of the other measures essential to the analysis? Just the completed FFQ?

Answer:
We have reworded this paragraph to highlight the importance to include participants with valid dietary records (line 101):

For this analysis, among the 833 participants in the EVIDENT 2 study, we included a total of 791 individuals. The remaining 42 participants did not have a valid dietary records at the baseline assessment visit, collected using a food frequency questionnaire (FFQ). Other measures included in this study (cardiovascular risk factors and obesity indexes) were present in the 791 participants included.

A reference is required for line 101 to show that this is a valid way to calculate a sample size.

Answer:
Taking into account that this is a subanalysis of the EVIDENT 2 study, we have calculated the statistical power to detect a minimum difference of 3% in the cardiovascular risk, with the 791 subjects included. This minimum difference was based on the results found after a diet and aerobic exercise program intervention, which achieved a reduction of 3.0 points on cardiovascular risk [14]. The calculation was made taking into account the standard deviation of cardiovascular risk in the sample (10.4%) and assuming an alpha risk of 0.05 and a beta risk of 0.2 in bilateral contrast. We have reworded this paragraph to improve the clarity of the sentence (line 111):
The 791 participants who meet the selection criteria allow detecting a minimum difference in cardiovascular risk of three percentage points between two of the three groups into which we have classified AD adherence, assuming an alpha risk of 0.05 and a beta risk of 0.2 in bilateral contrast. This minimum difference was based on the results found after a diet and aerobic exercise program intervention, which achieved a reduction of 3.0 points on cardiovascular risk.

Other dietary scores have been validated using biological markers or nutrients according to the score.

Answer: In effect, other dietary scores have been validated using biological markers or nutrients according to the score. We have included the table 4 with the nutritional composition according to the score of the Atlantic diet.

In addition, we have included one more biological variable in Table 5, fibrinogen, a marker considered of cardiovascular risk by clinical practice guidelines. This value does not show differences between the groups studied.

Line 103. What is the DÁgostino scale and why has it been used as the outcome marker for this score? What is the direct link from the AD score to this scale? Also, why has this scale been used for CVD risk when other more validated measures, such as the Framingham exist?

Answer: The use of this score as the outcome marker is because it is a global score that includes risk factors as the age, total cholesterol, high-density lipoprotein cholesterol, systolic blood pressure, gender, drug treatment for hypertension, smoking and history of diabetes mellitus. The inclusion on the text the clarification “D'Agostino scale” could be confusing. With this, we wanted to highlight one of the main authors of the Framingham scale. We have corrected the paragraph and now, reads, as follows (line 170):

Cardiovascular risk assessment (CVR): This was estimated using the published risk equation based on the Framingham study to assess general cardiovascular disease risk and risk of individual cardiovascular events (coronary, cerebrovascular, and peripheral arterial disease and heart failure). Risk factors used include age, total cholesterol, high-density lipoprotein cholesterol and SBP as quantitative variables, and gender, drug treatment for hypertension, smoking and history of diabetes mellitus as dichotomous variables.

Line 116: What is the name of this FFQ?

Answer: This FFQ does not have a characteristic name. The questionnaire was developed at the University of Navarra by the PREDIMED group.

Line 117: How was the FFQ validated eg: energy, nutrients, against another method, biomarkers etc? How is the FFQ validated for this kind of diet type?

Answer: The FFQ was validated against a 3 day dietary records. We have added this information in the text (line 126):

This questionnaire has been validated against a 3-days dietary records in Spain.

Line 123: “The results allowed us to calculate...” Why was any kind of analysis done prior to this? This process needs to be included as part of your methods going forward.

Answer: We have reworded the paragraph to improve the clarity of the sentence (line 133):

With the data of the FFQ, we have calculated an index of adherence to the Atlantic Diet, adapting the recommendations provided by Calvo-Malvar et al. [17] and Vaz Velho et al. [10].
A lot more detail needs to be added as to HOW the score was put together. What is the validation of using them from other people? Has their work shown them to be successful and if so, why do you need to develop another method?

Answer:
We have added more details about the calculation of the score, completing the information found in the first version (line 133).

With the data of the FFQ, we have calculated an index of adherence to the Atlantic Diet, adapting the recommendations provided by Oliveira et al. [11], Calvo-Malvar et al. [17] and Vaz Velho et al. [10]. Oliveira et al. [11] developed an index based on a food frequency questionnaire. This index consists of nine food groups (fresh fish, dried salt cod, red meat and pork products, dairy products, legumes and vegetables, vegetable soup, potatoes, whole-grain bread, and wine). Subsequently, Calvo-Malvar et al. [17] established a series of recommendations for good compliance with this dietary pattern which, in addition to previous ones, included olive oil, fruit, eggs, nuts and other additional items to reduce the consumption of foods rich in animal fats, sweets or sugar-sweetened beverages. Finally, Vaz Velho [10], and Tojo et al. [18] included in the AD pyramid performing daily physical activity moderate to high intensity. We wanted to put together all these recommendations for the calculation of a 14-item index (Table 1). Compliance with each of the criteria defined in Table 1 scored one point, with the overall score ranging from 0 to 14 points (the higher the score, the greater the adherence).

Why are the score allocated with the weighting? Surely some of the factors here should be weighted more heavily because of their relationship with CVD prevention? Some justification for the scoring with relation to CVD biology needs to be added if the score is to related to CVD prevention, not diet. The lack of weighting may have impacted on results provided here, especially in relation to PA.

Answer:
We have tried to create an index for quick assessment of adherence to this dietary pattern, in the same way, which was created the Mediterranean Diet adherence screener (MEDAS) [19] composed of 14 items. The MEDAS scores one point for every item. Individually, many of the components of AD have been associated with cardiovascular disease, including the clearest distinguishing aspect with respect to the Mediterranean diet or the DASH diet, which is a high consumption of fish [20]. The creation of this index allows measuring the combined effect of all these components, as well as their possible interactions, on cardiovascular risk or cardiovascular risk factors.

**Table 1**: What is considered to be a “serving size” for the foods in this list. How do they relate to country or international dietary recommendations?

Answer:
We have included what is considered as “serving size” in Table 1.

<table>
<thead>
<tr>
<th>Components</th>
<th>Frequency</th>
<th>Servings equivalents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bread, cereals, wholegrain cereals, rice, pasta, and potatoes</td>
<td>≥ 6 servings/day</td>
<td>1 serving: 75 g bread, 30 g cereals, 60 g rice, 60 g pasta, 150 g potatoes</td>
</tr>
<tr>
<td>Olive oil</td>
<td>≥ 3 servings/day</td>
<td>1 serving: 1 spoon</td>
</tr>
<tr>
<td>Fresh fruit</td>
<td>≥ 3 servings/day</td>
<td>1 serving: 1 piece or serving</td>
</tr>
<tr>
<td>Vegetables</td>
<td>≥ 2 servings/day</td>
<td>1 serving: 200 g</td>
</tr>
<tr>
<td>Dairy products</td>
<td>≥ 3 servings/day</td>
<td>1 serving: 200 g milk, 155 g yogurt, 50 g cheese</td>
</tr>
<tr>
<td>Fish and seafood</td>
<td>≥ 3 servings/week</td>
<td>1 serving: 130 g fish, 200 g seafood</td>
</tr>
<tr>
<td>Lean meat</td>
<td>≥ 3 servings/week</td>
<td>1 serving: 130 g</td>
</tr>
<tr>
<td>Eggs</td>
<td>≥ 3 servings/week</td>
<td>1 serving: quantity 1</td>
</tr>
<tr>
<td>Pulses</td>
<td>≥ 2 servings/week</td>
<td>1 serving: 150 g</td>
</tr>
<tr>
<td>Nuts, preferably chestnuts, walnuts, almonds, and hazelnuts</td>
<td>≥ 4 servings/week</td>
<td>1 serving: 30 g</td>
</tr>
<tr>
<td>Dietary Component</td>
<td>Frequency</td>
<td>Serving Size</td>
</tr>
<tr>
<td>---------------------------------</td>
<td>-----------------</td>
<td>-------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Fatty meat, cured sausage, margarine, butter</td>
<td>≤ 4 servings/month</td>
<td>1 serving: 50 g fatty meat or sausage, 12 g margarine or butter</td>
</tr>
<tr>
<td>Sweets, pastries, cakes, candies, ice cream</td>
<td>≤ 4 servings/month</td>
<td>1 serving: 50 g sweets, pastries or cakes, ice cream quantity 1</td>
</tr>
<tr>
<td>Sugar-sweetened beverages</td>
<td>≤ 4 servings/month</td>
<td>1 serving: 200 cc</td>
</tr>
<tr>
<td>Moderate and or vigorous physical activity</td>
<td>≥ 60 min/day</td>
<td></td>
</tr>
</tbody>
</table>

Each issue scored with one point if it is met

**Why is physical activity in the list and not smoking status?** Given that PA was included as a lifestyle factor, it is not logical that smoking is also not included.

**Answer:**
We have included the PA among the components of the index due to the inclusion of this in the Atlantic Diet Pyramid, by Vaz Velho et al. [10]. (see figure below). Physical activity and eating habits are the two lifestyles that are most commonly related one to each other. In the pyramid of the Mediterranean diet is also included the realization of daily physical activity (see figure below). In addition, the aims of the EVIDENT study are more related to the assessment of the influence of physical activity styles and eating habits. Our intention was that with the created index we could make an assessment of adherence to AD in the general population. Although the effect of tobacco on cardiovascular risk is contrasted, the percentage of smokers in the population is relatively low and this could alter the results.
Atlantic Diet Pyramid. Vaz Velho et al.[10]

Mediterranean Diet Pyramid

Mediterranean Diet Pyramid. 2009. Oldways Preservation and Exchange Trust
Line 138: Was LDL measure or just calculated using the equation?

Answer: There was a mistake. LDL cholesterol was estimated using the Friedewald equation except in subjects who had triglyceride levels ≥ 300 mg/dl (n=10), in which case we used 299 mg/dl for the calculation of triglycerides. We have included this information in the text (line 157).

Low density lipoprotein cholesterol (LDL-C) was estimated using the Friedewald equation except in subjects who had triglyceride levels ≥ 300 mg/dl (n=10), in which case we used 299 mg/dl for the calculation of triglycerides.

Line 165: Why was only one cohort used for arterial stiffness measures and how was this cohort different from the others?

Answer: The arterial stiffness measures was measured only in the cohort of Salamanca because this health center was the only that had the necessary devices to perform this measurements. We have carried out an analysis of the mean clinical characteristics (see table below). The 291 participants of this cohort has similar age and percentage of the women. We have added this information in the text (line 188).

Analysis of pulse wave velocity (PWV): Pulse wave velocity was recorded in the Salamanca cohort (N = 291). This cohort had similar age and gender distribution to that of the entire sample.

<table>
<thead>
<tr>
<th>Baseline characteristics by score of ATLANTIC diet and lifestyle index</th>
<th>Salamanca cohort (n=291) Mean or N (SD or %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>52.2 (10.2)</td>
</tr>
<tr>
<td>Gender, Female (n, %)</td>
<td>186 (63.9)</td>
</tr>
<tr>
<td>Hypertension (n, %)</td>
<td>75 (28.8)</td>
</tr>
<tr>
<td>Diabetes (n, %)</td>
<td>12 (4.1)</td>
</tr>
<tr>
<td>Antihypertensive agents (n, %)</td>
<td>61 (21.0)</td>
</tr>
<tr>
<td>Hypoglycemic agents (n, %)</td>
<td>12 (4.1)</td>
</tr>
<tr>
<td>Lipid-lowering agents (n, %)</td>
<td>40 (13.7)</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>121.4 (16.5)</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>74.5 (10.3)</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>67.6 (10.7)</td>
</tr>
<tr>
<td>Glycated hemoglobin (%)</td>
<td>5.4 (0.3)</td>
</tr>
<tr>
<td>Serum glucose (mg/dL)</td>
<td>85.5 (11.3)</td>
</tr>
<tr>
<td>Total cholesterol (mg/dL)</td>
<td>200.2 (31.9)</td>
</tr>
<tr>
<td>HDL-cholesterol (mg/dL)</td>
<td>60.1 (14.9)</td>
</tr>
<tr>
<td>LDL-cholesterol (mg/dL)</td>
<td>120.1 (28.9)</td>
</tr>
<tr>
<td>Tryglicerides (mg/dL)</td>
<td>99.9 (46.9)</td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
<td>27.3 (4.6)</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>92.9 (12.4)</td>
</tr>
<tr>
<td>Hip circumference (cm)</td>
<td>105.0 (9.5)</td>
</tr>
<tr>
<td>Waist-height ratio</td>
<td>0.57 (0.07)</td>
</tr>
<tr>
<td>Waist-hip ratio</td>
<td>0.88 (0.10)</td>
</tr>
<tr>
<td>Adiposity index</td>
<td>26.4 (5.9)</td>
</tr>
<tr>
<td>CVR</td>
<td>8.3 (8.7)</td>
</tr>
</tbody>
</table>

Categorical variables are expressed as n (%) and continuous variables as mean ± standard deviation.
SBP: Systolic blood pressure; DBP: Diastolic blood pressure; BMI: Body mass index; CVR: Cardiovascular risk; cPWV: Carotid femoral pulse wave velocity.

Line 179: Need to describe how cardiovascular risk was calculated to show that it doesn’t overlap with the other confounders mentioned.

Answer:
The calculation of the global cardiovascular risk score includes risk factors as the age, total cholesterol, high-density lipoprotein cholesterol, systolic blood pressure, sex, drug treatment for hypertension, smoking and history of diabetes mellitus. However, this variable was adjusted only for the energy intake on the adjusted model to avoid collinearity.

We have included this in the statistical analyses method (line 205):

This analysis was adjusted only for the energy intake in the case of the cardiovascular risk to avoid collinearity.

Line 199: Where are the p values reported here. Suggest putting in a table showing both unadjusted and adjusted values for the analyses run.

Answer:
Following the suggestions of the reviewer, we have put in a table both unadjusted and adjusted values. This table is the new table 5. As a consequence, we have deleted figures 1 and 2 that showed the adjusted values.

Results:

Line 188: Were any people removed for having unrealistic dietary values? Given that PA measures were available, it seems reasonable to be able to discover those who either under or over-reported their dietary intake.

Answer:
A frequency analysis has been carried out for the variable “energy” and other variables of nutritional composition but no anomalous values have been found. For the variable "energy", we find an average value of 2477 ± 786 kcal. The minimum value was 809 kcal and the maximum value 5550 kcal. Probably, the reason for these values is the overestimation of this method (FFQ). See following response.

Table 4: The energy value provided for the cohort seems very high to me. See earlier comment about over and under-reporting.

Answer:
It is true, however, that usually the estimation for energy intake and consumption of macronutrients shows higher values when the food intake frequency questionnaire is used, which reinforces the conclusions of many other studies which indicate that food frequency questionnaires may overestimate food consumption compared to other assessment instruments [21,22]. Recently, in a sample of 362 individuals in the EVIDENT study, an overestimation of the energy intake of more than 300 kcal of the FFQ was observed compared to the record made by the EVIDENT Smartphone application [23].

We have included a limitation in the discussion section adding this aspect (line 302):

Some studies indicate that FFQ may overestimate food consumption compared to other assessment instruments [21-23].

Discussion

From Line 249: The information provided here would be better placed in the methods, as this relates to how your score was derived.
Answer:
Following the recommendations of the reviewer, we have changed this paragraph from the discussion to the methods section.

**Line 256: Is this reference correct? It links to the validation paper.**

Answer:
We have changed the reference. Now, the text reads as follow (line 265):

The index created by our group, presented in this manuscript, includes all these recommendations, adapting the responses to a food frequency questionnaire widely used in other research [24,25].

The efficacy of the Mediterranean and DASH diets are well established, but what is unclear is how the differences in the Atlantic diet contribute to CVD prevention.

Answer:
We have added a paragraph some possible explanations to the results found (line 280):

Among the possible explanations for the results found in this study, we can point out that individually, many of the components of AD have been associated with cardiovascular disease, including the clearest distinguishing aspect with respect to the Mediterranean diet or the DASH diet, which is a high consumption of fish [20]. Nevertheless, the creation of this index allows measuring the combined effect of all these components, as well as their possible interactions, on cardiovascular risk or cardiovascular risk factors.

We have added other paragraph in the discussion (line 299):

The present study presents a series of limitations. The design of the study (being cross-sectional) does not allow causal relationships to be established between compliance with the recommendations of the AD and the variables studied, but it may be useful when proposing intervention or longitudinal studies to clarify the role of this dietary profile on health, like those developed for the DASH diet or the Mediterranean diet.

**Conclusion: It will be easier to see if this has not been over stated once adjusted and unadjusted values are presented together.**

Answer:
Following the suggestions of the reviewer, we have put in a table both unadjusted and adjusted values. This table is the new table 5. As a consequence, we have deleted figures 1 and 2 that showed the adjusted values.

**REFERENCES**

18. Tojo, R.; Leis, R. El papel de la Dieta Atlantica como contrapunto saludable a la Dieta Ocidental actual In La Dieta Atlantica, el pescado y las algas - Su importancia en el...


