REVIEW ARTICLE

Check for updates

Effect of the Mediterranean diet on incidence of heart failure in European countries: a systematic review and meta-analysis of cohort studies

Nicola Veronese[1]✉, Francesco Saverio Ragusa[1], Stefania Maggi[2], Oliver C. Witard[3], Lee Smith[4], Ligia J. Dominguez[1,5], Mario Barbagallo[1], Masoud Isanejad[6] and Konstantinos Prokopidis[6]

INTRODUCTION: Heart failure (HF) is one of the most common cardiovascular disorders, and its prevalence is increased due to age, genetics, and lifestyle factors. Emerging evidence suggests that the Mediterranean Diet (Med Diet) is linked to lower all-cause mortality in patients with increased cardiovascular disease risk, such as those with HF.
OBJECTIVE: To conduct a systematic review and meta-analysis of observational studies into the relationship between the Med Diet on HF risk.
DESIGN: Several databases (PubMed, Scopus, Web of Science and Cochrane Library) until the 01st of May 2023 were searched. Our research was conducted based on the updated 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Data were reported as risk ratios (RRs) with their 95% confidence intervals (CIs) as results of multivariate or univariate analyses.
RESULTS: From the original 1206 studies collected, six observational prospective studies were included, with a total of 216,385 European participants without evidence of HF at baseline. Over a mean period of 11 years of follow-up, a 1-point increase in the Med Diet score was associated with a significantly lower risk of HF (RR = 0.940; 95% CI: 0.912–0.969, $p < 0.0001$; $I^2 = 42.9\%$). Categorised by sex, a higher adherence to Med Diet was associated with a significantly lower incidence of HF in women (RR = 0.942; 95% CI: 0.912-0.973, $p = 0.001$; $I^2 = 41.8\%$), but not in men. The overall quality of included studies was good.
CONCLUSIONS: Higher adherence to Med Diet across European countries is associated with lower risk of HF, particularly in women.

European Journal of Clinical Nutrition; https://doi.org/10.1038/s41430-024-01519-4

INTRODUCTION

Cardiovascular disease (CVD) is among the most common causes of mortality and responsible for a substantial rise in hospitalizations and financial burden [1]. Heart failure (HF) is one of the most common cardiovascular disorders, and its prevalence increases primarily due to age, genetic predisposition, and lifestyle factors [2], leading to higher morbidity and mortality rates [3]. In particular, the prognosis following diagnosis of HF is poor, with a survival rate of ~50 and 10% within 5 and 10 years, respectively [4], affecting 1–2% of the adult population [5]; 1% of those aged 20–39 years to >20% in people aged 80 years and above [6]. Therefore, interventions aiding in improvements of primary HF prevention would result in decreased HF incidence, improving survival and hospitalization rates.

Emerging evidence suggests that the Mediterranean Diet (Med Diet) is linked to lower all-cause mortality in patients with increased CVD risk [7], including patients with HF [8]. Although nutritional treatment leading to improved odds of survival in this patient group could be fundamental to public health, observational studies investigating dietary patterns pertinent to the prevention of HF risk remain limited. For example, a large clinical trial with a median follow-up of 4.8 years indicated that following a Med Diet did not lead to reduced HF risk compared to controls [9], this finding is not universal [10]. There is one previous meta-analysis on this topic. However, this meta-analysis has several important limitations, for example, a small number of studies were included ($k = 3$), and data from incompatible study designs were merged, such as observational studies with randomized controlled trials [11].

Therefore, we conducted a systematic review and meta-analysis of published observational studies conducted across Europe in an attempt to update the current evidence around the impact of Med Diet on HF risk.

METHODS

This systematic review and meta-analysis was conducted based on the updated 2020 Preferred Reporting Items for Systematic

[1]Department of Health Promotion, Maternal and Infant Care, Internal Medicine and Medical Specialties, "G. D'Alessandro"-PROMISE-University of Palermo, Palermo, Italy. [2]Consiglio Nazionale delle Ricerche, Neuroscience Institute, Padova, Italy. [3]Faculty of Life Sciences and Medicine, Centre for Human and Applied Physiological Sciences, King's College London, London, UK. [4]Centre for Health Performance and Wellbeing, Anglia Ruskin University, Cambridge, UK. [5]Faculty of Medicine and Surgery, University of Enna "Kore", 94100 Enna, Italy. [6]Department of Musculoskeletal and Ageing Science, Institute of Life Course and Medical Sciences, University of Liverpool, Liverpool, UK.
✉email: nicola.veronese@unipa.it

Received: 2 June 2024 Revised: 21 September 2024 Accepted: 25 September 2024
Published online: 01 October 2024

Reviews and Meta-Analyses (PRISMA) guidelines [12]. The protocol has been registered in the International Prospective Register of Systematic Reviews (PROSPERO) (CRD42023429132).

Search strategy

Two independent reviewers (K.P. and S.R.) searched PubMed, Scopus, Web of Science and Cochrane Library from inception until 01st May 2023. The search strategy employed several terms for the concepts of Med Diet and HF, as detailed in Supplementary Table 1. Discrepancies in the literature search process were resolved by a third reviewer (N.V.).

Inclusion and exclusion criteria

Studies were included based on the following criteria: (i) prospective or retrospective cohort studies; (ii) adults ≥18 years old without history of HF at the baseline; and (iii) assessment of incidence of HF via hazard (HR) or risk ratios (RR), deriving from univariate or multivariate analyses, using a Cox's regression analysis. Articles were excluded if they (i) were reviews, letters, in vivo or in vitro experiments or commentaries; (ii) the participants were younger than 18 years-old.

Data extraction and risk of bias

Two reviewers (K. P. and S.R.) extracted data independently which included the name of the first author, date of publication, country of origin, study design. participant age, sample size, sex, definition of Med Diet, and years of study follow-up. Disagreements between reviewers were resolved by a third independent reviewer (N.V.). The Newcastle-Ottawa Scale (NOS) was utilized to assess study quality/risk of bias (RoB) [13]. NOS assigns a maximum of 9 points based on three quality parameters: selection, comparability, and outcome. The evaluation was made by two investigators (S.R. and N.V.). The risk of bias was classified as high (<5 points), moderate (6–7 points), or low (8–9 points) [14].

Statistical analysis

The primary analysis compared the incidence of HF from data derived from multivariate or univariate statistical analyses. RRs with their 95% confidence intervals (95% CIs) were then calculated. Statistical significance was assessed using the random effects model and inverse-variance method [15].

Statistical heterogeneity of outcome measurements between different studies was assessed using the overlap of their 95% CI and expressed as I^2. Classification of data with low heterogeneity was based on I^2 from 30 to 49%, moderate heterogeneity from 50 to 74%, and high heterogeneity from 75% and above [16]. We used an increase in one point to the Med Diet scores instead of categories (for example highest quantile vs. lowest in the adherence to Med Diet) to minimize statistical and clinical heterogeneity. Data about adherence to Med Diet were harmonized transforming the scales originally used in the manuscripts to a scale between 0 and 9 and calculating the association between an increase in 1 point and the risk of HF, using an approach similar to [17].

In case of high heterogeneity, a random-effect meta-regression was planned to explore potential sources of variability that could affect estimate rates among studies [18]. Mean age, number of adjustments in multivariate analyses (in univariate analyses equal to zero), and follow-up in years were considered potential confounders. However, the primary outcome did suffer on this issue and the number of studies (only six) did not permit this analysis.

Publication bias was assessed by visually inspecting funnel plots and using the Egger bias test [19]. In case of statistically significant publication bias, the trim-and-fill analysis was used [19]. A *P*-value of <0.05 was considered statistically significant and all analyses were conducted using STATA version 14.0 (StataCorp) and for forest plots MedCalc® Statistical Software version 22.023 (MedCalc Software Ltd, Ostend, Belgium; https://www.medcalc.org; 2024).

RESULTS

Literature search

The preliminary literature search yielded 682 publications. After excluding duplicates and abstracts, 10 full texts were eligible for inclusion in the systematic review and meta-analysis. Three of the 10 studies were discarded due to evaluating mortality risk in patients with HF, while one was a randomized controlled trial (RCT), as reported in Supplementary Table 2. This systematic review and meta-analysis comprised of six studies that investigated the incidence of HF depending on adherence to Med Diet (Fig. 1).

Descriptive data

As shown in Supplementary Table 3, the six prospective studies, giving information for nine independent cohorts [20–25] were performed in Europe and included a total of 216,385 participants without evidence of HF at baseline. Females represented 54.7% of the studied population. After a mean of 11 years of follow-up (range: 8.2–15 year), 6978 participants developed HF which is equivalent to a cumulative incidence of 3% of the initial population in all the included studies. The diagnosis of HF was made using medical records or death certificates (Supplementary Table 3).

Meta-analysis and sensitivity analyses

Figure 2 shows the primary data analysis. After adjusting for the potential confounders reported in Supplementary Table 3, an increase in one point in the Med Diet score was associated with a significantly lower risk of HF (RR = 0.940; 95% CI: 0.912–0.969, $p < 0.0001$; $I^2 = 42.9\%$). No publication bias (Egger's test: -0.68 ± 0.86; $p = 0.54$) was present for this outcome. The trim-and-fill-analysis did not modify our findings.

Since several cohorts reported datasets stratified according to sex, we also analysed the association between adherence to Med Diet and incidence of HF in men and women (Supplementary Fig. 1). In this regard, a positive association was observed in women (RR = 0.942; 95% CI: 0.912–0.973, $p = 0.001$; $I^2 = 41.8\%$), but not in men (interaction: $p = 0.94$). Similar results were evident when using categories (higher adherence vs. lower) instead of a one-point increase (RR = 0.591; 95% CI: 0.437–0.800, $p < 0.0001$), even if this analysis was characterized by a high heterogeneity ($I^2 = 88.2\%$) (Supplementary Fig. 2). Finally, in a sensitivity analysis, after removing the studies using univariate analyses (Bonaccio et al. [25]), the results were not different in magnitude (RR = 0.94; 95% CI: 0.91–0.96; $p < 0.0001$) with an important decrease in heterogeneity (I^2 from 42.9% to 8.3%).

Risk of bias

The risk of bias is fully reported in Supplementary Table 4. The overall quality of studies was good, except for one study included in the form of an abstract. The most common source of bias was the adequacy of follow-up of the cohorts that was not described in any of the studies included.

DISCUSSION

Our systematic review with meta-analysis included six studies with 216,385 community-dwelling adults living in Europe and without evidence of HF at baseline. We demonstrated that a higher adherence to Med Diet, as evaluated by Med Diet score, was associated with a significantly lower risk of HF, particularly in women.

Our meta-analysis confirms the important role of following the Med Diet in preventing CVD. A previous systematic review of 10,950 participants reported that following the Med Diet may protect against vascular diseases, but larger benefits were observed in smaller, single-centre studies with incomplete follow-up, hence there could be an overestimation of

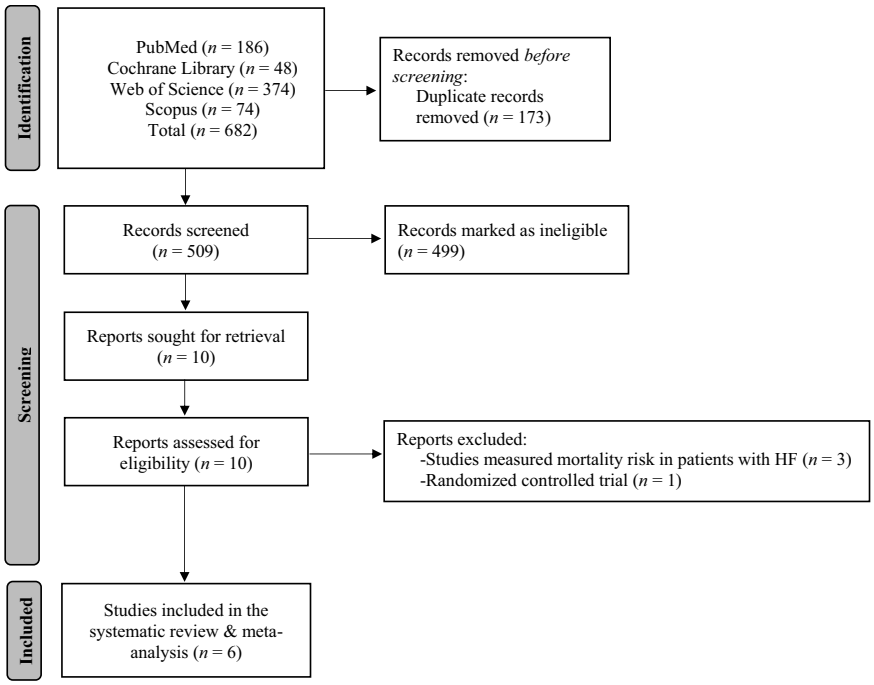

Fig. 1 Flowchart of the employed literature search.

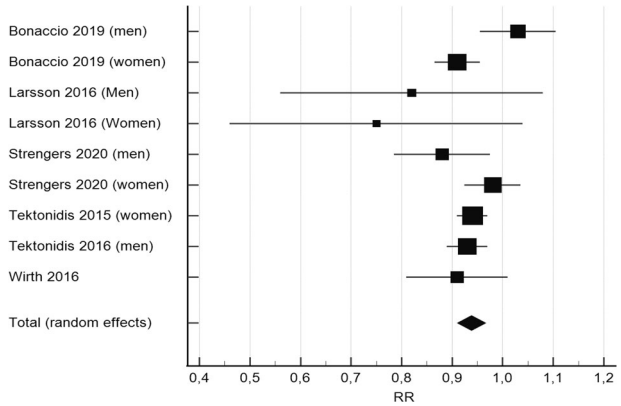

Fig. 2 Association between increase in one point in Med Diet score and incidence of heart failure.

benefits [26]. Moreover, a large-scale Italian study of 888,257 participants revealed a reduced risk of 40% for coronary heart disease, myocardial infarction and stroke with a higher adherence to Med Diet, highlighting the protective effects of olive oil, fruits, vegetables, and legumes [27]. However, this study also demonstrated an important heterogeneity of exposure categories included in the meta-analysis. The findings of our systematic review substantially confirmed these findings, adding to the concept that Med Diet could be protective for HF.

There may be several explanations for the apparent protective effect of a Med Diet against the incidence of HF. First, the Med Diet exhibits anti-inflammatory and antioxidant effects that could lower inflammation, oxidative stress, and endothelial dysfunction, which are the underlying complications leading to atherosclerosis, CVDs, and HF [28]. Accordingly, a study carried out in Greece on 3042 people described that higher adherence to the Med Diet was associated with an improved fasting glucose homeostasis, insulin levels, and an improved insulin resistance index (HOMA) in both normoglycemic individuals and diabetic participants [29]. This observation is particularly prudent given that diabetes is a known risk factor for HF [30]. Indeed, Med Diet could elicit lipid-lowering effects, protection against oxidative stress, inflammation and platelet aggregation, modification of hormones and growth factors involved in the pathogenesis of cancer and CVDs, inhibition of nutrient sensing pathways by specific amino acid restriction, and gut microbiota-mediated production of metabolites influencing metabolic health [31]. Finally, the Med Diet has been found to reduce levels of HF biomarkers, as revealed by a Spanish randomized controlled trial of 930 participants, where individuals at a high risk of CVDs who adopted this dietary pattern reduced their N-terminal pro-brain natriuretic peptide (NT-proBNP) compared with those assigned to a low-fat diet [32]. This observation was anticipated given the propensity for hypoxaemia to increase oxidative stress and release tumour necrosis factor-alpha (TNF-α), commonly associated with an increase in BNP levels in patients with chronic HF. This study also showed how a Med Diet could reduce plasma levels of TNF-α and of interleukin-1β (IL-1β) gene, with a consequent decrease of NT-proBNP release. This decline in NT-proBNP release results from a reduced volume expansion and wall stress leading to better blood pressure levels [32]. Otherwise, as demonstrated by a European study of 127 participants in patients with end-stage kidney disease, high adherence to Med Diet is associated with a progressive decrease of concentric and eccentric remodelling and lower left ventricular hypertrophy that are among the most important mechanisms for increasing HF risk [33].

Our meta-analysis suggests the relationship between Med Diet and HF risk may be sex specific since the association was statistically significant in women, but not in men. Previous studies have attempted to delineate the association between Med Diet and incidence of HF by sex. For instance, a British study of 23,232 men and women demonstrated that risk of stroke was significantly reduced in women with greater adherence to the Med Diet, but not in men, however, this study did not assess other CVDs risk factors such as atrial fibrillation [34]. Similarly, a Dutch study of 20,852 men and women demonstrated a significant relationship between adherence to the Med Diet and lower mortality in women only, with a rate advancement period of 15.1 years in women vs. 8.4 years in men [35]. However, there was no update of

dietary intake or other lifestyle data during the 10 years of follow-up, hence these findings may have sacrificed the precision of these associations. Moreover, a review revealed that consistent compliance to a Med Diet was associated with 21% lower odds of experiencing one additional risk factor (i.e., hypertension, hypercholesterolemia, diabetes, obesity) in women and with 14% lower odds in men [36]. Importantly, despite the relevant epidemiological evidence, no clear mechanism has been established to explain the association between Med Diet and CVDs, including HF, which is stronger in women than in men.

Finally, it should be acknowledged that, despite the significant results of our meta-analysis, some discrepancies across studies exist. First, there is considerable variability in study designs and populations. Second, despite efforts to ensure homogeneity, adherence to the Med Diet can vary significantly across different studies and regions. Mediterranean countries typically exhibit higher adherence due to their climate, lifestyle, and food production, whereas non-Mediterranean countries might show lower adherence, potentially impacting the outcomes of interest, namely, the incidence of HF. Third, the duration of follow-up varied greatly among the included studies, contributing to the observed heterogeneity. Finally, the quality of the included studies varies, with some, consisting of inadequate follow-up descriptions and inclusion of only European populations, may limit the generalizability of the findings. Therefore, these factors collectively contribute to the conflicting reports on the relationship between the Med Diet and HF risk. Further high-quality, interventional studies are needed to clarify the long-term effects of the Med Diet on HF prevention and related outcomes.

Limitations

Our research should be interpreted within the confines of several limitations. In our meta-analysis we included only six studies that embraced only European countries. However, even among European countries the best dietary pattern representing the Med Diet is observed in Mediterranean countries since the season, lifestyle, and food production (earth, season, weather etc.) are desirable for this dietary pattern. This may be different in non-Mediterranean European countries where climates and lifestyles differ (i.e., Netherlands, UK etc.). In this regard, a recent systematic review has found that Med Diet adherence has shown declines worldwide, and even in the Mediterranean region, therefore, this might have affected the results, even if we did not find a high statistical heterogeneity [37]. The dietary assessments of the included studies were performed during a period between 1994 and 2013, as shown in Supplementary Table 3, this could cause a limitation based on Med Diet decline. Second, several studies did not include the changes in the adherence to Med Diet during the follow-up period that was, on average, 11 years. Thus, inherent changes in dietary habits could modify our findings. Finally, the studies included were observational, which may incur biases that future interventional trials must explore. In particular, the heterogeneity in study designs and populations could affect the generalizability of the results.

In conclusion, our systematic review and meta-analysis revealed that higher adherence to Med Diet is associated with a significantly lower risk of HF; an observation particularly evident in women. Since CVDs remain the leading cause of death in our society, further research using interventional studies are warranted to better understand the long-term effects of the Med Diet on HF and its negative outcomes that accompany this condition.

REFERENCES

1. Clark KA, Reinhardt SW, Chouairi F, Miller PE, Kay B, Fuery M, et al. Trends in Heart Failure Hospitalizations in the US from 2008 to 2018. J Card Fail. 2022;28:171–80.
2. Velagaleti RS, Vasan RS. Heart failure in the twenty-first century: is it a coronary artery disease or hypertension problem? Cardiol Clin. 2007;25:487–95.
3. Rosamond W, Flegal K, Friday G, Furie K, Go A, Greenlund K, et al. Heart disease and stroke statistics—2007 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation. 2007;115:e69–e171.
4. Roger VL. Epidemiology of heart failure. Circ Res. 2013;113:646–59.
5. Savarese G, Lund LH. Global public health burden of heart failure. Card Fail Rev. 2017;3:7.
6. Lloyd-Jones DM, Larson MG, Leip EP, Beiser A, D'agostino RB, Kannel WB, et al. Lifetime risk for developing congestive heart failure: the Framingham Heart Study. Circulation. 2002;106:3068–72.
7. Karam G, Agarwal A, Sadeghirad B, Jalink M, Hitchcock CL, Ge L et al. Comparison of seven popular structured dietary programmes and risk of mortality and major cardiovascular events in patients at increased cardiovascular risk: systematic review and network meta-analysis. BMJ. 2023;380:e072003.
8. Chang C-Y, Lee C-L, Liu W-J, Wang J-S. Association of adherence to the mediterranean diet with all-cause mortality in subjects with heart failure. Nutrients. 2022;14:842.
9. Papadaki A, Martínez-González MÁ, Alonso-Gómez A, Rekondo J, Salas-Salvadó J, Corella D, et al. Mediterranean diet and risk of heart failure: results from the PREDIMED randomized controlled trial. Eur J Heart Fail. 2017;19:1179–85.
10. Singh RB, Dubnov G, Niaz MA, Ghosh S, Singh R, Rastogi SS, et al. Effect of an Indo-Mediterranean diet on progression of coronary artery disease in high risk patients (Indo-Mediterranean Diet Heart Study): a randomised single-blind trial. Lancet. 2002;360:1455–61.
11. Khan MS, Khan F, Fonarow GC, Sreenivasan J, Greene SJ, Khan SU, et al. Dietary interventions and nutritional supplements for heart failure: a systematic appraisal and evidence map. Eur J Heart Fail. 2021;23:1468–76.
12. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Int J Surg. 2021;88:105906.
13. Luchini C, Stubbs B, Solmi M, Veronese N. Assessing the quality of studies in meta-analyses: Advantages and limitations of the Newcastle Ottawa Scale. World J Meta Anal. 2017;5:80–4.
14. Luchini C, Veronese N, Nottegar A, Shin JI, Gentile G, Granziol U et al. Assessing the quality of studies in meta-research: Review/guidelines on the most important quality assessment tools. Pharm Stat. 2021;20:185–95. https://doi.org/10.1016/j.amjmed.2020.08.01510.1002/pst.2068.
15. DerSimonian R, Laird N. Meta-analysis in clinical trials. Controlled Clin trials. 1986;7:177–88.
16. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ. 2003;327:557–60.
17. Veronese N, Stubbs B, Volpato S, Zuliani G, Maggi S, Cesari M, et al. Association Between Gait Speed With Mortality, Cardiovascular Disease and Cancer: A Systematic Review and Meta-analysis of Prospective Cohort Studies. J Am Med Dir Assoc. 2018;19:981–88.e987. https://doi.org/10.1016/j.jamda.2018.06.007.
18. Cumpston M, Li T, Page MJ, Chandler J, Welch VA, Higgins JP, et al. Updated guidance for trusted systematic reviews: a new edition of the Cochrane Handbook for Systematic Reviews of Interventions. Cochrane Database Syst Rev. 2019;10:14651858.
19. Duval S, Tweedie R. A nonparametric "trim and fill" method of accounting for publication bias in meta-analysis. J Am Stat Assoc. 2000;95:89–98.
20. Larsson SC, Tektonidis TG, Gigante B, Akesson A, Wolk A. Healthy Lifestyle and Risk of Heart Failure: Results From 2 Prospective Cohort Studies. Circ Heart Fail. 2016;9:e002855 https://doi.org/10.1161/CIRCHEARTFAILURE.115.002855.
21. Strengers JG, den Ruijter HM, Boer JMA, Asselbergs FW, Verschuren WMM, van der Schouw YT, et al. The association of the Mediterranean diet with heart failure risk in a Dutch population. Nutr Metab Cardiovasc Dis. 2021;31:60–66. https://doi.org/10.1016/j.numecd.2020.08.003.
22. Tektonidis TG, Akesson A, Gigante B, Wolk A, Larsson SC. A Mediterranean diet and risk of myocardial infarction, heart failure and stroke: A population-based cohort study. Atherosclerosis. 2015;243:93–98. https://doi.org/10.1016/j.atherosclerosis.2015.08.039.
23. Tektonidis TG, Akesson A, Gigante B, Wolk A, Larsson SC. Adherence to a Mediterranean diet is associated with reduced risk of heart failure in men. Eur J Heart Fail. 2016;18:253–9. https://doi.org/10.1002/ejhf.481.
24. Wirth J, di Giuseppe R, Boeing H, Weikert C. A Mediterranean-style diet, its components and the risk of heart failure: a prospective population-based study in a non-Mediterranean country. Eur J Clin Nutr. 2016;70:1015–21. https://doi.org/10.1038/ejcn.2016.140.
25. Bonaccio M, Di Castelnuovo A, Costanzo S, Ruggiero E, Persichillo M, De Curtis A, et al. Mediterranean diet and risk of first hospitalization for heart failure and atrial fibrillation. Eur J Public Health. 2019;29:ckz185. 061.
26. Liyanage T, Ninomiya T, Wang A, Neal B, Jun M, Wong MG, et al. Effects of the Mediterranean diet on cardiovascular outcomes—a systematic review and meta-analysis. PLoS One. 2016;11:e0159252.

27. Grosso G, Marventano S, Yang J, Micek A, Pajak A, Scalfi L, et al. A comprehensive meta-analysis on evidence of Mediterranean diet and cardiovascular disease: are individual components equal? Crit Rev Food Sci Nutr. 2017;57:3218–32.
28. Richardson LA, Izuora K, Basu A. Mediterranean Diet and Its Association with Cardiovascular Disease Risk Factors: A Scoping Review. Int J Environ Res Public Health. 2022;19:12762.
29. Panagiotakos DB, Tzima N, Pitsavos C, Chrysohoou C, Zampelas A, Toussoulis D, et al. The association between adherence to the Mediterranean diet and fasting indices of glucose homoeostasis: the ATTICA Study. J Am Coll Nutr. 2007;26:32–8.
30. Lehrke M, Marx N. Diabetes mellitus and heart failure. Am J Cardiol. 2017;120:S37–S47.
31. Tosti V, Bertozzi B, Fontana L. Health benefits of the Mediterranean diet: metabolic and molecular mechanisms. J Gerontol Ser A. 2018;73:318–26.
32. Fitó M, Estruch R, Salas-Salvadó J, Martínez-Gonzalez MA, Arós F, Vila J, et al. Effect of the Mediterranean diet on heart failure biomarkers: a randomized sample from the PREDIMED trial. Eur J Heart Fail. 2014;16:543–50.
33. Bacharaki D, Petrakis I, Kyriazis P, Markaki A, Pleros C, Tsirpanlis G, et al. Adherence to the Mediterranean Diet Is Associated with a More Favorable Left Ventricular Geometry in Patients with End-Stage Kidney Disease. J Clin Med. 2022;11:5746.
34. Paterson KE, Myint PK, Jennings A, Bain LKM, Lentjes MAH, Khaw KT, et al. Mediterranean Diet Reduces Risk of Incident Stroke in a Population With Varying Cardiovascular Disease Risk Profiles. Stroke. 2018;49:2415–20. https://doi.org/10.1161/strokeaha.117.020258.
35. Van den Brandt PA. The impact of a Mediterranean diet and healthy lifestyle on premature mortality in men and women. Am J Clin Nutr. 2011;94:913–20.
36. Dontas AS, Zerefos NS, Panagiotakos DB, Valis DA. Mediterranean diet and prevention of coronary heart disease in the elderly. Clin Interventions Aging. 2007;2:109–15.
37. Damigou E, Faka A, Kouvari M, Anastasiou C, Kosti RI, Chalkias C, et al. Adherence to a Mediterranean type of diet in the world: a geographical analysis based on a systematic review of 57 studies with 1,125,560 participants. Int J food Sci Nutr. 2023;74:799–813.

AUTHOR CONTRIBUTIONS

Veronese, Ragusa, Witard: wrote the first draft of the manuscript; Veronese, Prokopidis: data analysis, methodology; Maggi, Barbagallo, Dominguez, Smith: critical revision of the work; Isanjead, Ragusa: data collection.

COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

Supplementary information The online version contains supplementary material available at https://doi.org/10.1038/s41430-024-01519-4.

Correspondence and requests for materials should be addressed to Nicola Veronese.

Reprints and permission information is available at http://www.nature.com/reprints

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.