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The role of the Mediterranean Diet on salt intake: a Systematized Review

O papel da Dieta Mediterrânica no consumo de sal: uma Revisão Sistematizada

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Resumo

Apesar de os benefícios para a saúde associados à Dieta Mediterrânica (MedDiet) serem bem conhecidos, os dados sobre a ingestão de sal dentro deste padrão alimentar são escassos. O objetivo da presente revisão foi investigar a associação entre a adesão à MedDiet e a ingestão de sal. A pesquisa bibliográfica foi realizada nas bases de dados Pubmed, Scopus e Web of Science. De um total de 28 estudos, foram encontradas associações positivas em oito estudos (n=1 apenas em homens) e associações inversas em nove estudos (n=1 apenas em homens). A maioria dos estudos incluídos (n=10) não comprovou a associação entre a adesão à MedDiet e a ingestão de sal/sódio. Um estudo encontrou resultados distintos, conforme o método utilizado para avaliar a ingestão de sal/sódio. Os resultados inconsistentes desta revisão, bem como a baixa qualidade dos estudos realizados sobre este tema, destacam a importância da realização de pesquisas mais robustas para uma melhor compreensão da possível relação entre a MedDiet e a ingestão de sal/sódio.

Palavras-chave: Dieta Mediterrânica, sal, sódio

Abstract

Despite all the well-known health benefits associated with the Mediterranean Diet (MedDiet), data on salt intake within this dietary pattern are scarce. The aim of the present review was to investigate the association between the adherence to the MedDiet and salt intake. Literature search was conducted in Pubmed, Scopus and Web of Science. Of a total of 28 studies, positive associations were found in eight studies (n=1 only in men) and inverse associations in nine studies (n=1 only in men). Most of the included studies (n=10) didn't prove any association between the adherence to MedDiet and salt/sodium intake. One study found different results, depending on the method used to evaluate salt/sodium intake. The inconsistent findings found in this review, as well as the low quality of the studies conducted in this area, highlight the importance of implementing more robust research in order to better understand the possible relation between MedDiet and salt/sodium intake.

Keywords: Mediterranean Diet, salt, sodium

List of abbreviations and acronyms

aMed Score – Alternate Mediterranean Diet Score

CG – Control Group

CKD – Chronic Kidney Disease

CVD - Cardiovascular Diseases

EPHPP - Effective Public Health Practice Project

FFQ - Food Frequency Questionnaire

Japanese-adapted Mediterranean Diet score - jMD score

MEDAS - Mediterranean Diet Adherence Score

MedDiet - Mediterranean Diet

NU-AGE - New dietary strategies addressing the specific needs of the elderly population for healthy ageing in Europe

PRISMA - Preferred Reporting Items for Systematic Reviews and Meta-Analyses

RCT – Randomised Controlled Trial

T1DM – Type 1 Diabetes Mellitus

UNESCO - United Nations Educational, Scientific and Cultural Organization

USA – United States of America

WHO - World Health Organization

Summary

Introduction

The Mediterranean Diet (MedDiet) is currently considered one of the healthiest dietary models. Coined by Ancel Keys back in 1960[1], this term is now one of the most well-known dietary patterns worldwide and has been recognised by the United Nations Educational, Scientific and Cultural Organization (UNESCO) as Intangible Cultural Heritage of Humanity[2].

The traditional MedDiet is characterised by a high intake of plant foods such as fruit, vegetables, bread and other sources of cereals (usually minimally refined), potatoes, beans, nuts and seeds; minimally processed, seasonally fresh and locally grown foods; fresh fruit as typical dessert; a high intake of olive oil used as the principal source of fat (especially virgin and extra-virgin olive oil); a moderate intake of dairy products; a moderate intake of eggs; fish and poultry consumed in low to moderate amounts; red meat consumed in low amounts; and wine in moderation, consumed with meals[3].

The most recent evidence shows that the MedDiet is related to very positive health outcomes as it is associated with a reduction of cardiovascular diseases (CVD) incidence and mortality, type 2 diabetes and metabolic syndrome, incidence of some cancers and cognitive function. The evidence on other outcomes, including the incidence of specific cancers is promising and strongly suggestive evidence indicates that the MedDiet does not increase adiposity or obesity, and it may even reduce these outcomes[3]. This dietary pattern has also been associated with a reduced risk of general cognitive decline as some of its main components (predominantly fruit and vegetables) are able to decrease brain damage induced

by reactive oxygen species (ROS), by improving antioxidant defences and lowering lipid oxidation and platelet aggregation[4, 5].

Although MedDiet is known to have a protective effect on CVD, data is still scarce on its association with salt/sodium intake. Sodium intake is a frequently ignored issue in the MedDiet definition[6] and the acceptable salt intake amount is not specified[7].

The World Health Organization (WHO) strongly recommends a reduction in sodium intake to reduce stroke and coronary heart disease in adults, control blood pressure in both children and adults and above all reduce the risk of CVD[8], the leading cause of death globally, representing 32% of all global deaths[9]. The recommendation is <2g/day sodium (5g/day salt) in adults and this value should be adjusted downward based on the energy requirements of children relative to those of adults[8].

It is known that dietary sodium is associated with blood pressure, a leading risk factor for CVD and with target organ damage independent of blood pressure. High dietary salt has been shown to cause or be associated with systemic vascular dysfunction, arterial stiffening, altered renal function, left ventricular hypertrophy, skin sodium deposition, cerebral circulatory dysfunction, alterations in sympathetic outflow and potential changes in bone content[10].

Despite its protective effect against CVD, it is essential to understand to what extent the MedDiet may be a source of hidden sodium.

Objective

To evaluate the association between adherence to the Mediterranean Diet and salt intake.

Methods

Study design

We conduct a systematized review according to the definition of Grant [11] which describes it as an "attempt to include elements of systematic review process while stopping short of systematic review". The present study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[12] as closely as possible.

Data Sources and Search Strategy

A systematic search was performed on the 7th of June using the databases Pubmed, Scopus and Web of Science databases. The same search expression was used in the three databases: ("Mediterranean Diet" OR "Mediterranean Pattern") AND (sodium OR salt). A total of 1227 references were exported to Endnote, where an automatic database clean-up was performed, yielding a total of 930 articles. After a manual cleaning of duplicates, 800 references were refined.

Inclusion and Exclusion Criteria

Initial screening was performed by the main author and it was based on title and abstracts. Only full-text articles in English and Portuguese languages were eligible. Studies conducted in animals and any type of review were excluded. Studies that did not evaluate the adherence to the MedDiet, salt intake or the

association between both were also excluded. No publication date was imposed. The full text of a total of 123 articles were analysed by two authors to make sure they met the inclusion criteria. All discrepancies were discussed and a final decision was deliberated by both. Figure 1[13] shows the results of the study selection process.
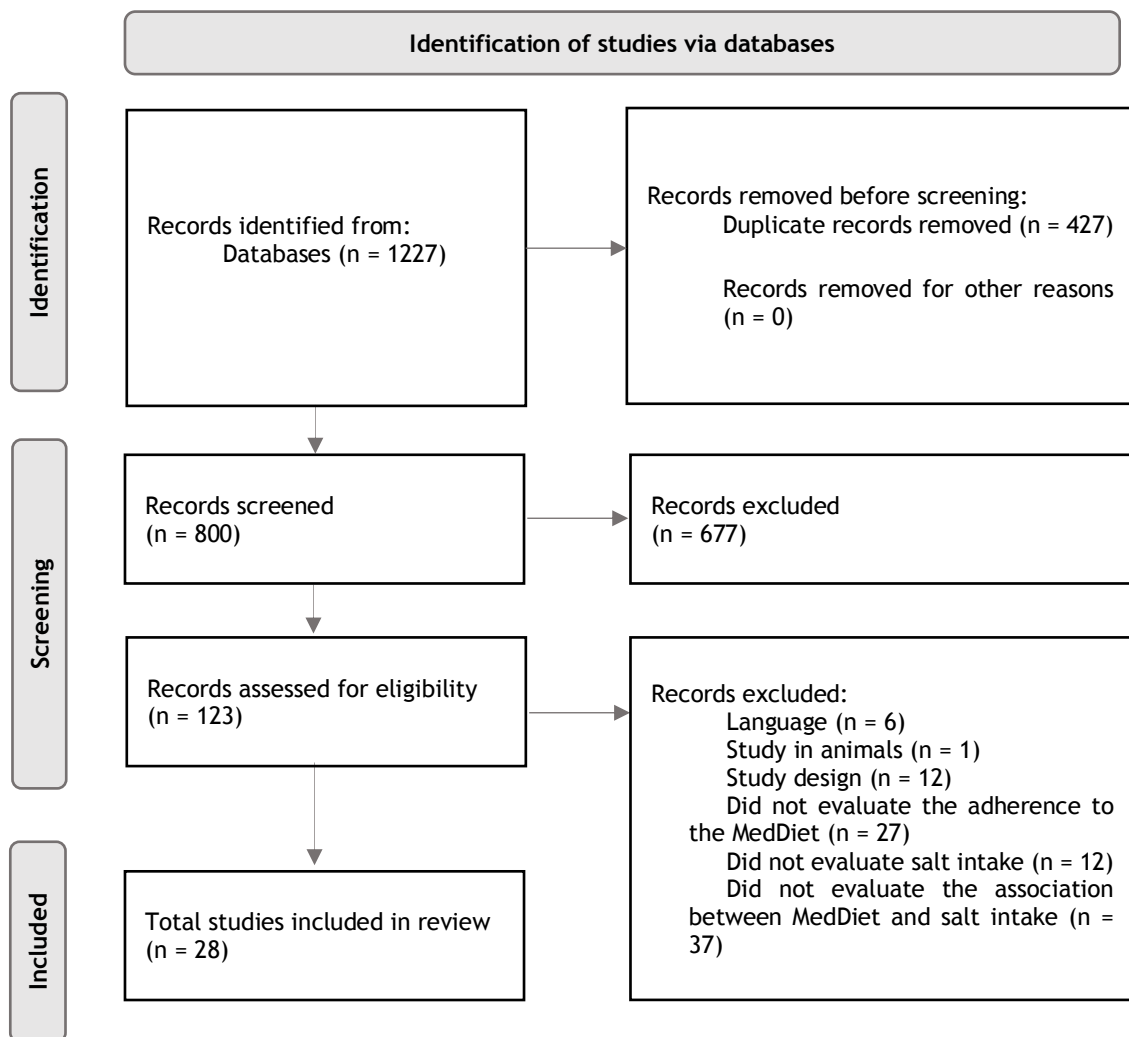

Figure 1. **PRISMA flow diagram search strategy**

Observational studies (cross-sectional studies, cohort studies and case-control studies) and experimental studies [randomized controlled trials (RCTs)] were included in this review. Studies that estimate salt/sodium intake through dietary assessment tools or urinary excretion, as well as those evaluating the adherence to the MedDiet, independently of the method, were eligible.

Quality Assessment

A total of 28 studies were included in this review and were assessed for quality using the Effective Public Health Practice Project—Quality Assessment Tool for Quantitative Studies (EPHPP)[14], a validated tool[15] for use in public health research. This tool consists of six criteria: selection bias, study design, confounders, blinding, data collection method, and withdrawals/dropouts. According to the dictionary of the tool[16], each criterion is rated as strong, moderate, or weak; the assessment of each study is determined by these ratings. According to the guidelines for the tool[17], studies with no weak ratings are classified as "strong"; studies with one weak rating are classified as "moderate"; and studies with two or more weak ratings are classified as "weak". The main reviewer performed the assessment of the quality of the included studies. All doubts were discussed with a second reviewer until a final decision was agreed upon. When doubt persisted, a third author was consulted.

Data Extraction and Data Synthesis

Considering the substantial heterogeneity in the methodology of the included studies, we decided to perform a qualitative synthesis to summarise the extracted data and to investigate the association between the MedDiet and salt intake.

Studies' information on author, year of publication, title, country/region, study design, main aim, population, method used to evaluate the adherence to the MedDiet and assess salt intake, outcome(s) of interest and main finding was entered into summary tables.

Results

<u>Study and sample characteristics</u>

Characteristics of included studies are summarised in Table 1 (from Appendix 1). In a total of 28 included studies, four[18-21] were conducted in the United States of America (USA), three studies each were conducted in Spain[22-24], two studies each were conducted in Portugal[25, 26], Iran[27, 28], Turkey[29, 30], Greece[31, 32], United Kingdom[33, 34], Canada[35, 36] and Japan[37, 38], one study each was conducted in Luxembourg[39], Australia[40], Italy[41], Netherlands[42], New Zealand[43]. One study was performed in several European countries[44] and one study did not mention its location[45].

The majority of the studies were cross sectional (n=13)[20, 25, 28-32, 36-39, 41, 43], followed by cohort studies (n=7)[18, 19, 21, 24, 33, 42, 45]. The total number of included RCTs was five[22, 23, 26, 40, 44]. One study each was classified as prospective[27], analysis of a RCT[35] and comparative pilot study[34].

The main aim of most studies (n=6)[19, 22, 23, 34, 42, 44] was related only to CVD and 3 studies[31, 32, 41] aimed to directly evaluate sodium intake. Only two studies[25, 26] intended to evaluate the association between Na excretion and the adherence to MedDiet as its main objective. The remaining articles (n=17) focused on various health-related outcomes[28, 29, 35, 39], including chronic diseases such as Type 1 Diabetes Mellitus (T1DM)[36], Chronic Kidney Disease (CKD)[18], obesity[37], as well

as kidney stones[45], metabolic risk factors[38], diet and weight status indicators[24, 27, 33], socio-demographic and lifestyle factors[43], cognitive function[21, 40] and depressive symptoms[20].

Population

The sample size of the studies ranged from 23 to 193 527 participants.

The majority included general adult populations (n=20), five studies[21, 25, 40, 43, 44] focused specifically on people 65 years old or older and three other studies used a younger population[29, 31, 33], up to 18 years old.

Methods used for data collection

A great diversity of tools was used to assess the adherence to the MedDiet. Of the ten studies that used the MedDiet Score, six[27, 28, 35, 38-40] based their method on Trichopoulou[46]; one[36] on Goulet[47]; one[32] was specially developed for the ATTICA study[48] and two didn't mention its main reference[21, 33]. A total of five studies[18-20, 26, 45] used the Alternate Mediterranean Diet Score (aMed score) based on Trichopoulou[46]. A total of five studies[22, 23, 25, 30, 34] used the Mediterranean Diet Adherence Score (MEDAS) questionnaire, derived from PREDIMED[49]. The KIDMED questionnaire was used in two studies[29, 31]. The "New dietary strategies addressing the specific needs of the elderly population for healthy ageing in Europe"-index (NU-AGE index), used in one study[44], was developed to evaluate the adherence to guidance based on nutrient reference values and food-based dietary guidelines for elderly individuals and nutrient requirements from the European Community[50]. The jMD score was specifically developed to evaluate Japanese eating behaviours in one study[37]. The Italian Mediterranean Index was developed by adapting the Greek Mediterranean Index to typical Italian eating

behaviour[41]. The study that used the Greek MedDiet[42] score didn't mention its main reference. In two studies[24, 43] it was not possible to understand what method was used.

To estimate salt/sodium intake, 20 studies reported data on sodium intake assessed through dietary assessment: Food Frequency Questionnaires (FFQs) (n=11)[18, 19, 21, 23, 24, 28, 31, 37, 39, 41, 43] were the most used method while dietary records (up to 4 days) (n=6)[22, 33-36, 38, 40] and dietary recalls (24 hours) (n=3)[20, 29, 30] were the least used methods. The second most frequent method to assess sodium was the 24-hour urinary excretion (n=7)[25-27, 32, 42, 44, 45].

Risk of Bias

According to the EPHPP Quality Assessment Tool, 25 of the total included articles were assessed as weak, three as moderate[23, 26, 45] and none was assessed as strong (Table 2 from Appendix 1).

Main Outcomes

Of the total 28 included studies, seven have suggested a positive association between the adherence to the MedDiet and sodium intake in the whole sample[18, 19, 21, 31, 37-39]. One demonstrated this positive association in men only[25]. An inverse association between these two factors was found in eight studies[20, 22-24, 27, 30, 36, 45]. One study described this negative association in men only[44]. In a total of ten studies[26, 28, 29, 32-35, 41-43], an association between the adherence to the MedDiet and salt/sodium intake was not found. One study[40] found an inverse association between the adherence to the MedDiet and sodium intake when estimated by a three-day food record, but no association was proved when sodium excretion was measured by a 24-hour urinary collection.

Discussion

To our knowledge, this is the first review that aimed to summarise data on the association between the adherence to MedDiet and salt/sodium intake.

Our literature search suggests that the majority of the included articles didn't find any association[26, 28, 29, 32-35, 41-43], seven found a positive association[18, 19, 21, 31, 37-39] and eight showed a negative association[20, 22-24, 27, 30, 36, 45]. Two studies only found associations between MedDiet and salt intake in male participants[25, 44]. It is important to note that one study[40] found different results according to the used methods to estimate sodium intake. This last study illustrates that the methodology used to evaluate the adherence to MedDiet and salt/sodium intake may justify different results concerning our outcome of interest.

One of the possible justifications for the heterogeneity of observed results is related to the poor validity of estimating sodium intake through dietary assessment[51]. The 'gold standard' method for estimating salt intake is a 24-hour urine collection, as 85% to 90% of sodium ingested over a 24-hour period is excreted in the urine. When estimates from a urinary sodium excretion and FFQs are compared, poor agreement is often found[51]. Dietary assessment often under-estimates salt intake due to under-reporting and difficulties quantifying sodium concentration in a variety of recipes, as well as discretionary salt intake[52]. Therefore, different accuracies between the methods used to assess sodium intake may condition the accuracy of the results on the association between the adherence to MedDiet and salt/sodium intake.

In addition, a great diversity of tools was used to assess the adherence to the MedDiet, as shown in our results. Also, one may say that occasionally different

methods were based on the same reference (MedDiet score and aMed) and that there were several ranges of scoring within the same method (MedDiet score). Among the methods used to evaluate the adherence to the MedDiet, discrepancies in validity and reliability were found. MedDiet score based on Trichopoulou is valid[53] but information on its reliability was not found. MedDiet score developed for ATTICA study showed to be valid[54]. NU-AGE index's validity still needs to be studied[50] and it provides reliable[55] data to evaluate short-term current dietary intake. The information on validity and reliability on the aMedDiet score based on Trichopoulou, jMed, MedDiet score based on Goulet and Italian and Greek scores is still scarce. MEDAS is found to be valid and reliable[56], as well as KIDMED[57], being the most accurate methods used among the included studies. This high heterogeneity of tools to assess the adherence to the MedDiet also contributes to the difficulty in comparing the results between studies and, therefore, the interpretation of the results on the association between the adherence to MedDiet and salt/sodium intake.

One of the studies that used urinary sodium excretion as the method to evaluate salt intake demonstrated a positive association between the adherence to the MedDiet and Na excretion in men, but not in women[25]. Men frequently choose processed foods with sizeable salt contents and add salt to the table more often than women, who are more likely to report limiting their consumption of salt and processed foods[58, 59]. Processed foods are not a predominant element of the MedDiet and it is therefore expected that the greatest source of sodium comes from added salt, something that is commonly ignored. Another factor that may influence the amount of sodium intake is the quantity of ingested food; the higher the amount of ingested food, the higher the sodium intake is expected to be[25].

Men's dietary intake is usually higher than women's due to their higher energy requirements, which may explain this dominant outcome in men.

According to the EPHPP Quality Assessment Tool, from the total of 28 articles included in this review, 25 were classified as weak, three as moderate[23, 26, 45] and none as strong. The majority of the included studies did not indicate the percentage of relevant confounders that were controlled, which led to a mostly weak classification in the "confounders" section.

Although it might have been useful to include grey literature in this review due to the small number of articles found on the topic, it would have been expected that the number of eligible results would have been small.

Conclusions

The discrepancy in methodologies used to assess both sodium intake and MedDiet adherence, as well as the low quality of the studies conducted in this area, may justify the inconsistent findings found in this review. It also highlights the importance implement more robust research in order to a better understanding of the possible relation between MedDiet and salt/sodium intake. Further studies focusing on this association are needed in the future, especially using a gold-standard methodology to estimate sodium, which is the gold standard method for evaluating sodium intake, as well as using the most suitable method to evaluate the adherence to the MedDiet, according to the population characteristics.

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APPENDIX 1

Table 1- General study characteristics of included studies

Title/Year/Country	Study Design	Main Aim	Population	Method Used to Evaluate the Adherence to The MedDiet	Method Used to Evaluate Salt Intake	Outcome	Main Finding
Cross-comparison of diet quality indices for predicting chronic disease risk: Findings from the Observation of Cardiovascular Risk Factors in Luxemburg[39] (2015, Luxembourg)	Nationwide cross-sectional population-based survey	To compare the ability of 5 diet quality indices, to detect changes in chronic disease risk biomarkers	N= 1352 non-institutionalized general adult population, 18-69 years	MedDiet Score as described by Trichopoulou	134-item semi-quantitative FFQ	Spearman's correlation coefficient for Na and MedDiet Score was 0,12 (p<0,001)	A higher adherence to the MedDiet was associated with a higher Na intake
Older Australians Can Achieve High Adherence to the MedDiet during a 6 Month Randomized Intervention; Results from the Medley Study[40] (2017, Australia)	Randomized controlled trial (6-month randomized controlled clinical dietary intervention trial)	To determine if an older population could adhere to a MedDiet, assessing the effect of this dietary pattern on cognitive function after 6 months, compared to the habitual Australian diet	N= 137 participants (70 in the MedDiet group, 67 in the Habitual Diet group), ≥ 65 years at baseline	15-point MedDiet Score, adapted from Trichopoulou	3-day weighed food record (Na intake) 24-h Urinary (Na excretion)	Assessed by a 3-day weighed food record, the mean Na intake was 264,5±8,8mg/MJ at baseline and 202,3± 6,8mg/MJ after 4 months of intervention (p<0,001). At 4 months, the control group (CG) had a Na intake of 259,5±7,0mg/MJ, significantly higher than the MedDiet group (p<0,001). Also, K intake at 4 months was higher in the MedDiet group than in the CG, 442,5±9,0mg/MJ and 403,1±9,3mg/MJ, respectively (p<0,01). Assessed by 24h urinary Na excretion, the values in baseline and after 6 months were 113,9±5,4mmol/24h and 107,8±4,9mmol/24h, respectively, with a p value of 0,85. The excretion of K was 79,7±2,7 at baseline and 80,7±3,0 (p=1). For both Na and K excretion, there were not significant differences between the MedDiet and CG (p=0,47 and 0,24, respectively)	The adherence to the MedDiet was associated with a lower Na intake, but a inverse association was not proved to NA excretion compared to the CG
MedDiet reduces 24-hour ambulatory blood pressure, blood glucose, and	Randomized controlled trial	To understand the mechanisms of CVD protection	N= 235 participants (56,5% women; aged 60-80 and 43,5% men aged 55-80), at	MEDAS	Dietary records	Although no recommendations on the use of salt were given, Na intake decreased in all MedDiet groups and CG by 10 to 15 mmol/d (0,6-0,9 g of salt) from a	Na intake decreased in all groups at the end of

lipids: one-year randomized, clinical trial[22] (2014, Spain)		related to the MedDiet, supplemented with extravirgin olive oil or nuts	high cardiovascular risk, but with no CVD at enrollment			moderate baseline intake of 92 to 98 mmol/d (5-6 g of salt).	the intervention. Good adherence to the MedDiet seems to be associated with moderate Na intake
Association between Cardiometabolic Profile and Dietary Characteristics among Adults with Type 1 Diabetes Mellitus[36] (2015, Canada)	Cross Sectional	To examine the association between cardiometabolic profile and alignment of the diet with Canadian nutrient recommendations for T1DM and with a Mediterranean-style dietary pattern among adults with T1DM	N= 118 adults with T1DM, ≥18 years	MedDiet score (range- 0 to 44) adapted from Goulet	3-day food record	58 participants were classified as having a Lower MedDiet Score (<19) and 60 a Higher MedDiet Score (≥ 19). The ones with the lower adherence to this dietary pattern had a mean Na consumption of 3222±1420 mg/day and those with the higher adherence had an intake of 2677±840mg/day (p=0,01)	Higher adherence to the MedDiet was associated with a lower Na intake. Participants with a higher MedDiet score had lower Na intakes
A remote nutritional intervention to change the dietary habits of patients undergoing ablation of atrial fibrillation: Randomized controlled trial[23] (2020, Spain)	Randomized Controlled Trial (single-blinded trial)	To assess the effectiveness of a MedDiet-based nutritional intervention in obtaining favorable dietary changes in the context of a secondary prevention trial of atrial fibrillation	N= 720 participants. 549 were men (76%) and 171 were women (24%), mean age was 59.7±10.7 years	MEDAS	147-item semiquantitative FFQ	The intervention group had a mean baseline Na intake of 3390mg/day. After 1 year in intervention, ie following a MedDiet, this group's mean Na intake was 2831mg/day, showing a mean decrease of 558,4mg/day (p=0,002). At 2 years follow up, this group's mean Na intake was 2586mg/day, showing a decrease of 803,6mg/day in the daily Na intake (p <0,001), IC 95%	The group with higher adherence to MedDiet had a decrease in the intake of Na, when compared to the CG
Adherence to Healthy Dietary Patterns and Risk of CKD Progression and	Prospective cohort	To define the associations of 4 healthy dietary patterns with	N= 2403 men and women, with an estimated glomerular filtration	aMed score (0 to 9), based on Trichopoulou	National Cancer Institute 124-item Diet	Participants were divided in tertiles. Participants in Tertile 1 had a baseline median aMed score of 2 and showed a mean Na intake of 2521±1237 mg/day.	Participants with higher adherence to aMed seems

Study	Design	Objective	Population	Index	Na measurement	Results	Conclusion
All-Cause Mortality: Findings from the CRIC (Chronic Renal Insufficiency Cohort) Study[18] (2021, USA)		risk of CKD progression and all-cause mortality among people with CKD	rate 20-70 ml/min/1.73 m2, 21-74 years		History Questionnaire (FFQ) and Diet*Calc software	Participants in Tertile 3 had a median aMed score of 6,5 and showed a 3275±388 mg/day	to have a higher Na intake
Mediterranean-Style Diet Improves Systolic Blood Pressure and Arterial Stiffness in Older Adults[44] (2019, Italy, UK, Netherlands, Poland, France)	Randomized controlled trial	To determine the effect of a Mediterranean-style diet on blood pressure and arterial stiffness	N= 1128 participants, 65 to 79 years	NU-AGE index	24h Urinary Na excretion	After 1 year of follow-up, the participants in the intervention group (focus in increase adherence to MedDiet) had a decrease in levels of 24h urinary Na concentrations, compared to CG (between-group difference: -5,5 mmol/L; 95% CI, -19,6 to 8,6; p=0,45). Only in males, it was found a significant decrease in levels of 24h urinary Na concentrations (between-group difference -27,1 mmol/L; 95% CI, -53,3 to -1,0; p=0,04)	Male participants with better adherence to the MedDiet had lower Na intake
Diet quality is independently associated with weight status in children aged 9-10 years[33] (2011, UK)	Cohort	To develop modified dietary indexes for use in children and to determine if they were associated with indicators of weight status and dietary intake	N= 2064 children (926 boys, 1138 girls), 9-10 years	MedDiet Score	4 day dietary records	Quintiles 1 and 5 of the MedDiet Score didn't differ for Na [P > 0,05 (ANCOVA)]	No differences in salt intake were found between groups with higher adherence to the MedDiet, versus lower adherence
Development of a MedDiet score adapted to Japan and its relation to obesity risk[37] (2016, Japan)	Cross-sectional	To develop an instrument to measure MedDiet adherence adapted to a Japanese diet and to examine its association with obesity risk	N= 1048 participants (645 men and 403 women), 18-68 years	jMD score, focusing on 13 components	58-item self-administered dietary history questionnaire (FFQ)	Participants with jMD score 0-4 (low adherence to MD) (n=310) had a salt intake of 12,4±3,2g/day. Participants with jMD score 5-7 (n=616) had a salt intake of 13,7±3,2 g/day. Participants with jMD score 8-13 (higher adherence to MedDiet) (n=122) had a salt intake of 15,9±3,9 g/day (p<0,001)	A higher adherence to the jMD was associated with a higher salt intake
Nutritional status and adherence to the MedDiet in children with epilepsy[29] (2022, Turkey)	Cross-sectional	To determine the nutritional status of children with epilepsy and to evaluate compliance with the MedDiet	N= 85 children diagnosed with epilepsy for at least 1 year, 2-18 years	KIDMED score	24h dietary recall	Kids with a high adherence to the MedDiet (≥ 8 points) had a mean Na intake of 1814,18±1207,48 mg/day; Kids with moderate adherence (4-7 points) had a mean Na intake of 1026,58±650,65mg/day and those with low adherence (≤3 points) had a mean Na intake of 1300,748±883,87mg/day (p=0,005). The relation between the adherence to MedDiet and Na was r=0,011 (Pearson correlation); (p=0,954)	No relation was found between the adherence to the MedDiet and salt intake
High Na intake of children through	Cross-sectional,	To identificate the total Na	N= 4580 children, 10-12 years	KIDMED score	Semi-quantitative	Children with a low total Na intake (<1500mg/day) showed a mean KIDMED score of 3,55± 2,17. Children	Kids with high Na intake

'hidden' food sources and its association with the MedDiet: the GRECO study[31] (2011, Greece)	population-based survey	intake, as well as 'hidden' Na intake from food sources in a young population			food frequency questionnaire	with a moderate total Na intake (1500-2200 mg/day) had a mean KIDMED score of 4,21±2,12. The ones with a high total Na intake (>2200 mg/day) had a mean KIDMED score of 3,86±2,25. Only 4.5% of children had an optimal adherence to the MedDiet	seem to have higher adherence to the MedDiet
Na and K Content of Foods Consumed in an Italian Population and the Impact of Adherence to a MedDiet on Their Intake[41] (2021, Italy)	Cross Sectional	To assess dietary Na and K and to evaluate how they may be influenced by adherence to dietary patterns known to be healthy, namely those related to the MedDiet	N= 719 participants, (319 men and 400 women) residents in one of the studied italian provinces, > 18 years	Italian Mediterranean Index	FFQ, implemented within the 'European Prospective Investigation into Cancer and Nutrition' project	Participants with Italian MedDiet Index below the median (< 4) (N = 275) had a mean daily Na intake of 2164,7mg. Participants with score above the median (≥ 4) (N = 444) had a mean daily Na intake of 2143,8mg. p=0,755 (t-test)	Higher adherence to MedDiet and MIND patterns have no effect on Na intake. But may have influence on K, favoring the decrease in the Na/K ratio
Associations of 24-Hour Urinary Na and K Excretion with Cardiac Biomarkers: The Maastricht Study[42] (2020, Netherlands)	Cohort study	To examine associations of 24h urinary Na and K excretion with markers of cardiomyocyte injury and cardiac dysfunction	N= 2961 participants, 40-75 years	Greek MedDiet score	24h urinary Na excretion	Participants were divided into quintiles, according to their 24h urinary Na excretion levels. Q1 (n = 592) had a mean Greek MedDiet score of 5 (3-6); Q2 (n = 593) 4 (3-6); Q3 (n = 592) 4 (3-6); Q4 (n = 592) 5 (3-6) and Q5 (n = 592) 4 (3-5)	No association was found between the adherence to the MedDiet and salt intake
Urinary Na-to-K ratio: a simple and useful indicator of diet quality in population-based studies[27] (2021, Iran)	Prospective study	To investigate if urinary Na-to-K ratio could be related to dietary patterns, and how their index can be used as an indicator of diet quality	N= 1864 adults, ≥ 19 years	MedDiet score, based on Trichopoulou	24h urinary Na excretion (measured in the morning spot urine samples)	The adherence to the MedDiet was divided into tertiles. Tertile 1 had a mean Na excretion of 136.5 ± 54.58 mmol/L; Tertile 2 128.0 ± 54.79mmol/L; Tertile 3 128.2 ± 55.94mmol/L. P=0.007. MedDietary pattern (β = − 0.07; 95% CI − 0.09, − 0.01) were inversely associated with urinary Na-to-K ratio. This association was made with a multivariable-adjusted linear regression.	A higher adherence to the MedDiet was associated with a lower Na-to-K ratio (higher intake of vegetables)
Association between adherence to the MedDiet and renal function biomarkers and cardiovascular risk factors among	Cross-sectional	To determine the association between level of adherence to a MedDiet, renal and CVD risk	N= 270 participants with Diabetes Nephropathy, Mean age 65.91 ± 9.71	MedDiet score, based on Trichopoulou	168-semi-quantitative food frequency questionnaire	Participants were classified into tertiles, according to their adherence to the MedDiet. Participants in Tertile 1 had a mean Na intake of 6343.00 ± 11061,31mg/d. Tertile 2 (6156,11 ± 11016,22mg/d). Tertile 3 (531,55 ± 11378,44mg/d). P=0,273 was	No association was found between higher adherence to

diabetic patients with nephropathy[28] (2020, Iran)		factors among patients with Diabetes Nephropathy				calculated using an analysis of covariance. P < 0,05 was considered significant	the MedDiet and Na intake
Urinary Na Excretion and Adherence to the MedDiet in Older Adults[25] (2021, Portugal)	Cross-sectional observational	To quantify the association between Na excretion and the adherence to the MedDiet in the elderly	N= 1321 Portuguese adults (766 women and 555 men), ≥65 years	MEDAS	24h urinary Na excrection	Odds ratios was calculated for the association between the adherence to the MedDiet and adequacy of Na excretion. Excessive Na excretion was associated with a high adherence to the MedDiet in men (OR = 1,94; 95% CI: 1,03–3,65). No such association was observed in women (OR = 0,91; 95% CI: 0,62-1,34)	A higher adherence to the MedDiet was associated with a higher Na excretion only in men
Dietary patterns, their nutrients, and associations with socio-demographic and lifestyle factors in older new zealand adults[43] (2020, New Zealand)	Cross-sectional	To identify and describe the dietary patterns in an older population, and to examine associations between dietary patterns and socio-demographic and lifestyle factors	65-74 year old men and women living in Auckland, New Zealand	Standardised dietary pattern scores	109-item Food Frequency Questionnaire (FFQ)	Effect size of correlations (adjusted R2) between MedDiet adherence and nutrients was calculated. Nutrients were all significant after Bonferroni adjustment (adjusted p-value < 0,05). However, no correlation was found between MedDiet and Na.	No association/c orrelation was found between the adherence to the MedDiet and Na intake
Diet quality scores in relation to metabolic risk factors in Japanese adults: a cross-sectional analysis from the 2012 National Health and Nutrition Survey[38] (2019, Japan)	Cross-sectional	To study the associations between the overall quality of japanese diets and metabolic risk factors	N=15618 participants (6552 men and 9066 women), >20 years old	MedDiet score 0-9, adapted from Trichopoulou	1-day weighed dietary record	A linear regression was made. MEN: Na intake (mg/4184 kJ) ß=82.66; SE=5.58; P< 0.0001. WOMEN: Na (mg/4184 kJ) ß=101.62; SE=5.05; P< 0.0001. In both man and women, a higher adherence is associated with a higher Na intake (ß is positive) and that increase is statistically significant	A higher adherence to the MedDiet was associated with a higher Na intake
Adherence to a Mediterranean style eating pattern and risk of diabetes in a U.S. prospective cohort study[19] (2020, USA)	Prospective cohort study	To investigate atherosclerosis etiology and clinical sequelae and to assess how CVD risk factors differ by race, sex, place, and time	N= 11991 participants free of chronic disease at baseline, 45-65 years	aMed score, adapted from Trichopoulou	66-item semi-quantitative FFQ	Participants were divided into quintiles, based on their aMed scores. The Quintile 1: aMed score 0-2 (n = 2430), had a mean Na intake of 877 ± 185,2mg/1000 kcal. The Quintile 2: aMed score 3-4 (n = 4573) had a mean Na intake of 905 ± 182,7mg/1000 kcal. The Quintile 3: aMed score of 5 (n = 2152) showed a mean Na intake of 929 ± 171,5mg/1000 kcal. The Quintile 4: aMed score of 6 (n = 1589) had a mean Na intake of 951 ± 166,5mg/1000 kcal.	Na intake was higher for higher quintiles of adherence to MedDiet

Title	Study type	Objective	Sample	Score	Dietary assessment	Results	Conclusion
						The Quintile 5: aMed score 7-9 (n = 1247) had a mean Na intake of 963 ± 162,4mg/1000 kcal	
Adherence to a MedDiet Is Associated with Lower Depressive Symptoms among U.S. Adults[20] (2022, USA)	Cross-sectional	To understand the role of dietary patterns on depressive symptoms	N= 11769 adults with depressive symptoms 20-79 years	aMed score, adapted from Trichopoulou	24h diet recall	Participants were divided into quintiles, according to their aMED scores. People in the Q1 aMED (n=3621) had a mean Na intake of 1688,0±11,7mg/day; Q2 aMED (n=2689) had a mean Na intake of 1695,0±13,2mg/day. Q3 aMED (n=4155) had a mean Na intake of 1695,6± 9,5mg/day. Q4 aMED had a mean Na intake of 1628,9±15,9 mg/day. (n=1304)	Participants in the highest quintile of adherence to MedDiet have the lowest salt intake
Low MedDiet scores are associated with reduced kidney function and health related quality of life but not other markers of cardiovascular risk in adults with diabetes and chronic kidney disease[35] (2021, Canada)	Post-hoc analysis of a Randomized Control Trial and longitudinal study	To investigate the association between diet quality, using MedDiet Score and health outcomes	N= 50 adults with T1 or T2 DM and Stage 1-4 CKD who were not vitamin D deficient, 18-80 years	MedDiet Score. 0-9, adapted from Trichopoulou	3-day food records	People were divided into 3 groups, according to their MedDiet Score. The ones with Low MedDiet Score (0 to 2) (n=8) had a mean Na intake of 3772 (2435-5092) mg/day; Moderate MEDDIET SCORE (3 to 5) (n=30) had a mean Na intake of 2288 (1697-3152) mg/day. High MEDDIET SCORE (>=6) had a mean Na intake of 1932 (1495-2506) mg/day (p=0.64)	No association was found between higher adherence to the MedDiet and Na intake
MedDiet adherence and risk of incident kidney stones[45] (2020, Location not available)	Prospective cohort study, longitudinal	To study the association between adherence to the MedDiet and the risk of incident kidney stones	N= 193527 participants, 25-75 years	aMed score, adapted from Trichopoulou	24h urinary Na excrection	24-h urinary Na was calculated for different aMed scores. aMed=0: 158mmol; aMed=1: 151mmol; aMed=2: 154mmol; aMed=3: 155mmol; aMed=4: 152mmol; aMed=5: 149mmol; aMed=6: 152mmol; aMed=7: 152mmol; aMed=8-9: 143mmol. P value for trend was <0,001	The highest adherence to a MedDiet was associated with a lower Na excretion
Contrasting effects of short-term Mediterranean and vegan diets on microvascular function and cholesterol in younger adults: A comparative pilot study[34] (2018, UK)	Comparative Pilot Study	To understand the influence of 2 dietary patterns (MedDiet and Vegan Diet) on CVD markers	N= 23 participants 18-35 years	MEDAS	A 3-day food diary; Nutritics™ software and its proprietary databank (Nutritics Ltd product version 1.7, Dublin, Ireland)	The participants were exposed to the MedDiet, increasing their adherence to it during the intervention. The pre-intervention sodium intake was 1569±763mg/day; the post-intervention sodium intake was 2146±785 mg/day, Δ Sodium (MedDiet = 577 ± (914), p> 0.05 within the group and p ≤ 0.05, between groups. Post-intervention, differences between groups emerged for Sodium (MedDiet = 2146 ± (785), VD = 1161 ± 852, p = 0.018; d = 1.10), Δ Sodium (MD = 577 ± (914), VD = −931 (586), p = ≥ 0.001; d = 1.95)	No association was found within the group
Increasing MedDiet adaptation in adults decreases energy	Cross-sectional	To determine the relationship between	N= 307, 18-64 years	MEDAS	24h dietary recall	Female participants with a low MedDiet Score (≤ 5)(n=85) had a mean sodium intake of 1715±794 mg/day and the ones with a medium MedDiet Score	A higher adherence to the MedDiet

intake[30] (2021, Turkey)		MedDiet and nutritional status in adult individuals				(6-10) (n=75) had a mean of 1591,7±672,3mg/day (p=0,294). Male participants with a low MDS (≤ 5)(n=92) had a mean sodium intake of 2478,7±1277 mg/day and the ones with a medium MedDiet Score (6-10) (n=55) had a mean of 2065,9±1017,3mg/day (p=0,043). The analysis of all participants data showed that the ones who had low MedDiet Score (<=5)(n=177) had a mean sodium intake of 2111,9±1135,9 mg/day and the ones with a medium MDS (6-10) (n=130) had a mean of 1792,3±864,8mg/day (p=0,005). P values were calculated with a Two independent samples t test	was associated with a lower Na intake in MALES and in the whole sample. No association was found in females
Na and K Intake in Healthy Adults in Thessaloniki Greater Metropolitan Area- The Salt Intake in Northern Greece (SING) Study[32] (2017, Greece)	Cross-sectional survey	To assess dietary Na and K intakes in a sample in Greece and to determine if adherence to a MedDiet is related to different Na intakes or Na-to-K ratio	N= 252 participants, (45.2% men and 54.8% women), 18-75 years	11-item MedDiet Score (range 0-55), specially developed for ATTICA study	24h urinary Na excretion	People were divided into quartiles, according to their MedDiet Scores. Each quartil had the following mean sodium intake: Q1 (MedDietScore≤28)- 4079± 1893mg/day; Q2 (>28, ≤31)- 4361±1746mg/day; Q3 (>31, ≤34)- 3972±1565mg/day; Q4 (>34)- 4424±1636mg/day. P value, calculated by ANOVA was 0,453	There were no significant differences in sodium across MedDietScore quartiles
High Adherence to MedDiet Is Not Associated with an Improved Na and K Intake[26] (2021, Portugal)	Randomized control study	To quantify Na and K excretion and assess its association with the adherence to a Mediterranean dietary pattern in adults	N= 102 participants, (48% male, 52% female) >18 years	aMED score, adapted from Trichopoulou	24h urinary Na excretion	The mean sodium urinary excretion was 3216±1307 mg/day (8.98 g/d of salt). No statistically significant differences were found when comparing mean sodium excretion in the low-moderate versus high adherence to MedDiet category in both sexes (respectively, 3868±1390 vs. 3807 ± 1179 mg/day, in men, and 2591±966 vs. 2768±1116 mg/day, in women	No statistically significant differences were found when in the low-moderate versus high adherence to MedDiet
Prospective study of Dietary Approaches to Stop Hypertension-and Mediterranean-style dietary patterns and age-related cognitive change: The Cache County Study on Memory, Health and Aging[21] (2013, USA)	Cohort study	To examine associations between Dietary Approaches to Stop Hypertension, Mediterranean-style dietary patterns and cognitive changes	N= 3580 participants, ≥65 years	MedDiet Score, 8 components	Food-frequency questionnaire	Participants in the quintile 1 had a mean sodium intake of 2555,4; 712,9 (mg), in the quintile 2 had 2574,1; 583,8 (mg), in the quintile 3 had 2611,9; 506,5 (mg), in the quintile 4 had 2625,6; 500,0 (mg) and in the quintile 5 had 2623,5; 577,3; p = 0,011	Higher adherence to MedDiet was associated with higher sodium intake

Dietary patterns and nutritional adequacy in a Mediterranean country[24] (2009, Spain)	Prospective cohort study	To analyse the adequacy of nutrient intake of a posteriori defined MedDiet and Western Diet patterns in the Seguimiento Universidad de Navarra (SUN) cohort	N= 17197 participants of the SUN cohort, <80 years	Everyone received a factor score for each identified pattern. A higher score suggests better adherence to a certain dietary pattern	Food-frequency questionnaire	Participants were classified into quintiles, according to their adherence to the MedDiet. Participants in Q1 (n=3439) had a mean sodium intake of 4178±2023 mg/day; Q2 (n=3440) 4064±2061mg/day. Q3 (n=3439) 3958 ± 1939mg/day; Q4 (n=3440) 3906±2528mg/day; Q5 (n=3439) 3616±1926mg/day.	A higher adherence to the MedDiet was associated with a lower Na intake

Table 2- Quality Assessment of included studies

Title/Year	Selection Bias	Study Design	Confounders	Blinding	Data Collection Methods	Withdrawals and Drop-Outs	Global Rating
Cross-comparison of diet quality indices for predicting chronic disease risk: Findings from the Observation of Cardiovascular Risk Factors in Luxembourg (ORISCAV-LUX) study[39] (2015)	WEAK	WEAK	WEAK	WEAK	MODERATE	WEAK	WEAK
Older Australians Can Achieve High Adherence to the MedDiet during a 6 Month Randomized Intervention; Results from the Medley Study[40] (2017)	WEAK	STRONG	WEAK	WEAK	MODERATE	STRONG	WEAK
MedDiet reduces 24-hour ambulatory blood pressure, blood glucose, and lipids: one-year randomized, clinical trial[22] (2014)	MODERATE	STRONG	WEAK	MODERATE	WEAK	STRONG	WEAK
Association between Cardiometabolic Profile and Dietary Characteristics among Adults with Type 1 Diabetes Mellitus[36] (2015)	MODERATE	WEAK	WEAK	MODERATE	MODERATE	STRONG	WEAK
A remote nutritional intervention to change the dietary habits of patients undergoing ablation of atrial fibrillation: Randomized controlled trial[23] (2020)	MODERATE	STRONG	WEAK	MODERATE	MODERATE	STRONG	MODERATE
Adherence to Healthy Dietary Patterns and Risk of CKD Progression and All-Cause Mortality: Findings from the CRIC (Chronic Renal Insufficiency Cohort) Study[18]. (2021)	MODERATE	WEAK	WEAK	WEAK	MODERATE	MODERATE	WEAK
Mediterranean-Style Diet Improves Systolic Blood Pressure and Arterial Stiffness in Older Adults[44]. (2019)	WEAK	STRONG	WEAK	WEAK	WEAK	STRONG	WEAK
Diet quality is independently associated with weight status in children aged 9-10 years[33] (2011)	MODERATE	WEAK	WEAK	WEAK	MODERATE	STRONG	WEAK
Development of a MedDiet score adapted to Japan and its relation to obesity risk[37] (2016)	MODERATE	WEAK	WEAK	WEAK	MODERATE	WEAK	WEAK
Nutritional status and adherence to the MedDiet in children with epilepsy[29] (2022)	MODERATE	WEAK	WEAK	MODERATE	WEAK	STRONG	WEAK
High Na intake of children through 'hidden' food sources and its association with the MedDiet: the GRECO study[31](2011)	STRONG	WEAK	WEAK	MODERATE	STRONG	STRONG	WEAK
Na and K Content of Foods Consumed in an Italian Population and the Impact of Adherence to a MedDiet on Their Intake[41] (2021)	WEAK	WEAK	WEAK	MODERATE	MODERATE	STRONG	WEAK
Associations of 24-Hour Urinary Na and K Excretion with Cardiac Biomarkers: The Maastricht Study[42] (2020)	MODERATE	WEAK	WEAK	MODERATE	MODERATE	WEAK	WEAK
Urinary Na-to-K ratio: a simple and useful indicator of diet quality in population-based studies[27] (2021)	MODERATE	WEAK	WEAK	MODERATE	STRONG	WEAK	WEAK

Association between adherence to the MedDiet and renal function biomarkers and cardiovascular risk factors among diabetic patients with nephropathy[28] (2020)	MODERATE	WEAK	WEAK	MODERATE	STRONG	WEAK	WEAK
Urinary Na Excretion and Adherence to the MedDiet in Older Adults[25] (2021)	MODERATE	WEAK	WEAK	MODERATE	STRONG	WEAK	WEAK
Dietary patterns, their nutrients, and associations with socio-demographic and lifestyle factors in older new zealand adults[43] (2020)	MODERATE	WEAK	WEAK	MODERATE	MODERATE	WEAK	WEAK
Diet quality scores in relation to metabolic risk factors in Japanese adults: a cross-sectional analysis from the 2012 National Health and Nutrition Survey[38] (2019)	MODERATE	WEAK	WEAK	MODERATE	WEAK	WEAK	WEAK
Adherence to a Mediterranean style eating pattern and risk of diabetes in a U.S. prospective cohort study[19] (2020)	MODERATE	WEAK	WEAK	MODERATE	MODERATE	WEAK	WEAK
Adherence to a MedDiet Is Associated with Lower Depressive Symptoms among U.S. Adults[20] (2022)	STRONG	WEAK	WEAK	MODERATE	STRONG	STRONG	WEAK
Low MedDiet scores are associated with reduced kidney function and health related quality of life but not other markers of cardiovascular risk in adults with diabetes and chronic kidney disease[35] (2021)	WEAK	STRONG	WEAK	MODERATE	STRONG	WEAK	WEAK
MedDiet adherence and risk of incident kidney stones[45] (2020)	MODERATE	MODERATE	WEAK	MODERATE	STRONG	STRONG	MODERATE
Contrasting effects of short-term Mediterranean and vegan diets on microvascular function and cholesterol in younger adults: A comparative pilot study[34] (2018)	MODERATE	WEAK	WEAK	MODERATE	STRONG	STRONG	WEAK
Increasing MedDiet adaptation in adults decreases energy intake[30] (2021)	WEAK	WEAK	WEAK	MODERATE	STRONG	STRONG	WEAK
Na and K Intake in Healthy Adults in Thessaloniki Greater Metropolitan Area-The Salt Intake in Northern Greece (SING) Study[32] (2017)	MODERATE	WEAK	WEAK	MODERATE	STRONG	WEAK	WEAK
High Adherence to MedDiet Is Not Associated with an Improved Na and K Intake[26] (2021)	MODERATE	STRONG	WEAK	MODERATE	STRONG	STRONG	MODERATE
Prospective study of Dietary Approaches to Stop Hypertension-and Mediterranean-style dietary patterns and age-related cognitive change: The Cache County Study on Memory, Health and Aging[21] (2013)	STRONG	WEAK	WEAK	MODERATE	STRONG	STRONG	WEAK
Dietary patterns and nutritional adequacy in a Mediterranean country[24] (2009)	MODERATE	WEAK	WEAK	MODERATE	MODERATE	STRONG	WEAK