Beyond Diabetes, Obesity, and Cardiovascular Disease: An Evidence Map of Anti-Inflammatory Diet and Related Dietary Interventions for the Prevention and Management of Chronic Health Conditions

October 2024

U.S. Department of Veterans Affairs
Veterans Health Administration
Health Systems Research

Recommended citation: Newberry S, Chen D, Shekelle P, Mak S, Begashaw M, De Vries G, Miake-Lye I. Beyond Diabetes, Obesity, and Cardiovascular Disease: An Evidence Map of Anti-Inflammatory Diet and Related Dietary Interventions for the Prevention and Management of Chronic Health Conditions. Washington, DC: Evidence Synthesis Program, Health Systems Research, Office of Research and Development, Department of Veterans Affairs. VA ESP Project #05-226; 2024.

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PREFACE

The VA Evidence Synthesis Program (ESP) was established in 2007 to conduct timely, rigorous, and independent systematic reviews to support VA clinicians, program leadership, and policymakers improve the health of Veterans. ESP reviews have been used to develop evidence-informed clinical policies, practice guidelines, and performance measures; to guide implementation of programs and services that improve Veterans' health and wellbeing; and to set the direction of research to close important evidence gaps. Four ESP Centers are located across the US. Centers are led by recognized experts in evidence synthesis, often with roles as practicing VA clinicians. The Coordinating Center, located in Portland, Oregon, manages program operations, ensures methodological consistency and quality of products, engages with stakeholders, and addresses urgent evidence synthesis needs.

Nominations of review topics are solicited several times each year and submitted via the ESP website. Topics are selected based on the availability of relevant evidence and the likelihood that a review on the topic would be feasible and have broad utility across the VA system. If selected, topics are refined with input from Operational Partners (below), ESP staff, and additional subject matter experts. Draft ESP reviews undergo external peer review to ensure they are methodologically sound, unbiased, and include all important evidence on the topic. Peer reviewers must disclose any relevant financial or non-financial conflicts of interest. In seeking broad expertise and perspectives during review development, conflicting viewpoints are common and often result in productive scientific discourse that improves the relevance and rigor of the review. The ESP works to balance divergent views and to manage or mitigate potential conflicts of interest.

ACKNOWLEDGMENTS

The authors are grateful to Kathryn Vela for literature searching, Zhaoping Li for content expertise, external peer reviewers, and the following individuals for their contributions to this project:

Operational Partners

Operational partners are system-level stakeholders who help ensure relevance of the review topic to the VA, contribute to the development of and approve final project scope and timeframe for completion, provide feedback on the draft report, and provide consultation on strategies for dissemination of the report to the field and relevant groups.

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Technical Expert Panel

To ensure robust, scientifically relevant work, the technical expert panel (TEP) guides topic refinement; provides input on key questions and eligibility criteria, advising on substantive issues or possibly overlooked areas of research; assures VA relevance; and provides feedback on work in progress. TEP members included:

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Disclosures

This report was prepared by the Evidence Synthesis Program Center located at the **VA Greater Los Angeles Healthcare System,** directed by Paul Shekelle, MD, PhD and Isomi Miake-Lye, PhD and funded by the Department of Veterans Affairs, Veterans Health Administration, Health Systems Research.

The findings and conclusions in this document are those of the author(s) who are responsible for its contents and do not necessarily represent the views of the Department of Veterans Affairs or the United States government. Therefore, no statement in this article should be construed as an official position of the Department of Veterans Affairs. The final research questions, methodology, and/or conclusions may not necessarily represent the views of contributing operational and content experts. No investigators have affiliations or financial involvement (*eg*, employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties) that conflict with material presented in the report.

Executive Summary

KEY FINDINGS

- Proposed impacts of anti-inflammatory dietary patterns on—or associations of these dietary patterns with—risks for some chronic diseases and mortality lack a strong evidence base. This is partly due to the small numbers of original studies, most of which are observational in design.
- Although multiple anti-inflammatory dietary patterns, including the DASH diet, Mediterranean diet, and to a lesser extent, vegetarian/plant-based diets, appear to be associated with lower risks for some chronic conditions, including hypertension, some types of cancer, and liver diseases, these observations could be due to foods excluded from these dietary patterns, foods they include, or both.
- This evidence map was not intended to support recommendations regarding adoption of particular diets. Despite lack of a full understanding of how anti-inflammatory diets might be beneficial for preventing and managing some chronic conditions, the demonstrated benefits for other conditions and apparent lack of harms suggest that there may be no downside to adopting one of these diets. However, the larger finding is the gap in the evidence base underlying the possible effect of the diets on the conditions covered in this report.

BACKGROUND

Six out of 10 adults in the United States have at least one chronic health condition, and chronic diseases are the nation's leading cause of death and disability (causing 7 in 10 deaths each year). Chronic health conditions include heart disease, cancer, diabetes, chronic pain, asthma, inflammatory gastrointestinal disorders, degenerative diseases, obesity, and Alzheimer's disease/dementia. Some evidence supports a common role for inflammation as a contributory factor across these conditions. Other lines of evidence have supported a role for particular diets in reducing markers of inflammation. Thus, there is considerable interest in assessing the role of diets with anti-inflammatory properties in preventing or managing chronic disease conditions. Evidence is plentiful for some conditions, such as diabetes, obesity, and cardiovascular disease, but sparse for others. The aim of this synthesis is to develop evidence maps that provide a visual overview of the distribution of evidence for the role of anti-inflammatory dietary patterns on the prevention and management of chronic health conditions where anti-inflammatory diet and related interventions are not yet established as one standard of care. The evidence maps have accompanying narrative that helps stakeholders interpret the state of the evidence to inform policy and clinical decision-making. The aim of this report is to summarize the body of evidence to date linking dietary patterns believed to have anti-inflammatory properties with outcomes for a set of relatively understudied health conditions; this report is not intended to issue recommendations about pursuing any particular dietary pattern.

METHODS

DATA SOURCES AND SEARCHES

Search strategies were developed with an experienced medical librarian who is expert in literature reviews. Searches were conducted in bibliographic databases conducted searches from inception to July

2023 in bibliographic databases (Medline, Cumulated Index to Nursing and Allied Health Literature [CINAHL], Cochrane Database of Systematic Reviews [CDSR]), non-bibliographic databases (Canadian Agency for Drugs and Technologies in Health [CADTH]), National Center for Biotechnology Information [NCBI] Bookshelf, VA Dimensions), and in PROSPERO for reviews in development.

STUDY SELECTION

Titles of potentially eligible reviews were screened in duplicate for relevance by 5 authors independently; any article chosen by at least 1 reviewer based on the title went on for abstract screening. Abstracts were then reviewed in duplicate, with any discrepancies resolved by group discussion. All titles and abstracts were selected based on the eligibility criteria described in the section below.

Eligible publications were systematic reviews (SRs) of studies of 1) adults that examined the efficacy or effectiveness of 2) the Dietary Approaches to Stop Hypertension (DASH) diet, Mediterranean-type diets (MD), the Dietary Inflammatory Index (DII), vegetarian/plant-based diets, or other anti-inflammatory diets 3) for preventing or managing clinical outcomes related to blood pressure, cancer, autoimmune diseases, frailty, cognitive function, liver disease conditions, all-cause mortality, or mortality related to the conditions named; or assessed associations of adherence to these diets or diet indexes with those outcomes and 4) assessed the certainty of evidence using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) or a comparable method.

DATA ABSTRACTION AND ASSESSMENT

Each included systematic review had data abstracted by 2 reviewers. Abstracted data included but were not limited to number of studies included in the review that had one of the diets of interest as the intervention or exposure, condition, type of diet, comparators, certainty of evidence rating, and certainty of evidence conclusion(s) relevant to the outcomes of interest.

SYNTHESIS

Our evidence mapping process resulted in visual depictions of the evidence for the role of anti-inflammatory dietary patterns on the prevention and management of chronic health conditions, excluding diabetes, obesity, and cardiovascular disease, as well as an accompanying narrative and table. Each visual depiction or evidence map uses a bubble plot format to display information on 4 dimensions: bubble size (numbers of relevant studies included in the review), bubble shape/color (study designs), bubble label (health condition), and y-axis (certainty of evidence underlying the conclusion). Each bubble represents a conclusion from an included systematic review. Thus, a systematic review may be represented multiple times, either in one map or multiple maps, but each conclusion appears only once.

RESULTS

We identified 2,309 potentially relevant citations. A total of 320 publications were retained and reviewed at full text. We excluded 292 publications for study design, outcomes that were not within scope, or failure to grade evidence, leaving 28 included publications. Based on these reviews, we created 6 evidence maps, one for each category of dietary patterns (*ie*, Mediterranean diet, DASH diet,

Dietary Inflammatory Index, vegetarian/plant-based diet, vegan diet, and other anti-inflammatory diets).

Of the 28 included studies, 4 reviewed more than 1 type of diet, while the other 24 focused on a single diet. While there are 28 included publications in total, some of those studies are counted multiple times across different diet categories because they examine more than 1 diet. From these reviews, 52 conclusions were made about 6 different types of diets. Two of the 6 diets were exclusively low or very low certainty of evidence. Of the 52 conclusions, 22 were drawn from 14 included reviews for the MD, 16 conclusions from 9 included reviews for the DASH diet, 5 conclusions from 5 included reviews for the DII, 5 conclusions from 4 included reviews for the vegetarian/plant-based diet, 3 conclusions from 3 included reviews for the anti-inflammatory diet, and 1 conclusion from 1 included review for the vegan diet (see Table 1).

Among the reviews that met our inclusion criteria of moderate or high certainty of evidence, 10 conclusions from 7 reviews considered the MD, 10 conclusions from 7 reviews considered the DASH diet, 3 conclusions from 3 reviews considered the DII, and 2 conclusions from 1 review considered the vegetarian/plant-based diet, for a total of 25 conclusions. Across the reviews of these 4 dietary patterns, 6 conclusions from the Mediterranean and DASH diets were supported by high certainty of evidence (see Table 8):

- The DASH diet was associated with significant reductions in systolic and diastolic blood pressure, compared with the consumption of other diets.
- A network meta-analysis suggested that the DASH diet might be the most effective dietary measure to reduce blood pressure among individuals with hypertension or pre-hypertension.
- A 5-point increase in adherence to the DASH diet reduced cancer-related mortality by 3%.
- A 5-point increase in adherence to the DASH diet reduced the risk for all-cause mortality by 5%.
- Better adherence to a Mediterranean diet was associated with decreased risk of frailty and pre-frailty (based on the findings of both randomized controlled trials and observational studies).

Moderate certainty of evidence supported 18 conclusions regarding the diets investigated and associated health outcomes, mainly the Mediterranean and DASH diets (See Table 9):

- SRs of observational studies found associations of the Mediterranean Diet, DASH diet, and lower DII scores with reductions in various cancer risk outcomes. For example, higher adherence to the Mediterranean diet and the DASH diet and lower DII scores are associated with lower risks for colorectal cancer and hepatocellular carcinoma and lower cancer-associated mortality.
- Adherence to both the Mediterranean diet and the DASH diet and lower DII scores are associated with lower risks for cirrhosis and nonalcoholic fatty liver disease (NAFLD).
- Adherence to the Mediterranean diet is associated with reduced risk for cognitive decline.

DISCUSSION

KEY FINDINGS AND CERTAINTY OF EVIDENCE

The proposed impacts of anti-inflammatory dietary patterns on—or associations of these dietary patterns with—risks for the chronic disease outcomes within scope of this study mostly lack a strong evidence base. This is partly due to small numbers of original studies and the challenges in examining these relationships via randomized controlled trials using clinical outcomes, rather than observational studies on biomarkers or other intermediate outcomes.

Multiple anti-inflammatory dietary patterns, including the DASH diet, Mediterranean diet, and to a lesser extent, vegetarian/plant-based diets, appear to be associated with lower risks for some chronic conditions, including high blood pressure, some types of cancer, and liver diseases (cirrhosis and NAFLD). However, these observations could be due to foods excluded from these dietary patterns as much as to foods or food combinations they include.

Despite lack of understanding of how anti-inflammatory diets might be beneficial for preventing and managing some chronic conditions, the demonstrated benefits for other conditions and apparent lack of harms suggest that there is no downside to promoting these diets.

This evidence map has a number of limitations, some inherent to the research and some inherent to the mapping process. As mentioned, most studies aimed at assessing the role of dietary patterns or individual foods or nutrients on chronic disease endpoints are relatively low-quality observational studies that rely on self-report or other potentially inaccurate methods of assessing exposures and adherence and on measures of intermediate outcomes of unclear value. In addition, because of the relatively large numbers of existing systematic reviews for some disease conditions of interest, we selected the most recent or most inclusive reviews for our map. Thus, we might have missed reviews that arrived at different conclusions. That being said, the proportion of reviews that assessed the certainty of the evidence supporting their conclusions was small for all outcomes and conditions of interest.

FUTURE RESEARCH

Definitively determining the impact of diets that might have anti-inflammatory properties on the risk of developing chronic diseases depends on first identifying several missing pieces in the biological plausibility chain. Most importantly, intermediate outcomes such as biomarkers that have consistent, significant associations—positive or negative—with disease risk must be identified and ideally, some chain of causality must be established. Inflammation is a natural process that serves vital physiological roles: Thus, the idea that a dietary pattern that non-selectively suppresses inflammation might have health benefits needs extensive clarification. Then it will be necessary to determine whether certain combinations of foods or nutrients or certain overall dietary patterns or the avoidance of certain foods or eating patterns are responsible for the observed health outcomes and whether these outcomes are also affected by other modifiable lifestyle characteristics.

CONCLUSIONS

Moderate or high certainty evidence linking diets with anti-inflammatory characteristics to chronic disease prevention or management outcomes is relatively sparse for conditions other than cardiovascular disease, diabetes, and obesity. Nevertheless, the evidence suggests that adherence to

diets such as DASH and Mediterranean-type eating patterns might have beneficial associations with reduction or management of chronic disease risks associated with blood pressure, liver diseases, cognitive function, and some types of cancer. Moreover, adverse events or harms associated with these diets are essentially non-existent.

Main Report

Evidence Synthesis Program

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ABBREVIATIONS TABLE

Abbreviation	Definition
AHRQ	Agency for Healthcare Research & Quality
AMED	Alternate mediterranean diet
BP	Blood pressure
CRC	Colorectal cancer
DAS28	Disease activity score in 28 joints
DASH	Dietary Approaches to Stop Hypertension
DBP	Diastolic blood pressure
DGA	Dietary Guidelines for Americans
DGC	Dietary Guidelines Committee
DII	Dietary Inflammatory Index
DRIs	Dietary Reference Intakes
EPC	Evidence-based Practice Center
ESP	Evidence Synthesis Program
GRADE	Grading of Recommendations, Assessment, Development and Evaluations
HCC	Hepatocellular carcinoma
MD	Mediterranean diet
MDS	Mediterranean Diet Score
MEDAS	Mediterranean Diet Adherence Screener
MIND	Mediterranean-Dietary Approaches to Stop Hypertension Intervention for Neurodegenerative Delay
MSDPS	Mediterranean-style Dietary Pattern Score
NAFLD	Nonalcoholic fatty liver disease
SBP	Systolic blood pressure
SR	Systematic review
TEP	Technical Expert Panel
UGI	Upper gastrointestinal
VA	Veterans Affairs
VHA	Veterans Health Administration

BACKGROUND

Chronic health conditions include heart disease, cancer, diabetes, chronic pain, asthma, inflammatory gastrointestinal disorders, degenerative diseases, obesity, and Alzheimer's disease/dementia. Six out of 10 adults in the United States have at least 1 chronic condition, and chronic diseases are the nation's leading cause of death and disability (causing 7 in 10 deaths each year).[1]

Nutrition and Chronic Disease

Research on the role of diet, particularly the role of saturated fat, in the risk for and progression of chronic diseases dates as far back as World War II, with the landmark study of Keys.[2] The 1977 report of the US Senate Select Committee on Nutrition and Human Needs (the McGovern Report) represents the first attempt of the federal government to set dietary goals to address chronic diseases among the US population.[3] As of 2024, studies attempting to assess the role of dietary patterns and individual nutrients in specific chronic diseases as well as chronic disease in general number in the thousands, yet the strength of the evidence regarding which dietary patterns and nutrients have the greatest impact—and by what mechanisms—remains unclear.

Since the mid-2000s, the Food and Nutrition Board of the National Academy of Sciences' Health and Medicine Division, which is responsible for developing the Dietary Reference Intakes (DRIs), has been focusing on methods for including chronic disease endpoints in determining DRIs.[4] However, major barriers must be overcome to design and execute studies of sufficient quality to establish a body of work that can be judged to provide at least moderate evidence. Thus, the nutrition community has been faced with basing dietary guidelines for chronic disease management on the best available evidence, largely prospective cohort studies of relatively short-term duration assessing shorter term indicators of chronic disease.

Inflammation and Chronic Disease

Inflammation can be defined in various ways but basically refers to a normal, localized or systemic physiologic process in which the mammalian immune system initiates a series of orchestrated events, including reddening, swelling, and increasing temperature, often in response to acute injury or infection.[5] Inflammation can be acute or chronic.

Over at least the past quarter century, indirect evidence has increasingly supported an association between (chronic) inflammation and most if not all chronic diseases, including cancer, cardiovascular disease, degenerative joint diseases, Type 2 diabetes, and cognitive decline associated with aging.[6] Although mechanisms for these associations have been proposed and are the subject of extensive research, direct evidence is generally lacking. Whether inflammation is a cause or consequence of various disease processes remains unclear, and animal models are limited in their application to human disease.

Anti-Inflammatory Diet and Chronic Disease

Despite the lack of understanding of the mechanisms by which inflammation might increase the risk for or the progression of chronic diseases, some evidence suggests that some nutrients, *eg*, simple carbohydrates and saturated fat, may promote inflammation. Likewise, some dietary patterns have been associated with chronic disease risk.[7] A high level of evidence from randomized controlled trials supports the role of the DASH (Dietary Approaches to Stop Hypertension) eating plan in preventing

and managing hypertension.[8] The DASH diet emphasizes higher intakes of fruits, vegetables, whole grains, beans, lean meats, fish, and low-fat dairy foods, and limited intakes of saturated fats, refined carbohydrates, sweets, and sodium; it is also rich in the minerals potassium, calcium, and magnesium, as well as in dietary fiber and protein compared with the average US diet. The DASH plan was not developed as an anti-inflammatory diet, and whether this diet exerts its effects through an anti-inflammatory mechanism is unclear, but it closely resembles dietary patterns identified as anti-inflammatory and is likely the most thoroughly studied diet in terms of research quality.

Likewise, evidence from population studies dating back to the late 1950s seems to support an association between what has come to be known as the Mediterranean diet (MD) and reduced risk for cardiovascular disease and other chronic conditions.[9] The MD pattern (based originally on eating patterns identified in Italy and Greece) has been characterized as one that emphasizes high intakes of fruits, vegetables, legumes, grains, unsaturated fats, moderate intakes of fish, and lower intakes of meats and dairy foods. Measuring adherence to the MD has spawned at least 4 different methods or indices, including the Alternate Mediterranean Diet, the Mediterranean-Style Dietary Pattern Score (MSDPS), the Mediterranean Diet Score, and the Mediterranean Diet Adherence Screener, some food based and some nutrient based.[10] The MSDPS attempts to calculate intakes of more than 20 nutrients: energy, dietary fiber, glycemic index, added sugar, b-carotene, lycopene, folate, vitamins C and E, calcium, magnesium, potassium, alcohol, saturated and trans fats, monounsaturated fat, oleic acid, polyunsaturated fatty acids (FA), omega-6 (n-6) FA, omega-3 (n-3) FA, linoleic acid, linolenic acid, n-6/n-3 ratio, and the combination of two n-3 FA, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA).

Finally, some evidence has shown an association between adherence to various vegetarian diets and vegan (plant-based) diets and risk for chronic disease. One mechanism that has been proposed to explain how each of these diets might lower disease risk is via anti-inflammatory properties of some or all of the nutrients or the absence of other nutrients.

What Are Dietary Patterns and What Is the Definition of an Anti-Inflammatory Diet?

A challenge in conducting research on the role of nutrition in health is that the traditional focus on single nutrients ignores the importance of nutrient interactions and overall dietary patterns—the totality of what individuals and groups tend to eat over time; thus, current research increasingly has focused on the role of overall diet. The 2010 *Dietary Guidelines for Americans*[11] (DGA) report introduced the concept of assessing the role of overall dietary patterns—the kinds of foods people tend to eat—in morbidity and mortality. Prior to that report, the DGA (which is issued every 5 years) had focused on individual nutrients and their roles in health and disease. But the 2010 DGA report drew few conclusions about the role of dietary patterns beyond the need to increase focus on them, because, as the committee acknowledged, they are exceedingly difficult to measure with any precision. And because they are difficult to measure, it is even more challenging to try to establish a causal relationship with any health outcomes. Following release of the 2010 DGA, the Dietary Patterns Methods Project was launched. This project has sought to gather or establish methods to score adherence of an individual's or population's food intake to a particular diet or standard, such as the DASH diet score, the MD score, the Healthy Eating Index, and the Dietary Inflammatory Index (DII).[12] The 2015 DGA sought to focus mainly on the association of dietary patterns and health outcomes, while acknowledging that individual nutrients could interact—either in opposition or in synergy—and that particular foods could affect the bioavailability of the nutrients contained within them or in other foods in ways that cannot be accounted for.[13]

The Dietary Patterns Subcommittee of the 2020 Dietary Guidelines Committee (DGC) conducted a systematic review of the associations of various dietary patterns with all-cause mortality, in collaboration with United States Department of Agriculture's systematic review team.[14] The review, which included 153 articles, reported:

> *"Strong evidence demonstrates that dietary patterns in adults and older adults characterized by vegetables, fruits, legumes, nuts, whole grains, unsaturated vegetable oils, and fish, lean meat or poultry when meat was included, are associated with decreased risk of all-cause mortality. These patterns were also relatively low in red and processed meat, high-fat dairy, and refined carbohydrates or sweets. Some of these dietary patterns also included alcoholic beverages in moderation."*

Of the studies included in the 2020 DGC review, one assessed adherence to the DII, and several others considered anti-inflammatory diet properties as exposures. However, the report did not draw specific conclusions on the impact of an anti-inflammatory diet as such. Numerous included studies investigated the DASH diet, vegetarian, and vegan dietary patterns.

What exactly is an anti-inflammatory diet or dietary pattern? The DII is based on evidence gathered from studies—cross-sectional and cohort—on the association between intakes of any nutrient (and presumptive nutrients like some phytochemicals) and levels of 6 inflammatory biomarkers: interleukin (IL)-1β, IL-4, IL-6, IL10, Tumor Necrosis Factor (TNF)-α, and C-reactive protein (CRP).[12] The original DII, developed in 2009, was updated in 2014 to include more studies and refine some aspects of the algorithm. The current DII comprises 45 food component parameters, including (but not limited to) mono- and polyunsaturated fatty acids, fiber, most of the known vitamins and minerals, other antioxidants, phytochemicals that include flavonoids and anthocyanins, caffeine, cholesterol, macronutrients, alcohol, and green and black tea. Particular foods are considered anti-inflammatory (*eg*, fatty fish, nuts, berries), whereas others are considered pro-inflammatory (*eg*, processed meats, foods high in saturated fat, sugar-sweetened beverages, refined grains), as discussed above. Thus, several other dietary patterns, including the DASH diet, MD, and some vegetarian and vegan diets, are anti-inflammatory.

This Evidence Map

In response to increasing interest in the potential role for anti-inflammatory diets as a standard of care for preventing and managing chronic disease, the Veterans Health Administration (VHA) Clinical Nutrition Committee requested a review of reviews (evidence map) of available evidence on the health effects of anti-inflammatory diets. The current body of literature—and literature reviews—on this topic is large, particularly in the areas of cardiovascular disease, diabetes, and obesity. Benefits of anti-inflammatory diets in preventing and managing these conditions is widely accepted, as evidenced by recommendations of organizations like the American Diabetes Association, the American Heart Association, and the Academy of Nutrition and Dietetics to follow diets such as the Mediterranean diet and the DASH diet. Therefore, to make the body of evidence more manageable for evidence maps, we chose to focus on conditions that may have been less studied but are of considerable importance for the VA population, including cancer, chronic pain, liver disease, and frailty. Thus, the purpose of this map was to catalog existing systematic reviews in areas of interest with less established bodies of research and to identify evidence gaps.

Findings from this review will be used by the Clinical Nutrition Committee to inform the development of clinical guidance for dietitians and the clinical team. Guidance will include national education calls,

training courses for VA staff, and national education materials for Veterans. Additionally, the evidence will inform the development of standards for anti-inflammatory diet classes for Veterans. Lastly, evidence will support the Eating for Whole Health faculty (of the Office of Patient Centered Care and Cultural Transformation) to improve the nutrition courses that are taught and developed for all VA staff.

METHODS

TOPIC DEVELOPMENT

This topic was developed in response to a nomination from Tessa Johnson, MS, RDN, IFNCP, RYT, Nutrition and Food Service Clinical Nutrition Committee, Integrative and Functional Nutrition Workgroup; Katherine Dignan, MS, RD, LD, CDCES, Nutrition and Food Service Clinical Nutrition Committee, Integrative and Functional Nutrition Workgroup; Kwynn Mason, MPH, RDN, LDN, CLS, IFNCP, Nutrition and Food Service Clinical Nutrition Committee, Integrative and Functional Nutrition Workgroup; and Glory Rodriguez-Gomez, MS, RDN, CDCES, LD, IFNCP, Nutrition and Food Service Clinical Nutrition Committee, Integrative and Functional Nutrition Workgroup.

The scope was further developed with input from the topic nominator, the ESP Coordinating Center, and the review team. The scope of this report includes: 1) one or more evidence maps that provide a visual overview of the distribution of evidence for the role of anti-inflammatory dietary patterns on the prevention and management of chronic health conditions, excluding diabetes, obesity, and cardiovascular disease, and 2) an accompanying narrative that helps stakeholders interpret the state of the evidence to inform policy and clinical decision-making. A draft version of this report was reviewed by external peer reviewers; their comments and author responses are located in the Appendix.

KEY QUESTIONS AND ELIGIBILITY CRITERIA

The aim of this synthesis is to develop evidence maps that provide a visual overview of the distribution of evidence for the role of anti-inflammatory dietary patterns on the prevention and management of chronic health conditions, excluding diabetes, obesity, and cardiovascular disease, with accompanying narrative that helps stakeholders interpret the state of the evidence to inform policy and clinical decision-making. We will focus on clinical topic areas where anti-inflammatory diet and related interventions are not yet established as one standard of care.

STUDY SELECTION

Titles of potentially eligible reviews were screened in duplicate for relevance by 5 authors independently; any article chosen by at least 1 reviewer based on the title went on for abstract screening. Abstracts were then reviewed in duplicate, with any discrepancies resolved by group discussion. All titles and abstracts were selected based on the eligibility criteria described in the section below.

To further define the scope by clinical topic areas and outcomes of interest, we recorded condition type when initially reviewing abstracts and presented a preliminary evidence mapping of clinical topic areas and diets for which we found reviews to the operational partners to determine which areas were of interest to the VA; clinical topic areas not selected by the operational partners were therefore excluded from further review. Operational partners elected to focus on clinical topic areas other than body weight, obesity, diabetes, and most cardiovascular diseases—as described in the next paragraph—because an extensive body of literature has provided moderate to high certainty evidence of an association between adopting anti-inflammatory dietary patterns and endpoints related to these conditions, and these dietary patterns have been widely incorporated into health practitioners' guidelines as recommendations to prevent or manage these outcomes.[15]

We included reviews on hypertension, including the continuous measure of blood pressure (BP), in our map, as hypertension has been shown to be a strong predictor of many non-cardiovascular related chronic conditions (*eg*, dementia, cancer);[16] synthesizing evidence on diet and hypertension could provide important insights on the relationship between dietary patterns and other (non-cardiovascular) chronic conditions, where evidence is still lacking, to drive the use of dietary interventions to reduce the disease burden.[15,17] With the exception of including reviews on BP, we did not include studies in which the only outcomes were intermediary outcomes or biomarkers.

We further restricted eligibility to reviews that used formal methods to assess the certainty of the evidence for conclusions. Most reviews that assessed the certainty of evidence used the widely accepted Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach.[18] However, other formal methods were accepted, such as the approach developed by the Agency for Healthcare Research & Quality (AHRQ) Evidence-based Practice Center (EPC) program[19] and Nutrigrade.[20] To remain eligible, a systematic review had to 1) state or cite the method used to formally assess the certainty of included evidence, and 2) report the certainty of evidence for the effect of the dietary pattern on an outcome of interest. The assessment needed to be applied to specific conclusions, not individual studies or multiple combined conclusions.

ELIGIBILITY CRITERIA

The ESP included studies that met the following criteria:

	Eligibility Criteria
Population	Adults (*ie,* individuals over 18 years old), either reported on exclusively or both adult and pediatric populations but reported results specifically for adults, were included.
Intervention	• Studies that considered anti-inflammatory dietary patterns, including the MD, DASH (not DASH low sodium), Mediterranean-Dietary Approaches to Stop Hypertension Intervention for Neurodegenerative Delay (MIND), and plant-based/vegetarian, were included.[a] • Studies that focus on supplements, specific ingredients (*eg*, olive oil), eating habits, or on diets that are generic without a specific diet intervention (*eg,* terms like “dietary support," “process,” and “dietary factors”) and dietary patterns that are not considered anti-inflammatory are excluded. • Reviews that included studies of other interventions were eligible if results for specific anti-inflammatory diets were reported separately (*eg,* a review comparing various types of lifestyle interventions, including anti-inflammatory diets, aimed at lowering risk for breast cancer).
Comparator	No determination about eligibility was made based on comparators.
Outcomes	• Prevention and management of chronic health conditions excluding diabetes (including gestational diabetes, metabolic syndrome), obesity (including weight), and cardiovascular disease (*eg,* myocardial infarction, angina, heart failure, and stroke). We included hypertension/BP, as described in the narrative above. • We included clinically relevant outcomes (including biomarkers) for conditions of interest. Biomarkers were required to be commonly used in clinical decision making, otherwise they were excluded (*eg,* liver enzymes for nonalcoholic fatty liver disease, or NAFLD).
Study Design	• Systematic reviews were included. • Reviews of reviews (*eg,* umbrella reviews) and reviews that did not employ traditional systematic review methods (*eg,* narrative reviews, scoping reviews) for identifying and critically appraising studies were excluded.

Notes. [a]Due to a lack of consensus on the criteria defining an anti-inflammatory diet, the decision regarding which diets to include was made by the research team in consultation with several subject matter experts and was approved by the Clinical Nutrition Committee.

SEARCHING AND SCREENING

Search strategies were developed in consultation with a medical librarian who is expert in literature reviews. We used a combination of MeSH keywords (*eg, anti-inflammat**, *DASH*, *Mediterranean*, *MIND*, *vegetarian*, *plant-based*, *vegan*) and conducted searches from inception to July 2023 in bibliographic databases (Medline, Cumulated Index to Nursing and Allied Health Literature [CINAHL], Cochrane Database of Systematic Reviews [CDSR]), non-bibliographic databases (Canadian Agency for Drugs and Technologies in Health [CADTH], National Center for Biotechnology Information [NCBI] Bookshelf, VA Dimensions), and in PROSPERO for reviews in development (see Appendix for complete search strategies). Additional citations were identified from hand-searching reference lists and consultation with content experts. English-language titles, abstracts, and full-text articles were independently reviewed by 2 investigators, and disagreements were resolved by consensus.

DATA ABSTRACTION

Data were abstracted from each included systematic review by 1 reviewer and verified by a second reviewer. Abstracted data included, but were not limited to, descriptors to assess publication relevance and critical information about relevant conclusions. Because many systematic reviews covered a range of clinical topics, diets, or populations, we focused our data abstraction on relevant certainty of evidence conclusions rather than entire systematic reviews. For each conclusion, we determined the following: certainty of evidence assessment, study design for studies used in reaching conclusion, number of studies used in reaching conclusion, description of clinical topic area, dietary pattern or intervention characteristics, and the conclusion itself.

SYNTHESIS

Our evidence mapping process resulted in a visual depiction of the evidence for the role of anti-inflammatory dietary patterns on the prevention and management of chronic health conditions, excluding diabetes, obesity, and cardiovascular disease, as well as an accompanying narrative and table. Each visual depiction or evidence map uses a bubble plot format to display information on 5 dimensions: bubble size (size of study/studies), bubble shape/color (study design[s]), bubble label (condition), x-axis (reported benefit vs no benefit), and y-axis (certainty of evidence). Each bubble represents a conclusion from an included systematic review. Thus, a systematic review may be represented multiple times, either in 1 map or multiple maps, but each conclusion appears only once. The maps provide the following types of information about each included conclusion from a systematic review, with each map representing a different diet:

Number of articles used to formulate conclusion (bubble size): The size of each bubble corresponds to the number of relevant primary research studies used to formulate the specific conclusion from a systematic review. Overlap between primary studies included in reviews (*ie,* that would be represented in more than 1 bubble) is discussed narratively.

Clinical topic area (bubble label): Each bubble is labeled with the clinical topic area discussed by that conclusion.

Shapes and colors: Included study characteristics for each conclusion are presented using colors and shapes: a yellow square denotes that this conclusion was based on observational studies only, a blue

triangle denotes that this conclusion was based on randomized control trials only, and a green diamond denotes that this conclusion was based on a mix of the 2 study designs.

Strength of findings (y-axis): Each conclusion is plotted on the map based on the certainty of evidence statement as reported in the systematic review. We have 3 categories: "Conclusion is rated as low or very low certainty," Conclusion is rated moderate certainty," and "Conclusion is rated as high or strong certainty."

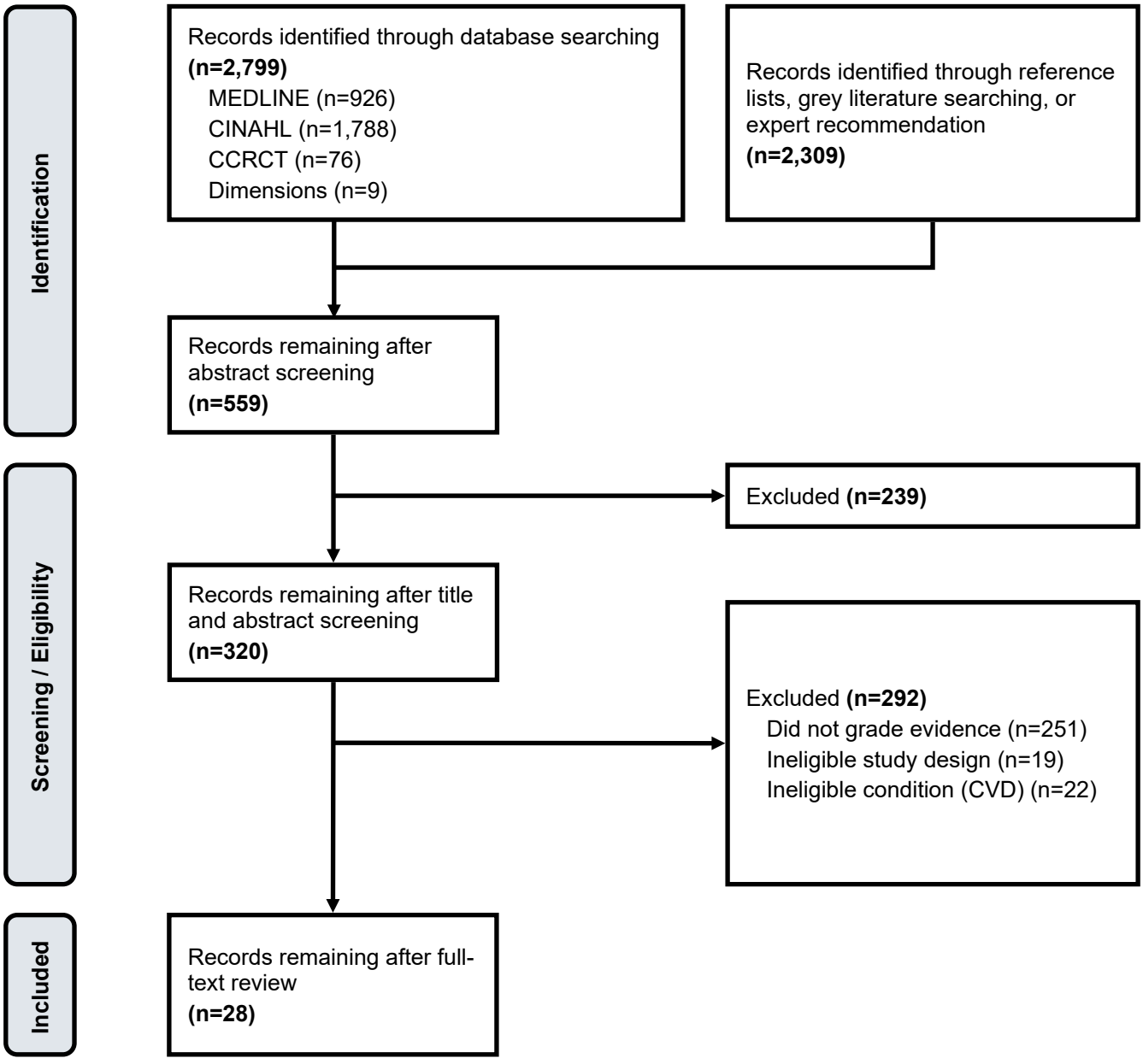
Dietary pattern or intervention (x-axis): Each conclusion is plotted as showing either "potential benefit" or "no benefit."

Accompanying each map is a narrative synthesis that expands upon the visual evidence map to provide a summary of high and moderate conclusions from the map and a table of conclusions organized by health condition. The narrative does not discuss low and very low certainty of evidence conclusions, because the level of certainty or strength of these conclusions is not sufficient to consider them as supporting or not supporting the conclusions (the benefit or lack of benefit of the dietary pattern). The GRADE definition of low certainty of evidence is "Our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of effect." The definition of very low certainty of evidence is "We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect."[18] Implicit in these definitions is that there is a (very) high likelihood that new evidence could change the conclusion. Details about all the conclusions in each map are included in the corresponding table.

RESULTS

LITERATURE FLOW DIAGRAM

The literature flow diagram summarizes the results of the study selection process. A full list of excluded studies is provided in the Appendix.



Abbreviations. CVD=cardiovascular disease.

OVERVIEW OF INCLUDED STUDIES

We identified 2,309 potentially relevant citations. After applying the inclusion and exclusion criteria to the 2,309 titles, 559 abstracts were reviewed. From these, a total of 239 abstracts were excluded based on several criteria related to study design, population, focus, and topic. At the full-text stage, 320 publications were reviewed. From these, 292 publications were excluded for the following reasons: did not grade evidence ($N = 251$), study design ($N = 19$), and cardiovascular disease topic other than blood pressure/hypertension ($N = 22$). A full list of excluded reviews from the full-text review is included in the Appendix. We included 28 publications in the maps.

Characteristics of Included Reviews and Their Conclusions

The 28 included systematic reviews drew 52 individual conclusions. These conclusions can be categorized into 6 dietary patterns of interest and 22 clinical topic areas or outcomes of interest.

Of the 52 conclusions, 22 were drawn from 14 included reviews for the MD, 16 conclusions from 9 included reviews for the DASH diet, 5 conclusions from 5 included reviews for the DII, 5 conclusions from 4 included reviews for the vegetarian/plant-based diet, 3 conclusions from 3 included reviews for the anti-inflammatory diet, and 1 conclusion from 1 included review for the vegan diet (see Table 1).

Among the reviews that met our inclusion criteria with moderate or high certainty of evidence, 7 considered the Mediterranean diet, 7 considered the DASH diet, 3 considered the DII, and 2 considered vegetarian/plant-based diets, for a total of 19 conclusions.

The 52 conclusions could also be categorized into 22 clinical topic areas or outcomes: all-cause mortality and cancer mortality – general ($N = 1$ conclusion), all-cause mortality ($N = 7$), blood pressure ($N = 10$), cancer mortality – general ($N = 4$), cancer risk – general ($N = 1$), cancer risk – general and cancer mortality – general ($N = 1$), cognitive function ($N = 2$), depressive symptoms ($N = 1$), NAFLD and cirrhosis ($N = 2$), NAFLD, cirrhosis, and liver cancer ($N = 1$), neurodegenerative disease risk ($N = 1$), rheumatoid arthritis ($N = 1$), rheumatoid arthritis – pain ($N = 1$), risk of breast cancer ($N = 1$), risk of colorectal cancer ($N = 6$), risk of frailty ($N = 3$), risk of liver cancer ($N = 2$), risk of pancreatic cancer ($N = 1$), risk of upper GI cancer ($N = 2$), sarcopenia ($N = 1$), ulcerative colitis ($N = 2$), and various liver disease outcomes ($N = 1$).

The conclusions for clinical topic areas were grouped by diet, resulting in 6 maps (Figure 1–Figure 6), each representing a different diet. Of the conclusions, 7 had high certainty of evidence, 18 had moderate certainty of evidence, and 27 had low or very low certainty of evidence. The number of studies supporting each conclusion in the included reviews ranged from 1 study to 35 studies.

Table 1. A Crosswalk of Systematic Review Conclusions to Diets

Author, Year	Total	MD	DASH	DII	Vegetarian/Plant-Based	Anti-Inflammatory	Vegan
Ali Mohsenpour, 2019[21]	2		2				
Bloomfield, 2015[22]	1	1					
Bloomfield, 2016[23]	5	5					
Buzzetti, 2021[24]	1	1					
Diao, 2023[25]	1			1			
Filippou, 2020[26]	1		1				
Filippou, 2021[27]	1	1					
Gibbs, 2021[28]	4	1	1		2		1
Guo, 2021[29]	1			1			
Jabri, 2021[30]	1				1		
Jafari, 2022[31]	1				1		
Lee, 2020[32]	1				1		
Limketkai, 2019[33]	1					1	
Limketkai, 2022[34]	1					1	
Moazzen, 2020[35]	2	1		1			
Moazzen, 2021[36]	3	1	1	1			
Morze, 2020[37]	5		5				
Morze, 2021[38]	2	2					
Nelson, 2020[39]	1	1					
Nowson, 2018[40]	2	2					
Poursalehi, 2023[41]	2	2					
Quirk, 2013[42]	1	1					
Schonenberger, 2021[43]	1					1	
Schwingshackl, 2019[44]	1		1				
Soltani, 2019[45]	1	1					
Soltani, 2020[46]	2		2				
Theodoridis, 2023[47]	1		1				
Zheng, 2022[48]	5	2	2	1			
Total included conclusions	***52***	***22***	***16***	***5***	***5***	***3***	***1***

Abbreviations. DASH=Dietary Approaches to Stop Hypertension; DII=Dietary Inflammatory Index; MD=Mediterranean diet.

EVIDENCE MAPS

We constructed 4 evidence maps, one each for the following diets: MD, DASH diet, DII, and vegetarian/plant-based diet. Two additional diets that did not have any moderate or high certainty of evidence conclusions are included in the final section. In these figures, each shape represents a single conclusion from a single systematic review: Triangles are reviews of RCTs only, squares are reviews of only observational studies, and diamonds represent reviews of both RCTs and observational studies.

MEDITERRANEAN DIET

The main components of the MD as originally studied were described in the introduction and were based on dietary patterns found in Italy and Greece. Because dietary scores based on the original dietary patterns might not be appropriate for non-Mediterranean populations, the original assessment metrics have been adapted to create numerous spinoff definitions and measures of adherence or exposure. These include the Mediterranean Diet Score (MDS); Mediterranean-style Dietary Pattern Score (MSDPS), which is based on the original Mediterranean Dietary Pyramid food groups but also accounts for foods not included in the Pyramid; the Alternate Mediterranean Diet (AMED), which does not include legumes as a separate food group; or the 14-item Mediterranean Diet Adherence Screener (MEDAS).[10,49] Typically, these tools are either used to directly assess intakes of various food groups or they are applied to analyze dietary recall or other food frequency questionnaire data. The results are then expressed as servings from specific food groups or they are translated to some subset of nutrients provided by those food intakes. Each of the Mediterranean diet assessment tools also varies slightly in the panel of nutrients included (*eg,* including or excluding alcohol).

Thirteen systematic reviews that met inclusion criteria attempted to assess the effects of a MD on—or association of the MD with—health outcomes of interest (see Figure 1). Seven of the systematic reviews reported conclusions with moderate or high SoE.[27,28,38-41,48] Table 2 reports the conclusions, in order of condition, as described in the reviews.

RCTs included in the reviews had 1 of 2 designs: some provided participants with all their meals and snacks, and some provided menus for participants to follow. Both the RCTs and the observational studies included in each systematic review used various measures to assess adherence and intake, as described above.

Blood Pressure

Two reviews assessed the effects of the MD diet on BP in RCTs.[27,28] A 2021 systematic review and meta-analysis that pooled 35 RCTs reported that compared with maintaining usual diet, adopting a MD resulted in a small but significant decrease in both systolic blood pressure (SBP) and diastolic blood pressure (DBP) in both those with hypertension and those with normal BP. But when the MD was compared with adopting other active dietary interventions, there was no difference in blood pressure. This conclusion had a moderate certainty of evidence .[27] A second 2021 systematic review and meta-analysis identified eight RCTs assessing the effects of the MD on BP, 6 of which were included in the larger review; this review reported that the MD reduces both SBP and DBP (but did not distinguish the effects of the MD compared with standard diet from the effects of the MD compared with other active dietary interventions).[28] This conclusion also had a moderate certainty of evidence.

Frailty

The World Health Organization defines frailty as "a clinically recognizable state in which the ability of older people to cope with everyday or acute stressors is compromised by an increased vulnerability brought by age-associated declines in physiological reserve and function across multiple organ systems."[50]

One review conducted a dose-response meta-analysis on the association between MD adherence (2-point increases in MDS) and the risk for frailty in 12 cohort studies and 7 cross-sectional studies.[41] The authors reported that higher MDS was associated with a decreased risk for frailty and pre-frailty among older adults in both cohort and cross-sectional studies: Both conclusions (from each of the two sets of studies) reached a high certainty of evidence.

Cancer and All-Cause Mortality Outcomes

Five reviews assessed the association between MD and various outcomes related to cancer risk or incidence, cancer mortality, or all-cause mortality.

One review assessed the association between various anti-inflammatory diets and HCC, incident NAFLD, and cirrhosis and found an inverse association between adherence to MD and incidence of HCC (4 case control and 3 cohort studies), and incident NAFLD and cirrhosis (7 cohort studies).[48] These conclusions had a moderate certainty of evidence.

A second systematic review and meta-analysis, which updated an earlier review by the same research group, assessed the association between adherence to the MD and risks for cancer mortality, site-specific cancer in the general population, all-cause mortality, and cancer mortality, as well as cancer reoccurrence among cancer survivors.[37,38] The review included 117 studies and used Nutrigrade to assess certainty of evidence. Assessment of 1 RCT and 18 cohort studies showed a decrease in risk for mortality from all cancers with higher adherence to the MD; this conclusion had a moderate certainty of evidence. Analysis of 34 observational studies showed moderate certainty of evidence for a reduction in risk for CRC with higher adherence to the MD.

Cognition

One review assessed the association of MD with the risk for cognitive decline in older adults.[40] This review included 18 studies—1 RCT (the PREDIMED trial, 13 cohort studies, and 3 cross-sectional studies. Using an Australian method (also called GRADE), the reviewers assessed the certainty of evidence for a positive association between MD index scores and various measures of cognitive function as good (GRADE B or moderate).

Rheumatoid Arthritis

One review assessed the impact of following a MD (among various diets, intakes of specific foods, and uses of dietary supplements) on Disease Activity Score in 28 joints (DAS28).[39] The review identified 1 RCT that assessed the impact of a MD intervention and one that assessed the impact of a Mediterranean-style anti-inflammatory diet intervention. The reviewers assessed the certainty of evidence as moderate for a beneficial effect of the diet on DAS28, although one of the studies did not report an effect size.

The additional 12 conclusions in the evidence map were rated low or very low certainty of evidence and thus did not have sufficient certainty to be discussed here in detail. See Table 2 for details from all MD conclusions.

Figure 1. Evidence Map of Mediterranean Diet

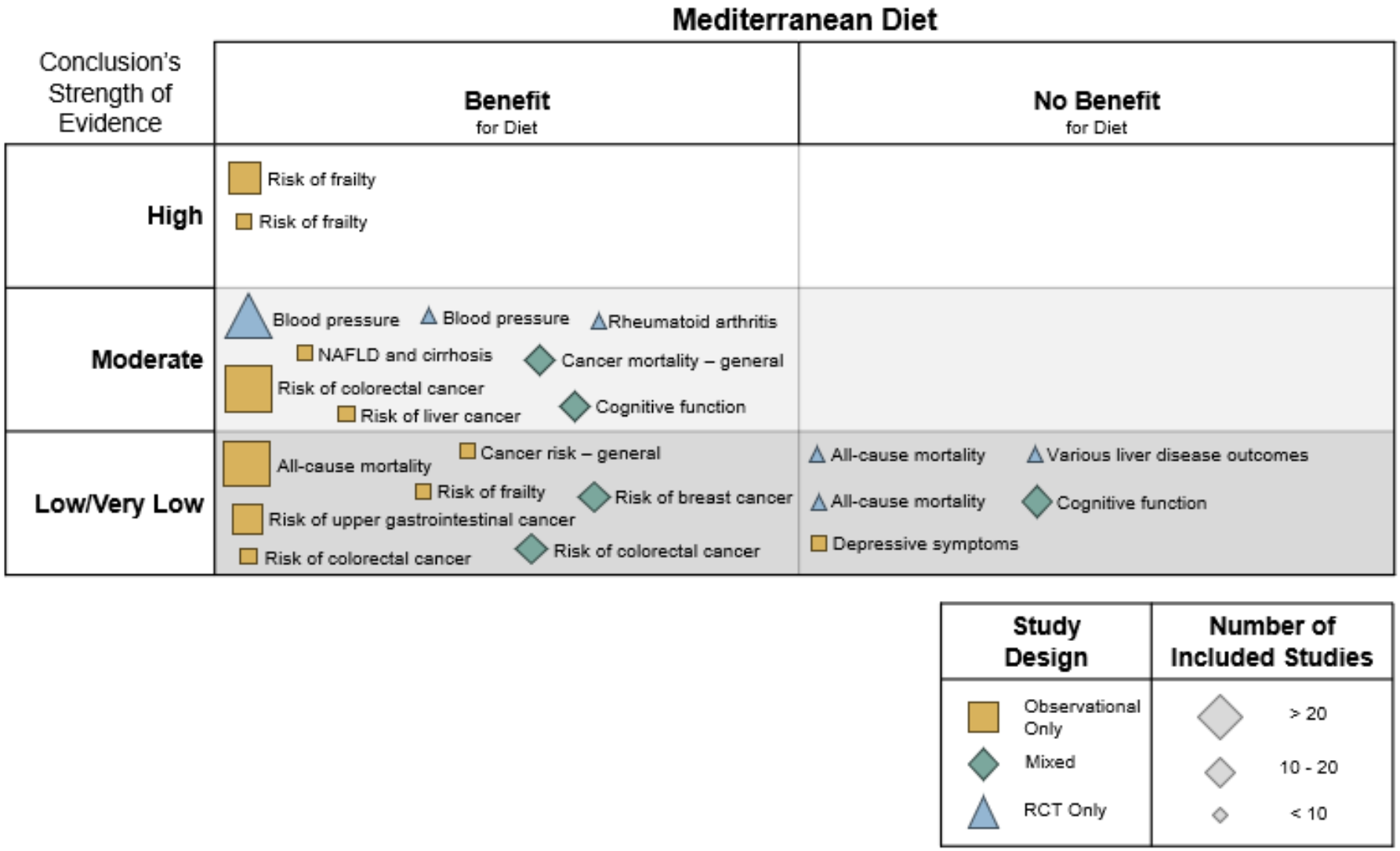


Table 2. Evidence Table of Mediterranean Diet Conclusions

Author, Year	Clinical Topic Area	Certainty of Evidence Primary Studies	Abridged Conclusion Text from Systematic Review
Bloomfield, 2015[22]	All-cause mortality	Low 3 RCT	"All cause mortality is about the same as the control diet."
Bloomfield, 2016[23]	All-cause mortality	Low 2 RCT	"Incidence of all-cause mortality was similar between the Mediterranean-like diet and the control diet groups."
Soltani, 2019[45]	All-cause mortality	Low 29 Observational studies	"Each 2-point increment in the adherence to a MD is associated with a 10% reduction in the risk of all-cause mortality."
Filippou, 2021[27]	BP	Moderate 35 RCT	"The adoption of the MD was accompanied by a relatively small, but yet significant BP reduction, while higher baseline SBP levels and longer follow-up duration enhanced the BP-lowering effect of the intervention."
Gibbs, 2021[28]	BP	Moderate 8 RCT	"Consumption of the MD was associated with statistically significant reduction in SBP and non-statistically significant reduction in DBP compared with the consumption of comparator diets."
Morze, 2021[38]	Cancer mortality – general	Moderate 19 Mixed studies	"The MD was related to lower risk of cancer mortality in the general population."
Bloomfield, 2016[23]	Cancer risk – general	Low 3 Observational studies	"Three large cohort studies reported highest conformity to a MD was associated with a reduction in total cancer incidence compared with lowest conformity (reference group)."
	Cognitive function	Low 17 Mixed studies	"Cognitive functioning [inconsistent/mixed results in observational studies and RCTs]."
Nowson, 2018[40]	Cognitive function	Moderate 18 Mixed studies	"A diet with MD characteristics is associated with reduced cognitive decline."
Quirk, 2013[42]	Depressive symptoms	Low 1 Observational study	"No association between a traditional MD and the likelihood of depressive symptoms."
Zheng, 2022[48]	NAFLD and cirrhosis	Moderate 7 Observational studies	"MDS and alternative MD was negatively associated with incident NAFLD and cirrhosis."
Nelson, 2020[39]	Rheumatoid arthritis	Moderate 2 RCT	"The MD reduced DAS28 in rheumatoid arthritis."

Author, Year	Clinical Topic Area	Certainty of Evidence Primary Studies	Abridged Conclusion Text from Systematic Review
Bloomfield, 2016[23]	Risk of breast cancer	Low 14 Mixed studies	"One RCT reported breast cancer incidence was lower in the combined MD groups compared to control; 13 cohort studies found breast cancer incidence was similar between the highest and lowest conformity groups."
	Risk of CRC	Low 9 Observational studies	"Highest conformity to a MD was associated with a reduction in CRC incidence compared with the lowest conformity."
Moazzen, 2021[36]	Risk of CRC	Very low 16 Mixed studies	"High diet quality quantified by the MDS was significantly associated with a lower risk of CRC."
Morze, 2021[38]	Risk of CRC	Moderate 34 Observational studies	"The MD was related to lower risk of CRC."
Nowson, 2018[40]	Risk of frailty	Low 3 Observational studies	"Following a diet with Mediterranean dietary characteristics may be associated with decreased likelihood of frailty."
Poursalehi, 2023[41]	Risk of frailty	High 7 Observational studies	"Better adherence to MD is associated with a decreased risk of frailty and pre-frailty among older adults."
		High 12 Observational studies	"Better adherence to MD is associated with a decreased risk of frailty and pre-frailty among older adults."
Zheng, 2022[48]	Risk of liver cancer	Moderate 5 Observational studies	"MDS and alternative MD was negatively associated with HCC."
Moazzen, 2020[35]	Risk of UGI cancer	Very low 11 Observational studies	"High scores in the MDS had a significant protective effect on the risk of upper gastrointestinal (UGI) cancer."
Buzzetti, 2021[24]	Various liver disease outcomes	Very low 1 RCT	"Associations were not estimable because 'there were no events in either group' (see table Summary of findings 1. starting on p6)."

Abbreviations. BP=blood pressure; CRC=colorectal cancer; DAS28=Disease Activity Score in 28 joints; DBP=diastolic blood pressure; HCC=hepatocellular carcinoma; NAFLD=nonalchoholic fatty liver disease; MD=Mediterranean diet; MDS=Mediterranean Diet Score; SBP=systolic blood pressure; UGI=upper gastrointestinal.

DASH DIET

The DASH diet pattern was described in the introduction. Seven of 9 systematic reviews that met inclusion criteria reported moderate or high certainty conclusions linking the DASH diet with beneficial health outcomes (see Figure 2 and Table 3).[21,26,28,37,44,46,48] Adherence or exposure to the DASH diet was typically measured using the DASH score when reported in observational studies, and assignment to the DASH treatment option was used in RCTs.

All-Cause Mortality

Two reviews assessed observational studies to examine associations between DASH diet scores and all-cause mortality, with both reaching conclusions that the DASH diet was associated with lower all-cause mortality (with moderate and high certainty of evidence). The first review and meta-analysis (of a variety of dietary indices used in cohort studies) identified 15 DASH score cohort studies and found that the highest DASH scores, when compared to lowest DASH scores, were inversely associated with risk of all-cause mortality (moderate certainty of evidence).[37] The second review, a systematic review and dose-response meta-analysis of prospective cohort studies on DASH diet and mortality, found 13 prospective cohort studies related to all-cause mortality.[46] The meta-analysis pooling these studies found that higher adherence to the DASH diet was associated with lower all-cause mortality (high certainty of evidence).

Blood Pressure

Four systematic reviews addressed the link between the DASH diet and blood pressure. Three of the reviews drew conclusions with high or moderate certainty of evidence.

The first meta-analysis focused exclusively on RCTs of DASH diet and BP, and found that among the 30 RCTs that compared DASH diet with control diets, DASH reduced SBP and DBP in adults with or without hypertension (moderate certainty of evidence).[26]

The second systematic review conducted meta-analyses for multiple diets including DASH and pooled 11 RCTs of DASH diet to reach a high certainty of evidence conclusion that DASH diet was associated with reductions in SBP and DBP when compared with other diets.[28]

The third review related to BP was a network meta-analysis of 67 trials comparing 13 dietary approaches, including 3 DASH diet trials, for both SBP and DBP.[44] The authors found that of the 13 dietary approaches, the DASH diet was most effective at reducing BP in both hypertensive and pre-hypertensive patients (high certainty of evidence).

Cancer Outcomes

Seven reviews assessed the evidence regarding a link between the DASH diet and cancer outcomes. Three reviews reported 4 conclusions with moderate to high certainty of evidence. Two of these were described above, as they also reported on all-cause mortality. The remaining 4 reviews reported conclusions with low to very low certainty of evidence.

The first dose-response meta-analysis described above in the all-cause mortality section also included another analysis of 10 prospective cohort studies and found that DASH diet lowered cancer mortality (high certainty of evidence).[46]

The second review described above also concluded that the DASH diet was inversely associated with risk of cancer, with 25 cohort studies included.[37] Their moderate certainty of evidence conclusion also included an inverse association between DASH diet and cancer incidence.

The third review, also a systematic review and meta-analysis of cohort studies, included 2 conclusions, both relating to DASH diet cancer outcomes.[21] The first conclusion, based on 9 cohort studies, found that higher adherence to DASH diet decreased cancer mortality, similar to the findings in the other 2 reviews (moderate certainty of evidence). The second conclusion was that adherence to a DASH diet decreased the risk of CRC (moderate certainty of evidence).

Liver

One review assessed the impact of multiple diets on NAFLD and HCC.[48] The review reached 1 conclusion, based on 4 observational studies, that the DASH diet was negatively associated with risk of NAFLD and liver cirrhosis (moderate certainty of evidence).

The additional 6 conclusions in the evidence map were rated low or very low certainty of evidence and thus did not have sufficient certainty to be discussed here in detail. See Table 3 for details from all DASH diet conclusions.

Figure 2. Evidence Map of DASH Diet

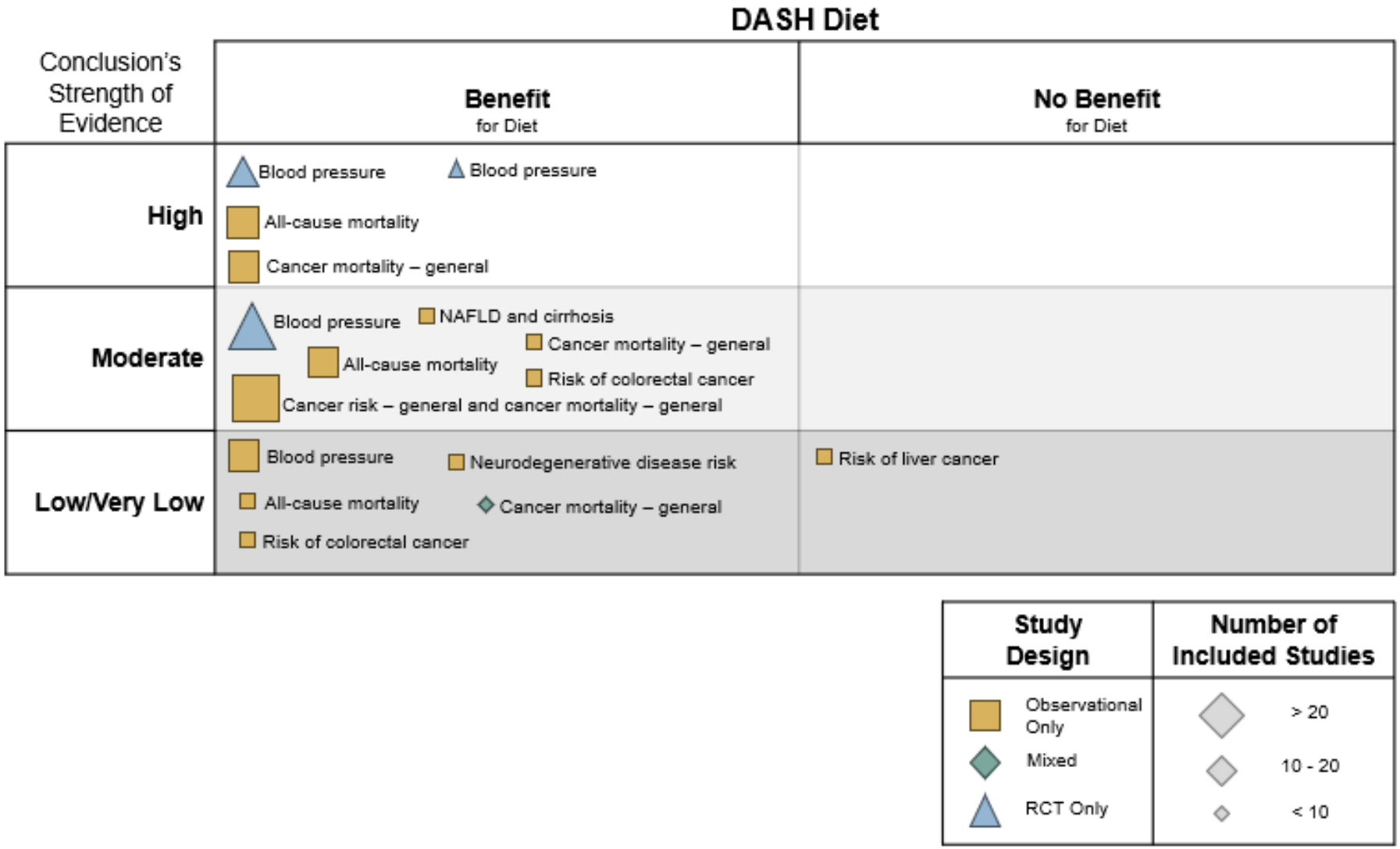


Table 3. Evidence Table of DASH Conclusions

Author, Year	Clinical Topic Area	Certainty of Evidence Primary Studies	Abridged Conclusion Text from Systematic Review
Morze, 2020[37]	All-cause mortality	Low 6 Observational studies	"Highest vs lowest category of diet quality (assessed by DASH score) were inversely associated with risk of all-cause mortality among cancer survivors."
		Moderate 15 Observational studies	"Highest vs lowest category of diet quality (assessed by DASH score) were inversely associated with risk of all-cause mortality."
Soltani, 2020[46]	All-cause mortality	High 13 Observational studies	"5-point increment in the adherence to the DASH diet could significantly lower the all-causes by 5%."
Filippou, 2020[26]	BP	Moderate 30 RCT	"Compared with a control diet, the DASH diet reduced both SBP and DBP, and hypertension status did not modify the effect on BP reduction."
Gibbs, 2021[28]	BP	High 11 RCT	"Consumption of the DASH diet was associated with statistically significant reductions in SBP and DBP compared with the consumption of comparator diets."
Schwingshackl, 2019[44]	BP	High 3 RCT	"The present network meta-analysis suggests that the DASH dietary approach might be the most effective dietary measure to reduce BP among hypertensive and pre-hypertensive patients based on high quality evidence."
Theodoridis, 2023[47]	BP	Very low 12 Observational studies	"The findings suggest that high adherence to the DASH diet has a positive effect on reducing hypertension risk compared to low adherence."
Ali Mohsenpour, 2019[21]	Cancer mortality – general	Moderate 9 Observational studies	"Highest vs lowest adherence to a DASH-style diet significantly decreased the risk of mortality from all cancer types."
Morze, 2020[37]	Cancer mortality – general	Low 6 Observational studies	"Highest vs lowest category of diet quality (assessed by DASH score) were inversely associated with risk of cancer mortality among cancer survivors."
Soltani, 2020[46]	Cancer mortality – general	High 10 Observational studies	"5-point increment in the adherence to the DASH diet could significantly lower the cancer mortality by 3%."
Morze, 2020[37]	Cancer risk – general and cancer mortality – general	Moderate 25 Observational studies	"Highest vs lowest category of diet quality (assessed by DASH score) were inversely associated with risk of cancer mortality or incidence."

Author, Year	Clinical Topic Area	Certainty of Evidence Primary Studies	Abridged Conclusion Text from Systematic Review
Zheng, 2022[48]	NAFLD and cirrhosis	Moderate 4 Observational studies	"DASH diet was negatively associated with incident NAFLD and cirrhosis."
Morze, 2020[37]	Neurodegenerative disease risk	Low 7 Observational studies	"Highest vs lowest category of diet quality (assessed by DASH score) were inversely associated with risk of neurodegenerative disease."
Ali Mohsenpour, 2019[21]	Risk of CRC	Moderate 4 Observational studies	"Highest vs lowest adherence to a DASH-style diet significantly decreased the risk of CRC."
Moazzen, 2021[36]	Risk of CRC	Very low 8 Mixed studies	"High diet quality quantified by the DASH score was significantly associated with a lower risk of CRC."
Zheng, 2022[48]	Risk of liver cancer	Very low 3 Observational studies	"DASH diet showed inconsistent association with HCC."

Abbreviations. BP=blood pressure; CRC=colorectal cancer; DASH=Dietary Approaches to Stop Hypertension; DBP=diastolic blood pressure; HCC=hepatocellular carcinoma; NAFLD=nonalchoholic fatty liver disease; SBP=systolic blood pressure.

DIETARY INFLAMMATORY INDEX

The Dietary Inflammatory Index was developed to enable the assessment of individual and group food intakes and dietary patterns for their inclusion of some 45 nutrients that have been associated with increased or decreased levels of biomarkers that have been associated with chronic inflammation (inflammatory cytokines) as well as with chronic disease risk (higher scores reflect inclusion of larger amounts of nutrients thought to promote inflammation).[12] The DII has undergone several modifications to reflect changes in the evidence and has been used to score measures of food intake across more than 10 countries (such as NHANES data for the US).

Five systematic reviews were identified that met inclusion criteria and assessed the association of DII scores on outcomes of interest (Figure 3 and Table 4).

Cancer Outcomes

Two reviews assessed the association of the DII, or pattern, on cancer—one on liver cancer (HCC) [48] and the second review on pancreatic cancer[29] (see Figure 3). Both reviews relied exclusively on observational data: The liver cancer review reported on 2 case-control studies and 1 cohort study, and the pancreatic cancer review reported on 2 cohort studies and 4 case-control studies. In the latter, the findings on pancreatic cancer were meta-analytically pooled. Both reviews found moderate certainty evidence that diets with a higher DII were associated with increasing progression of chronic liver disease to HCC[48] or development of pancreatic cancer.[29]

Frailty

An additional review that also meta-analytically combined observational data concluded that diets with a higher DII were associated with sarcopenia (with moderate certainty evidence), however 9 of the 11 included studies were cross-sectional in design, which precludes drawing conclusions even about association.[25] Point estimates from the cohort studies did not show any statistically significant association between higher DII and sarcopenia.

The additional 2 conclusions in the evidence map were rated very low certainty of evidence and thus did not have sufficient certainty to be discussed here in detail. See Table 4 for details from all DII diet conclusions.

Figure 3. Evidence Map of Dietary Inflammatory Index

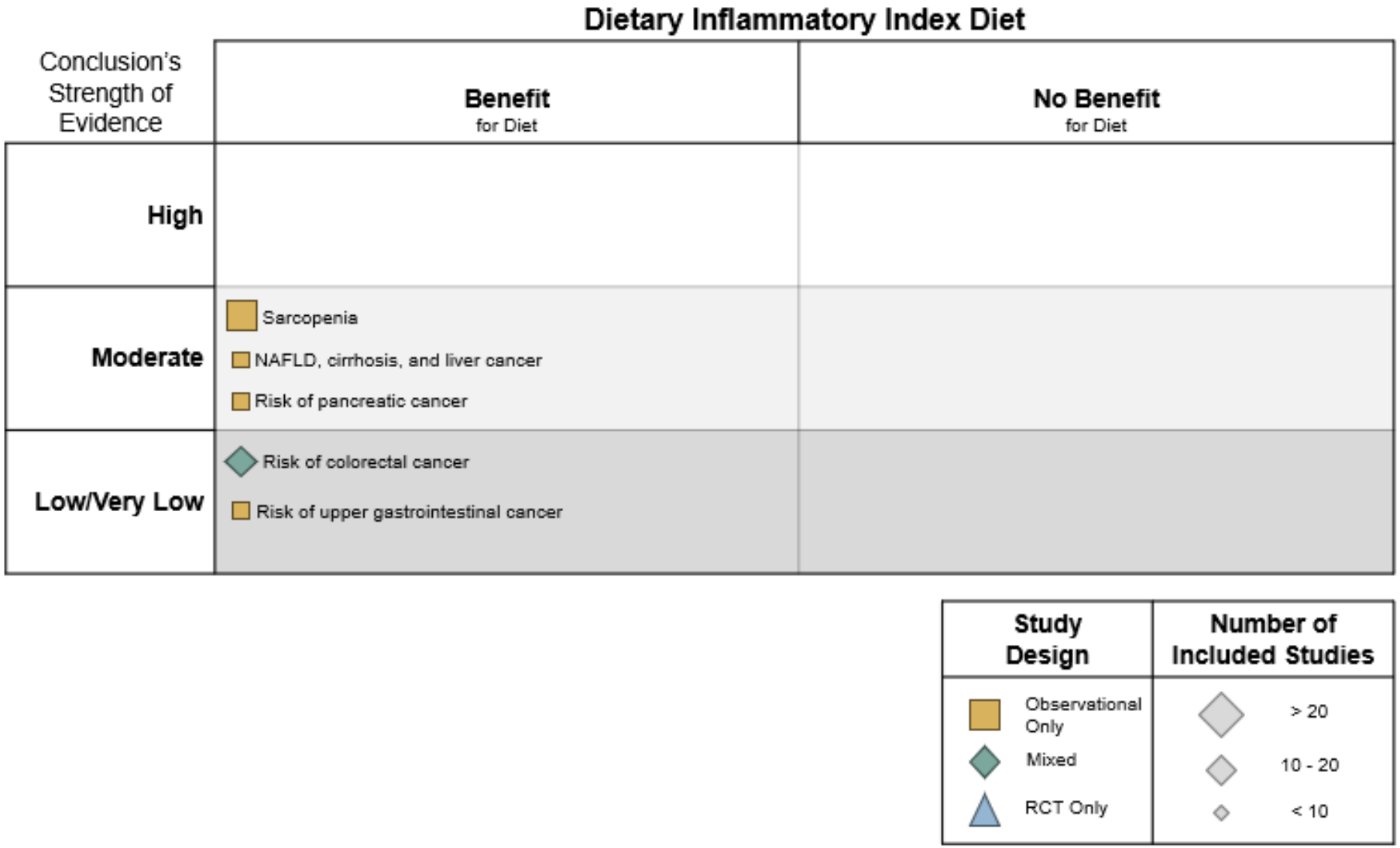


Table 4. Evidence Table of Dietary Inflammatory Index Conclusions

Author, Year	Clinical Topic Area	Certainty of Evidence Primary Studies	Abridged Conclusion Text from Systematic Review
Zheng, 2022[48]	NAFLD, cirrhosis, and liver cancer	Moderate 3 Observational studies	"DII was positively associated with incident NAFLD, cirrhosis, and HCC."
Moazzen, 2021[36]	Risk of CRC	Very low 11 Mixed studies	"High diet quality quantified by the DII was significantly associated with a lower risk of CRC."
Guo, 2021[29]	Risk of pancreatic cancer	Moderate 6 Observational studies	"Results suggested that dietary habits with high inflammatory features (high DII score compared to lower score) might increase pancreatic cancer risk."
Moazzen, 2020[35]	Risk of UGI cancer	Very low 9 Observational studies	"Low DII scores did indicate statistically significant protection against UGI cancer."
Diao, 2023[25]	Sarcopenia	Moderate 11 Observational studies	"The meta-analysis indicated that the DII is associated with sarcopenia. Meanwhile, the result of the dose–response analysis showed that sarcopenia increased by 1.22 times for each 1-point increase in the DII score."

Abbreviations. CRC=colorectal cancer; DII=Dietary Inflammatory Index; HCC=hepatocellular carcinoma; NAFLD=nonalchoholic fatty liver disease; UGI=upper gastrointestinal.

EVIDENCE MAP OF VEGETARIAN OR OTHER PLANT-BASED DIET

A large number of epidemiological studies have linked lower intakes of animal foods (non-lean meat and full-fat dairy products) with lower risks for chronic diseases, including obesity. However, the terms vegetarian diet or plant-based diet have no exact definitions or criteria in terms of the range of contents of animal products or even their overall nutritive values. Even vegan diets (covered in a separate section, below), which completely exclude any animal products and have also been associated with lower chronic disease risks, adhere to no criteria regarding nutrient contents. Thus, reviews of these diets entirely lack standardization of interventions or exposures. For this evidence map review, we identified 4 reviews that met inclusion criteria: 2 that included only RCTs and 2 that included only observational studies.

Blood Pressure

Two reviews of only RCTs concluded that compared to non-vegetarian diets in 5 clinical trials, plant-based dietary patterns were associated with lower SBP (high certainty evidence) and DBP (moderate certainty evidence) (see Figure 4 and Table 5).[28]

The additional 3 conclusions in the evidence map were rated very low certainty of evidence and thus did not have sufficient certainty to be discussed here in detail. See Table 5 for details from all vegetarian or other plant-based diet conclusions.

Figure 4. Evidence Map of Vegetarian/Plant-Based Diet

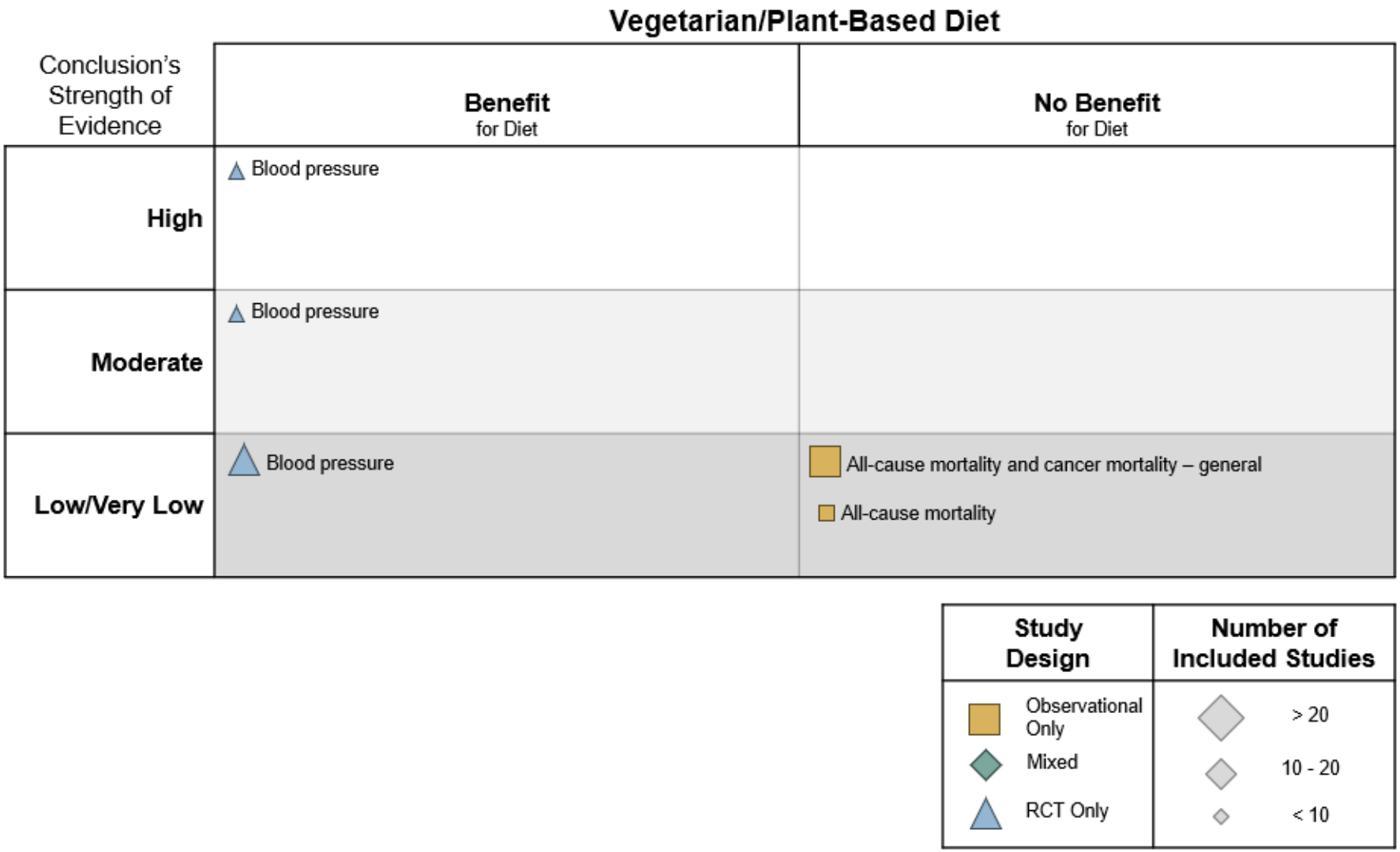


Table 5. Evidence Table of Vegetarian/Plant-Based Diet Conclusions

Author, Year	Clinical Topic Area	Certainty of Evidence Primary Studies	Abridged Conclusion Text from Systematic Review
Jabri, 2021[30]	All-cause mortality	Very low 8 Observational studies	"There was no association between vegetarian diet and [all-cause] mortality."
Jafari, 2022[31]	All-cause mortality and cancer mortality – general	Very low 12 Observational studies	"A decrease in hazard ratios for all-cause mortality and no association with any cancer mortality."
Gibbs, 2021[28]	BP	High 5 RCT	"Consumption of the lacto-ovo vegetarian diet was associated with statistically significant reductions in SBP and DBP compared with the consumption of comparator diets."
		Moderate 5 RCT	"Consumption of the lacto-ovo vegetarian diet was associated with statistically significant reductions in SBP and DBP compared with the consumption of comparator diets."
Lee, 2020[32]	BP	Very low 15 RCT	"Compared to meat diet, vegetarian dietary pattern significantly reduced SBP and DBP."

Abbreviations. BP=blood pressure; DBP=diastolic blood pressure; SBP=systolic blood pressure.

OTHER ANTI-INFLAMMATORY DIETS

Three reviews were identified that met inclusion criteria and considered studies of diets labeled as anti-inflammatory. The conclusions reached by these 3 reviews—2 on risk for inflammatory bowel disorder and 1 on chronic pain—were all deemed low or very low certainty of evidence conclusions (Figure 5 and Table 6).

Figure 5. Evidence Map of Anti-Inflammatory Diet

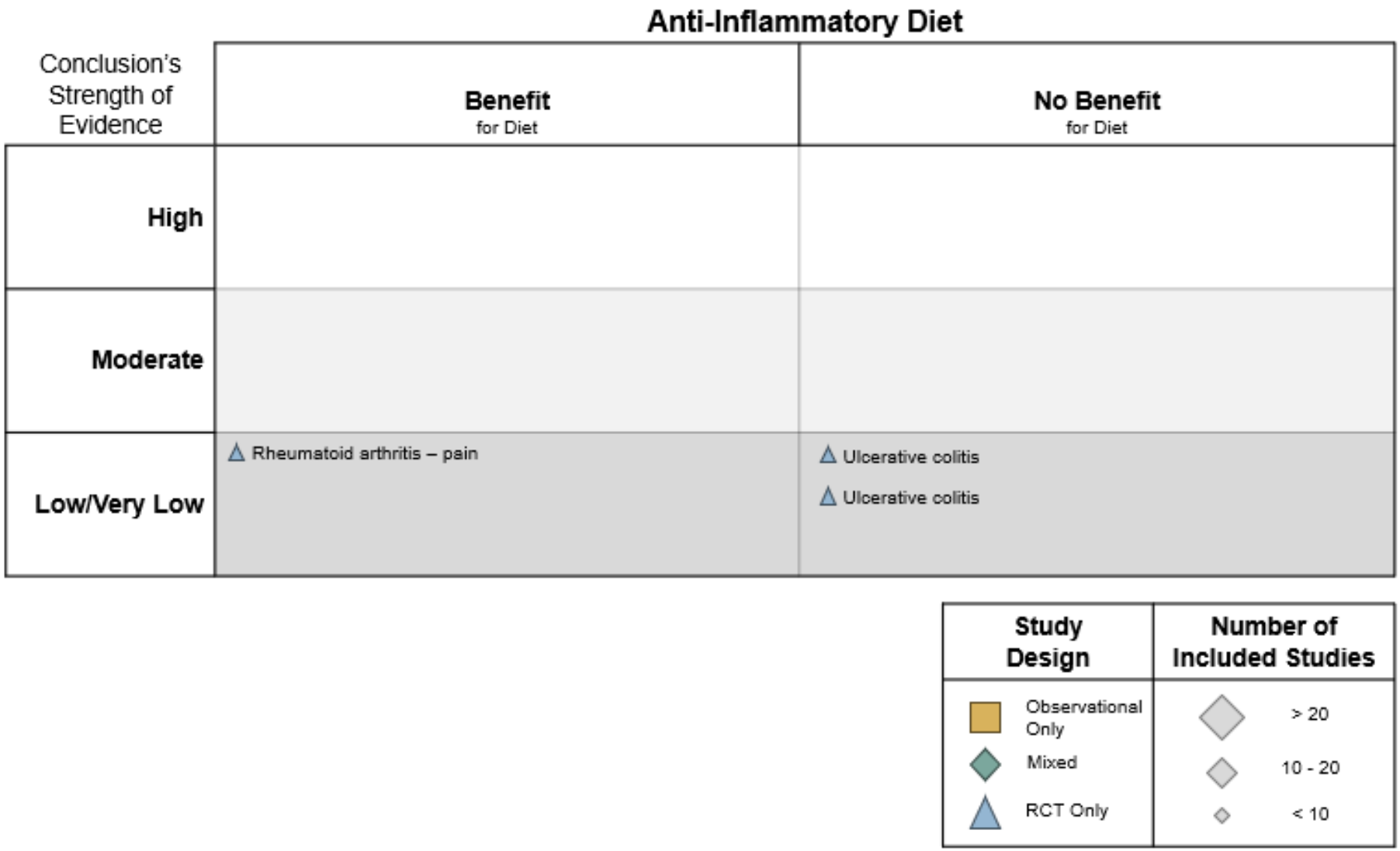


Table 6. Evidence Table of Anti-Inflammatory Diet Conclusions

Author, Year	Clinical Topic Area	Certainty of Evidence Primary Studies	Abridged Conclusion Text from Systematic Review
Schonenberger, 2021[43]	Rheumatoid arthritis - pain	Very low 7 RCT	"Our meta-analysis showed a significant improvement in pain in rheumatoid arthritis patients on anti-inflammatory diets compared with ordinary diets."
Limketkai, 2019[33]	Ulcerative colitis	Very low 1 RCT	“At 6 months, 36% (5/14) of participants in the Alberta-based anti-inflammatory diet group['s ulcerative colitis] relapsed compared to 29% (4/14) of participants in the control group.”
Limketkai, 2022[34]	Ulcerative colitis	Very low 1 RCT	“There was no observed benefit from [an] anti-inflammatory diet... for the maintenance of 26- to 52-week clinical remission, or for quality of life.”

VEGAN DIET

The 1 conclusion in the evidence map was rated low certainty of evidence and thus does not have sufficient certainty to be discussed here in detail. See Figure 6 and Table 7 for details from this vegan diet conclusion.

Figure 6. Evidence Map of Vegan Diet

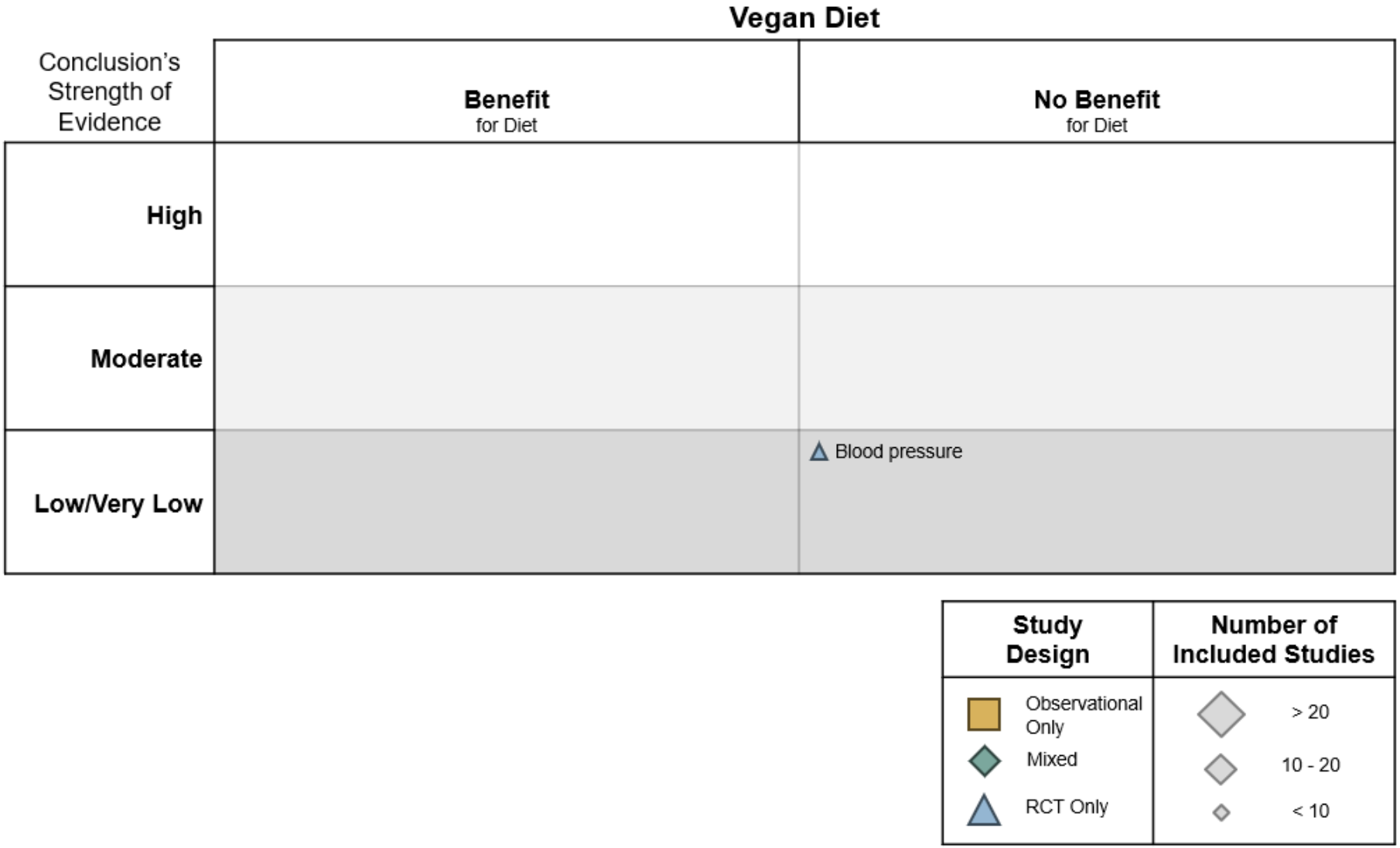


Table 7. Evidence Table of Vegan Diet Conclusions

Author, Year	Clinical Topic Area	Certainty of Evidence Primary Studies	Abridged Conclusion Text from Systematic Review
Gibbs, 2021[28]	BP	Low 9 RCT	"Consumption of the vegan diet was associated with non-statistically significant reductions in SBP and DBP compared with the consumption of comparator diets."

Abbreviations. BP=blood pressure; DBP=diastolic blood pressure; SBP=systolic blood pressure.

DISCUSSION

A large number of chronic health conditions have been associated with inflammation or inflammatory states, with varying amounts of evidence and plausible proposed mechanisms supporting those associations. The literature assessing the benefits of various diets that have been categorized as being potentially anti-inflammatory for these health conditions (or the association between adoption of such diets and risk for the conditions) is likewise vast.

For the purpose of producing an evidence map that focused on conditions of interest to the sponsor, for which no recent reviews of reviews (or umbrella reviews) were conducted, and that aimed to identify associations with at least moderate supporting evidence, we limited this review to systematic reviews that:

- Considered the MD (eating pattern), DASH diet, anti-inflammatory diet (as assessed by the DII), or vegan/vegetarian/plant-based diets.
- Assessed outcomes related to autoimmune disorders, blood pressure or hypertension, cancer, cognitive function, frailty, and liver diseases.
- Assessed the strength of the body of evidence underlying their conclusions using the GRADE method or a similar approach.

It is important to note that despite the variety of methods used to assess adherence to a Mediterranean dietary pattern (reflecting the many culture-specific variations) and the apparent differences among the eating patterns we considered in this report (especially the Mediterranean and DASH diets), these dietary patterns actually share many aspects in common. These include an emphasis on a variety of vegetables, legumes, fruits, (less processed) grains, nuts, (less-saturated) vegetable (over animal fats), and minimal intakes of red meat and full-fat dairy products. The nutrient profiles that the DII aims to capture also reflect those of the MD and DASH diets.

Among 18 reviews that met the inclusion criteria for this review, only 5 drew conclusions that the authors of those reviews judged as being supported by high-certainty evidence. Two of these conclusions were that the DASH diet, a diet that was originally developed as an approach to preventing or controlling hypertension, was shown to have a beneficial effect on blood pressure and to be associated with lower risk for all-cause or cancer mortality (see Table 8).

Two conclusions with high certainty of evidence, both from the same study, addressed the impact of the MD on—or the association of the diet with—risk for frailty. Both showed beneficial effects or associations.

Finally, the remaining conclusion with high certainty of evidence addressed the impact of vegetarian diet on blood pressure, finding that lacto-ovo vegetarian diets reduced systolic blood pressure.

Table 8. Conclusions with High Strengths of Evidence and Numbers and Types of Studies Supporting Them

Author, Year	Clinical Topic Area Primary Studies	Abridged Conclusion Text from Systematic Review
Gibbs, 2021[28]	BP 5 RCT	"Consumption of the lacto-ovo vegetarian diet was associated with statistically significant reductions in DBP compared with the consumption of comparator diets."
Soltani, 2020[46]	All-cause mortality 13 Observational studies	"5-point increment in the adherence to the DASH diet could significantly lower the all-causes by 5%."
Gibbs, 2021[28]	BP 11 RCT	"Consumption of the DASH diet was associated with statistically significant reductions in SBP and DBP compared with the consumption of comparator diets."
Schwingshackl, 2019[44]	BP 3 RCT	"The present network meta-analysis suggests that the DASH dietary approach might be the most effective dietary measure to reduce BP among hypertensive and pre-hypertensive patients based on high quality evidence."
Soltani, 2020[46]	Cancer mortality – general 10 Observational studies	"5-point increment in the adherence to the DASH diet could significantly lower the cancer mortality by 3%."
Poursalehi, 2023[41]	Risk of frailty 7 Observational studies	"Better adherence to MD is associated with a decreased risk of frailty and pre-frailty among older adults."
	Risk of frailty 12 Observational studies	"Better adherence to MD is associated with a decreased risk of frailty and pre-frailty among older adults."

Abbreviations. BP=blood pressure; DASH=Dietary Approaches to Stop Hypertension; DBP=diastolic blood pressure; MD=Mediterranean diet; SBP=systolic blood pressure.

Table 9. Conclusions with Moderate Strengths of Evidence and Numbers and Types of Studies Supporting Them

Author, Year	Clinical Topic Area	Abridged Conclusion Text from Systematic Review
Morze, 2020[37]	All-cause mortality 15 Observational studies	"Highest vs lowest category of diet quality (assessed by DASH score) were inversely associated with risk of all-cause mortality."
Filippou, 2021[27]	BP 35 RCT	"The adoption of the MD was accompanied by a relatively small, but yet significant BP reduction, while higher baseline SBP levels and longer follow-up duration enhanced the BP-lowering effect of the intervention."
Filippou, 2020[26]	BP 30 RCT	"Compared with a control diet, the DASH diet reduced both SBP and DBP, and hypertension status did not modify the effect on BP reduction."
Gibbs, 2021[28]	BP 8 RCT	"Consumption of the MD was associated with statistically significant reduction in SBP and non-statistically significant reduction in DBP compared with the consumption of comparator diets."
Gibbs, 2021[28]	BP 5 RCT	"Consumption of the lacto-ovo vegetarian diet was associated with statistically significant reductions in SBP and DBP compared with the consumption of comparator diets."
Morze, 2021[38]	Cancer mortality – general 19 Mixed studies	"The MD was related to lower risk of cancer mortality in the general population."
Ali Mohsenpour, 2019[21]	Cancer mortality – general 9 Observational studies	"Highest versus lowest adherence to a DASH-style diet significantly decreased the risk of mortality from all cancer types."
Morze, 2020[37]	Cancer risk – general and cancer mortality – general 25 Observational studies	"Highest vs lowest category of diet quality (assessed by DASH score) were inversely associated with risk of cancer mortality or incidence."
Nowson, 2018[40]	Cognitive function 18 Mixed studies	"A diet with MD characteristics is associated with reduced cognitive decline."

Abbreviations. BP=blood pressure; DASH=Dietary Approaches to Stop Hypertension; DBP=diastolic blood pressure; MD=Mediterranean diet; SBP=systolic blood pressure.

Moderate certainty of evidence supported 18 conclusions regarding the diets investigated and associated health outcomes: 8 conclusions about the MD, 6 conclusions about the DASH Diet, 3 conclusions regarding lower DII scores, and 1 conclusion regarding effects of vegetarian/plant-based diets.

SRs of RCTs examining the impact of the MD, DASH diet, and lacto-ovo vegetarian diets showed that a moderate certainty of evidence supported a role of these diets in reducing blood pressure. SRs of observational studies found associations of the MD, DASH diet, and lower DII scores with reductions in various cancer risk outcomes: for example, higher adherence to the MD and the DASH diet and lower DII scores were associated with lower risks for CRC and HCC and lower cancer-associated mortality. Moderate certainty of evidence supported associations of both the MD and the DASH diet and lower DII scores with lower risks for cirrhosis and NAFLD. Finally, a moderate certainty of evidence supported an association of the MD with reduced risk for cognitive decline and an association of lower DII scores with reduced risk for frailty.

Limitations

This evidence map had several limitations.

The first, common to all SRs, is that we might not have identified all the potentially eligible evidence. If a systematic review was published in a journal not indexed in any of the databases we searched, then we would have missed it. An extension to this limitation is that the included systematic reviews may themselves have missed some original research studies eligible for their review. An additional factor that limited inclusion of studies on some conditions of interest (such as depression, fibromyalgia, and myalgic encephalomyelitis/chronic fatigue syndrome) is that we included only systematic reviews that formally assessed the strength of the evidence; however, this stipulation can only have served to increase the quality of the reviews we included.

The second limitation, which pertains to evidence maps, is that we did not independently evaluate the source evidence; in other words, we took the conclusions of the authors of the systematic review at face value. That is the nature of an evidence map. As in all evidence-based products, and particularly in one such as this covering a large and complex evidence base, it is possible there are errors of data extraction and compilation. We used dual review to minimize the chance of such errors, but if we are notified of errors, we will correct them.

A third limitation, one that is common to all research on the role of nutrition in chronic disease prevention/etiology and management, is that most of the original studies, with the exception of the studies on BP, are observational, so the chance of identifiable and unidentifiable confounders is higher, and the certainty of evidence is usually not high. However, because we chose to include only reviews that graded the certainty of evidence supporting their conclusions, the quality of the original studies has at least been taken into account. Unfortunately, outcome measures for RCTs are likely to be relatively short term and are more likely to be biomarkers or other intermediate outcomes of unclear predictive value than longer-term clinical outcomes (except for studies on BP and hypertension, which are key risk factors for a variety of diseases), but well-designed observational studies of dietary patterns can yield important insights about long-term health and chronic disease outcomes.

A fourth limitation of this review, which is actually a limitation of the SRs and the original studies themselves, is the way that interventions or exposures are defined. For example, studies of the MD employ at least 9 different indices to measure adherence to the diet. SRs on the associations of MD

adherence with health outcomes typically disregarded the indices used by individual studies. Although we found no formal comparisons among these indices, and simply reported the conclusions of the SRs, we did ascertain that the various indices were capturing important aspects of the MD. Assessment of the association of adherence to an anti-inflammatory diet usually relied on use of the DII, rather than trials of specific dietary guidance or meal provision. But more concerning is that the data used to calculate these scores are self-reported food frequency or dietary recall data, whose limitations are well recognized.

A final limitation, which is actually a challenge to the field, is the lack of scientific consensus on what constitutes an anti-inflammatory eating pattern. The criteria used to define an anti-inflammatory eating pattern is not consistent across studies, and in fact, the criteria used to define specific diets and diet indices, such as the Mediterranean diet (for which there are at least 5 indices), are not consistent. Although this makes it difficult to compare the effects of one diet against another, the DASH diet and the many variations of the Mediterranean diet have much in common. Both promote increased consumption of fruits, vegetables, whole grains, legumes, and nuts and seeds, although the Mediterranean Diet promotes additional foods or ingredients with anti-inflammatory properties such as olive oil, fish, and herbs and spices. Studies that focus specifically on an anti-inflammatory diet, such as those that use the DII, are still too few in number and too limited in design to enable more far-reaching conclusions to be drawn.

FUTURE RESEARCH

Definitively determining the impact of diets that might have anti-inflammatory properties on the risk of developing chronic diseases depends on first identifying several missing pieces in the biological plausibility chain. Most importantly, intermediate outcomes such as biomarkers that have consistent, significant associations—positive or negative—with disease risk must be identified and ideally, some chain of causality must be established. Inflammation is a natural process that serves vital physiological roles: Thus, the idea that a dietary pattern that non-selectively suppresses inflammation might have health benefits needs extensive clarification. Then it will be necessary to determine whether certain combinations of foods or nutrients or certain overall dietary patterns or the avoidance of certain foods or patterns are responsible for the observed outcomes and whether the outcomes are affected by factors such as genetics and other lifestyle characteristics.

CONCLUSIONS

Moderate or high certainty evidence linking diets with anti-inflammatory characteristics to chronic disease prevention or management outcomes is strong for some conditions but remains relatively sparse for others. Nevertheless, the evidence suggests that adherence to diets such as DASH and Mediterranean-type eating patterns might have beneficial associations with a multitude of health risks. Moreover, adverse events or harms associated with these diets are essentially non-existent.

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Appendix

SEARCH STRATEGIES

Search Date: July 25, 2023			
1. Bibliographic Databases	**#**	**Search Statement**	**Results**
MEDLINE: Systematic Reviews Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations and Daily 1946 to July 25, 2023	1	Mediterranean Diet/ OR Diet, Vegetarian/ OR Diet, Vegan/	9322
	2	(((anti-inflammat* OR DASH OR Mediterranean OR MIND OR vegetarian OR plant?based OR vegan) adj3 diet*) OR MedDiet).ti,ab,kf,kw.	13174
	3	1 OR 2	16155
	4	(systematic review.ti. or meta-analysis.pt. or meta-analysis.ti. or systematic literature review.ti. or this systematic review.tw. or pooling project.tw. or (systematic review.ti,ab. and review.pt.) or meta synthesis.ti. or meta-analy*.ti. or integrative review.tw. or integrative research review.tw. or rapid review.tw. or umbrella review.tw. or consensus development conference.pt. or practice guideline.pt. or drug class reviews.ti. or cochrane database syst rev.jn. or acp journal club.jn. or health technol assess.jn. or evid rep technol assess summ.jn. or jbi database system rev implement rep.jn. or (clinical guideline and management).tw. or ((evidence based.ti. or evidence-based medicine/ or best practice*.ti. or evidence synthesis.ti,ab.) and (((review.pt. or diseases category/ or behavior.mp.) and behavior mechanisms/) or therapeutics/ or evaluation studies.pt. or validation studies.pt. or guideline.pt. or pmcbook.mp.)) or (((systematic or systematically).tw. or critical.ti,ab. or study selection.tw. or ((predetermined or inclusion) and criteri*).tw. or exclusion criteri*.tw. or main outcome measures.tw. or standard of care.tw. or standards of care.tw.) and ((survey or surveys).ti,ab. or overview*.tw. or review.ti,ab. or reviews.ti,ab. or search*.tw. or handsearch.tw. or analysis.ti. or critique.ti,ab. or appraisal.tw. or (reduction.tw. and (risk/ or risk.tw.) and (death or recurrence).mp.)) and ((literature or articles or publications or publication or bibliography or bibliographies or published).ti,ab. or pooled data.tw. or unpublished.tw. or citation.tw. or citations.tw. or database.ti,ab. or internet.ti,ab. or textbooks.ti,ab. or references.tw. or scales.tw. or papers.tw. or datasets.tw. or trials.ti,ab. or meta-analy*.tw. or (clinical and studies).ti,ab. or treatment outcome/ or treatment outcome.tw. or pmcbook.mp.))) not (letter or newspaper article).pt.	606863
	5	3 AND 4	944
CINAHL Ultimate	1	(MH "Mediterranean Diet") OR (MH "Vegetarianism") OR (MH "Plant-Based Diet")	12723
	2	TX (((anti-inflammat* OR DASH OR Mediterranean OR MIND OR vegetarian OR plant?based OR vegan) N3 diet*) OR MedDiet)	26079
	3	1 OR 2	31579
	4	(MH "meta analysis" OR MH "systematic review" OR MH "Technology, Medical/EV" OR PT "systematic review" OR PT	310465

		"meta analysis" OR (((TI systematic* OR AB systematic*) N3 ((TI review* OR AB review*) OR (TI overview* OR AB overview*))) OR ((TI methodologic* OR AB methodologic*) N3 ((TI review* OR AB review*) OR (TI overview* OR AB overview*)))) OR (((TI quantitative OR AB quantitative) N3 ((TI review* OR AB review*) OR (TI overview* OR AB overview*) OR (TI synthes* OR AB synthes*))) OR ((TI research OR AB research) N3 ((TI integrati* OR AB integrati*) OR (TI overview* OR AB overview*)))) OR (((TI integrative OR AB integrative) N3 ((TI review* OR AB review*) OR (TI overview* OR AB overview*))) OR ((TI collaborative OR AB collaborative) N3 ((TI review* OR AB review*) OR (TI overview* OR AB overview*))) OR ((TI pool* OR AB pool*) N3 (TI analy* OR AB analy*))) OR ((TI "data synthes*" OR AB "data synthes*") OR (TI "data extraction*" OR AB "data extraction*") OR (TI "data abstraction*" OR AB "data abstraction*")) OR ((TI handsearch* OR AB handsearch*) OR (TI "hand search*" OR AB "hand search*")) OR ((TI "mantel haenszel" OR AB "mantel haenszel") OR (TI peto OR AB peto) OR (TI "der simonian" OR AB "der simonian") OR (TI dersimonian OR AB dersimonian) OR (TI "fixed effect*" OR AB "fixed effect*") OR (TI "latin square*" OR AB "latin square*")) OR ((TI "met analy*" OR AB "met analy*") OR (TI metanaly* OR AB metanaly*) OR (TI "technology assessment*" OR AB "technology assessment*") OR (TI HTA OR AB HTA) OR (TI HTAs OR AB HTAs) OR (TI "technology overview*" OR AB "technology overview*") OR (TI "technology appraisal*" OR AB "technology appraisal*")) OR ((TI "meta regression*" OR AB "meta regression*") OR (TI metaregression* OR AB metaregression*)) OR (MW meta-analy* OR MW metaanaly* OR MW "systematic review*" OR MW "biomedical technology assessment*" OR MW "bio-medical technology assessment*") OR ((TI medline OR AB medline OR MW medline) OR (TI cochrane OR AB cochrane OR MW cochrane) OR (TI pubmed OR AB pubmed OR MW pubmed) OR (TI medlars OR AB medlars OR MW medlars) OR (TI embase OR AB embase OR MW embase) OR (TI cinahl OR AB cinahl OR MW cinahl)) OR (SO Cochrane OR SO health technology assessment OR SO evidence report) OR ((TI comparative OR AB comparative) N3 ((TI efficacy OR AB efficacy) OR (TI effectiveness OR AB effectiveness))) OR ((TI "outcomes research" OR AB "outcomes research") OR (TI "relative effectiveness" OR AB "relative effectiveness")) OR (((TI indirect OR AB indirect) OR (TI "indirect treatment" OR AB "indirect treatment") OR (TI mixed-treatment OR AB mixed-treatment) OR (TI bayesian OR AB bayesian)) N3 (TI comparison* OR AB comparison*)) OR ((TI multi* OR AB multi*) N3 (TI treatment OR AB treatment) N3 (TI comparison* OR AB comparison*)) OR ((TI mixed OR AB mixed) N3 (TI treatment OR AB treatment) N3 ((TI meta-analy* OR AB meta-analy*) OR (TI metaanaly* OR AB metaanaly*))) OR (TI "umbrella review*" OR AB "umbrella review*") OR ((TI multi* OR AB multi*) N2 (TI paramet* OR AB paramet*) N2 (TI evidence OR AB evidence) N2 (TI synthesis OR AB synthesis)) OR ((TI multiparamet* OR AB multiparamet*) N2 (TI evidence OR AB evidence) N2 (TI synthesis OR AB synthesis)) OR ((TI multi-paramet* OR AB	

		multi-paramet*) N2 (TI evidence OR AB evidence) N2 (TI synthesis OR AB synthesis))	
	5	3 AND 4	1812
CDSR: Protocols and Reviews April 1996-present	1	MeSH descriptor: [Diet, Mediterranean] this term only	768
	2	MeSH descriptor: [Diet, Vegetarian] this term only	242
	3	MeSH descriptor: [Diet, Vegan] this term only	38
	4	(((anti-inflammat* OR DASH OR Mediterranean OR MIND OR vegetarian OR plant?based OR vegan) near/3 diet*) OR MedDiet)	4013
	5	#1 OR #2 OR #3 OR #4	4013
	6	Limit 5 to protocols and reviews	76
Bibliographic databases			
Total results			2832
2. Non-Bibliographic Databases	**Search Statement/Description**		**Results**
AHRQ: evidence reports, technology assessments, U.S Preventative Services Task Force Evidence Synthesis	Mediterranean diet OR vegan diet OR vegetarian diet OR DASH diet OR plant-based diet OR anti-inflammatory diet		0
CADTH	Mediterranean diet OR vegan diet OR vegetarian diet OR DASH diet OR plant-based diet OR anti-inflammatory diet Anti-inflammatory Diets for Chronic, Non-Cancer Pain: Clinical Effectiveness and Guidelines Nutritional Interventions for the Delayed Progression or Reversal of Frailty: Clinical Effectiveness Low Carbohydrate Diets for Diabetes: A Review of the Clinical Effectiveness and Guidelines Dietary Interventions for Chronic Kidney Disease		4
EPPI-Centre	[Use browser search function [CNTL + F] for keyword search] Mediterranean diet OR vegan diet OR vegetarian diet OR DASH diet OR plant-based diet OR anti-inflammatory diet		0
NCBI Bookshelf	Mediterranean diet OR vegan diet OR vegetarian diet OR DASH diet OR plant-based diet OR anti-inflammatory diet Benefits and Harms of the Mediterranean Diet Compared to Other Diets [Internet].		3

	What National and Subnational Interventions and Policies Based on Mediterranean and Nordic Diets are Recommended or Implemented in the WHO European Region, and is there Evidence of Effectiveness in Reducing Noncommunicable Diseases? [Internet]. Diet and Health: Implications for Reducing Chronic Disease Risk.	
NHS Evidence	Not available	
VA: HSR&D	Mediterranean diet OR vegan diet OR vegetarian diet OR DASH diet OR plant-based diet OR anti-inflammatory diet	0
VA: ORD	Mediterranean diet OR vegan diet OR vegetarian diet OR DASH diet OR plant-based diet OR anti-inflammatory diet	0
VA: Dimensions	("Mediterranean diet" OR "vegan diet" OR "vegetarian diet" OR "DASH diet" OR "plant-based diet" OR "anti-inflammatory diet") AND review, limit to VA publications	9
3. Secondary Sources	**Search Statement/Description**	**Results**
BCBS Foundation Massachusetts	N/A	0
CMS Research Reports	N/A	0
Hayes	N/A	0
ICES	N/A	0
National Academies, Health & Medicine Division	N/A	0
McMaster Health Systems Evidence	N/A	0
Robert Wood Johnson Foundation	N/A	0
UBC Centre for Health Services & Policy Research	N/A	0
WHO Health Evidence Network	N/A	0
4. Reviews in development	**Search Statement/Description**	**Results**
AHRD topics in development (EPC status report)	[Email Charli Armstrong Charlotte.Armstrong1@va.gov] KV emailed 07-26-23 CA responded 07-26-23: no duplication	0
PROSPERO (SR registry)	Mediterranean diet OR vegan diet OR vegetarian diet OR DASH diet OR plant-based diet OR anti-inflammatory diet A meta-analysis of effects of Mediterranean diet in patients with nonalcoholic fatty liver disease	32

	A systematic review of diets for weight loss and remission of type 2 diabetes Adherence to a Mediterranean Diet and risk of Alzheimer's and Parkinson's Diseases: a systematic review of population-based studies and evidence from pre-clinical studies Adherence to a Mediterranean -style diet and risk of diabetes: A Systematic Review and Meta-Analysis of Prospective Studies Adherence to DASH diet and hypertension risk: a systematic review and meta-analysis Adherence to Mediterranean diet and risk of cancer: a systematic review and meta-analysis of observational studies Adherence to the Mediterranean diet in relation to all-cause mortality: a systematic review and dose-response meta-analysis of prospective cohort studies Anti-Inflammatory Diets for Patients with a Chronic Inflammatory Disease: Protocol for a Systematic Review and Meta-Analysis of Randomized Trials Association between Mediterranean diet and Parkinson's disease in adults: A systematic review and meta-analysis of cohort studies Benefits and harms of the Mediterranean diet compared to other dietary interventions Dietary interventions for non-alcoholic fatty liver disease: systematic review and meta-analysis Effectiveness of vegetarian and vegan diets in type 2 diabetes mellitus: Systematic review Evidence on vegan diet for health benefits and risks – an umbrella review of meta-analyses of observational and interventional studies Impact of Vegetarian, Vegan and Non-Vegetarian Diets on Cardiometabolic Disease Prevention, Secondary Prevention and Management in Adults The effectiveness of a low-fat vegan diet for the prevention and management of type 2 diabetes: a systematic review and meta-analysis of controlled trials Vegan and vegetarian diets vs. omnivore diets: implications on human health: a systematic review of randomized clinical trials	

	Effects of vegetarian and vegan diets on insulin sensitivity in people with overweight or type 2 diabetes: protocol for a systematic review and meta-analysis Efficacy of Plant-based Dietary Patterns in the management of type 2 diabetes mellitus: A Systematic Review and Meta-Analysis Healthy effects of vegetarian diets: evidence and mechanisms Nutritional and health outcomes associated with vegetarian diets: an umbrella systematic review of meta-analyses Role of Vegetarian and Plant-based diet in the prevention of Mild Cognitive Impairment and Dementia Systematic review and meta-analysis of the associations of vegan and vegetarian diets with inflammatory biomarkers Systematic review of the relationship between vegetarian diets and health-related outcomes Adherence to DASH diet and hypertension risk: a systematic review and meta-analysis Effect of anti-inflammatory diet on NAFLD: systematic review Effect of anti-inflammatory diets on inflammation markers in adult human populations: a systematic review of randomized controlled trials Update 2020-2023 Effect of Plant-Based Diets on Rheumatoid Arthritis: A Systematic Review Effect of Plant-based Dietary Patterns in Type 2 Diabetes Patients: A Systematic Review of Randomized Controlled Trials Effect of the level of adherence to the DASH diet on blood pressure: a systematic review and meta-analysis of observational studies Anti-Inflammatory Diets for Patients with a Chronic Inflammatory Disease: Protocol for a Systematic Review and Meta-Analysis of Randomized Trials The effects of an anti-inflammatory diet on chronic inflammation and disease activity in adults diagnosed with rheumatoid arthritis	

Summary	
Bibliographic databases	2832
Non-bibliographic databases	16
Secondary sources	0

Reviews in development	32
Total results	2880
Total after deduplication	2309

STUDIES EXCLUDED DURING FULL-TEXT SCREENING

No GRADE, *N = 251*

1. Abbas, N., et al., A Systematic Review of the Role of Diet in Ulcerative Colitis. Cureus, 2023. 15(5): p. e39350.
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PEER REVIEW COMMENTS AND RESPONSES

Comment #	Reviewer #	Comment	Author Response
Are the objectives, scope, and methods for this review clearly described?			
1	2	No - The rationale for examining the specific dietary patterns in this paper was not well documented. In addition, this is largely described as an evidence map - though in some placed referred to as an umbrella review - and clarity to type of evidence synthesis product and alignment with the methods would be helpful.	We have added a description of the rationale for the choice of dietary patterns we included.
2	3	Yes	N/A
3	4	Yes	N/A
4	5	Yes	N/A
5	6	Yes	N/A
6	7	Yes	N/A
7	8	Yes	N/A
Is there any indication of bias in our synthesis of the evidence?			
8	2	No	N/A
9	3	No	N/A
10	4	No	N/A
11	5	No	N/A
12	6	No	N/A
13	7	No	N/A
14	8	No	N/A
Are there any published or unpublished studies that we may have overlooked?			
15	2	No	N/A
16	3	Diet and Chronic Non-Cancer Pain: The State of the Art and Future Directions. Authors: Brain, K et. al. published 2021	We reviewed this publication, but it did not meet inclusion criteria as it is not a systematic review.
17	3	Dietary recommendations for the prevention of depression. Author: Opie et. al Published 2017	We reviewed this publication, but it did not meet inclusion criteria as it is not a systematic review.

Comment #	Reviewer #	Comment	Author Response
18	3	Effect of polyphenols in a Mediterranean diet on symptoms of depression: A systematic literature review. Authors: Bayes, J et. al.	We reviewed this publication, but it did not meet inclusion criteria as it about specific nutrients, and not diets of interest.
19	4	No	N/A
20	5	No	N/A
21	6	No	N/A
22	7	No	N/A
23	8	No	N/A
Additional suggestions or comments can be provided below.			
General			
24	3	I believe including the WHO definition of the clinical term "frailty" under evidenced maps where frailty is discussed (page 13) would be beneficial to clinicians who are not familiar. Frailty is an important factor in health and aging; and the clinical usefulness of reducing this risk would be a helpful acknowledgement in the report. Clinicians who are not familiar with the term may not understand the full impact of reducing its occurrence.	Added as text to the first results section that mentions frailty.
25	4	It may helpful to further emphasize the fact that studies on cardiovascular disease, diabetes, and obesity were omitted due to the assumption that it is widely accepted that anti-inflammatory diets are beneficial for prevention and treatment of these conditions. There is a wide body of evidence supporting this, and Mediterranean diets are recommended by the American Diabetes Association, American Heart Association, and Academy of Nutrition and Dietetics for these conditions. In order to make the body of evidence more manageable for an evidence map, we chose to exclude CVD, diabetes, and obesity and to focus on other conditions that have not been studied quite as much. This evidence makes it quite clear, that more high quality research is needed on anti-inflammatory diets, especially for cancer, liver disease, and frailty.	Added a version of this language to the executive summary
26	4	Another challenge highlighted by this evidence map, is the difficulty defining an anti-inflammatory eating pattern; the definition of anti-inflammatory eating pattern is not consistent across all studies, which makes it difficult to compare the effects. For example, DASH diets and Mediterranean Diets both promote	Added language to both the inclusion criteria table and the conclusions (limitations) to address this.

Comment #	Reviewer #	Comment	Author Response
		increased fruits, vegetables, whole grains, legumes, and nuts and seeds; however, the Mediterranean Diet includes additional anti-inflammatory properties such as olive oil, fish, and herbs and spices. Studies that focus specifically on anti-inflammatory diets, such as those that use the DII are so limited without any RCTs that it is hard to draw conclusions.	
27	5	I would not suggest including DASH diet. DASH diet may not always fall in the category of an anti-inflammatory plan.	We included DASH because it shares many of the anti-inflammatory properties endorsed by other diets, and when discussed during scoping conversations with our operations partners and technical experts, the group reached consensus to include it.
28	6	Please add IFNCP to the credentials for Kwynn Mason	Added IFNCP for Kwynn Mason.
29	8	Overall, great, thorough review. I was surprised there were no findings related to things like depression, anxiety, fibromyalgia, chronic fatigue, etc. I did a preliminary search for SRs related to these conditions and then found that the SRs I came across were listed under excluded studies. It might be helpful to include in the background or study selection sections some mention of these other conditions for which no findings are reported because the studies didn't meet inclusion criteria.	We added a statement to the limitations that addresses this point.
Executive Summary			
30	2	Page ii: I am a strong proponent of including the librarian or bioinformaticist that developed and execute the literature search as an author on the paper, rather than just mentioning their role in the acknowledgements. Developing a comprehensive literature search is fundamental to the review process, and I believe that role warrants authorship.	We often do include librarians as co-authors. For this project specifically, the librarian we worked with was unavailable during the drafting and report development, and as such we were unable to include her in the process and could not get her permission to be included as an author.
31	2	Page v, Key Findings: Given that this is an evidence map, and not a review of reviews or umbrella review, making recommendations on the basis of the findings may not be warranted. Recommendations should be based on a review, in which the risk of bias or quality of studies is evaluated, evidence is synthesized, and strength of evidence assessed.	We agree making recommendations on the effectiveness or efficacy of anti-inflammatory diets based on evidence maps would be inappropriate. We have revised the wording to clarify that our recommendations pertain to the strength of evidence, quality of existing literature, and gaps in the literature.
32	8	1) Pg v, lines 4-5 under Key Findings, 1st bullet point, 2nd statement uses studies/study 3 times.	Reworded
33	8	2) Pg v, line 8 – shouldn't "blood pressure" here be "high blood pressure" or "hypertension"?	Reworded

Comment #	Reviewer #	Comment	Author Response
34	8	3) Pg v, lines 9-10 – suggest changing “However, these observations could be due to foods excluded from these dietary patterns or to foods they include” to something like “The observed benefits could be related to the exclusion of particular foods from the dietary patterns, the inclusion of particular foods, or both.”	Reworded
35	8	4) Pg v, lines 10 – I’m not sure I agree that there is a “lack of understanding of how anti-inflammatory diets might be beneficial for preventing and managing some chronic conditions.” It is fairly well-established that inflammation plays an underlying role in many chronic conditions, as are the mechanisms by which various dietary compounds influence the synthesis of anti-inflammatory or pro-inflammatory cytokines. -- Edited to add that language on pg 4 "Proposed mechanisms and direct evidence are generally lacking. Whether inflammation is a cause or consequence of various disease processes remains unclear" is more clear.	We have reworded the language in this section.
36	8	5) Pg v, lines 32-33 – beginning of this sentence needs rewording (see pg vi, line 2-4).	Reworded
37	3	Page vi, line 14 down. Would be helpful to have all 18 moderately supported conclusions listed in one place instead of just a few. Either here or later on in the report.	The conclusions with high certainty of evidence are listed in the summary; We could create a table of the moderate CoE conclusions but given that this is an evidence map, we would hesitate to give them that much weight.
38	8	6) Pg viii, lines 7-9 – same as comment #1 above regarding repetitious use of the word studies/study.	We revised the sentence.
39	8	7) Pg viii, line 15-17 – same as # 4 above: I’m not sure I agree that there is a “lack of understanding of how anti-inflammatory diets might be beneficial for preventing and managing some chronic conditions.” It is fairly well-established that inflammation plays an underlying role in many chronic conditions, as are the mechanisms by which various dietary compounds influence the synthesis of anti-inflammatory or pro-inflammatory cytokines. -- Edited to add that language on pg 4 "Proposed mechanisms and direct evidence are generally lacking. Whether inflammation is a cause or consequence of various disease processes remains unclear" is more clear.	We revised the wording, as indicated above.

Comment #	Reviewer #	Comment	Author Response
40	8	8) Pg viii, line 18 – Delete “Limitations” prior to “This evidence map has a number of limitations…”	We deleted “Limitations” and included transitional words for clarity.
41	8	9) Pg ix, line 18 – RE: “immutable factors such as genetics” – doesn’t seem to account for reality that genes don’t exist in a vacuum and diet affects gene expression (nutrigenomics).	Revised
42	8	10) Pg ix, line 24 – same as #2 above: shouldn’t “blood pressure” her be “high blood pressure” or “hypertension”?	Revised
43	4	Page ix, lines 20-26: The first two conclusions that were supported by high certainty of evidence seem very similar and could maybe be combined into one? The relationship between DASH diet and HTN is widely accepted; summarizing these two conclusions may give more clout to the others listed.	These conclusions are separated because one is based on a review of patients with hypertension, and the other was based on studies of people with normal BP or pre-hypertension.
Introduction			
44	2	Pg 4, introduction: The introduction is not adequately referenced. Numerous statements are made with no supporting citations provided.	Additional references have been added to the introduction.
45	8	11) Pg 4, line 10 – dietitian (as opposed to dietician) was adopted as the official spelling in 1930.	Spelling changed throughout the document.
46	3	Page 4, line 10. Dietitians is generally spelled with a T and to remain consistent in the publication would recommend changing "dieticians" to dietitians	Spelling changed throughout the document.
47	2	Pg 4, after Line 16: Consider adding a section to introduce “nutrition and inflammation.” The introduction addresses inflammation and health, and diet and chronic disease, but does not adequately set the stage for the relationship between diet and inflammation.	We cited at least one recent review on the evidence linking nutrition and inflammation, but since the purpose of this report is to compile the evidence linking nutrition and inflammation, we would not ordinarily do this.
48	2	Pg 4, line 33: It would be helpful to establishing the scope and purpose of this work to provide a definition of inflammation.	We have added this definition and elaborated on the link between chronic inflammation and disease.
49	2	Pg 5, Lines 5-7: While DASH is relatively lower in refined carbs and saturated fat, those are not the defining features of DASH – rather fruits, vegetables, lean meats, low-fat dairy, and lower sodium are. This sentence does not adequately define or describe the key features of the DASH pattern.	We greatly expanded on the description of the DASH diet.
50	8	12) Pg 5, line 5-7 – while it is true that the DASH diet is low in refined carbs and sat fat, it is specifically characterized as being	We have augmented the description of DASH.

Comment #	Reviewer #	Comment	Author Response
		high in fruits, vegetables, nuts, whole grains, and low-fat dairy and emphasizing fish, chicken and lean meats as animal protein sources.	
51	2	Pg 5, Line 23-25: I am unaware of any Mediterranean diet score that includes level of processing as a scoring feature. As with DASH, the Mediterranean diet is not defined on the basis of animal fats or simple carbohydrates – but rather fruits, vegetables, olive oil, lean meat and seafood, etc. This is an inadequate description of the pattern.	We have significantly modified this description with additional references.
Methods			
52	2	Page 6, Line 13: Here, this work is referred to as an umbrella review – whereas elsewhere its referred to as an evidence map. Those are fundamentally different products – with an umbrella review more often thought of as a systematic review of reviews that seeks to draw and grade conclusions from the evidence, and an evidence map as the result of scoping activity intended to describe what has been published on a topic – more descriptive in nature.	We have made the language consistent.
53	2	Pages 7-8, Eligibility criteria: This table would be easier for the reader to follow if it included separate columns for inclusion and exclusion criteria. As currently presented, its hard to easily sort through what is in and what is out.	This table is the standard format for our products.
54	2	Page 7, Lines 7-23: The authors have indicated an interest in focusing on a small set of specific dietary patterns, but have not provide clear rationale or justification for focusing on these patterns. Suggest adding content to the introduction and/or methods to provide justification.	We added text to the introduction elaborating on the rationale. We were asked to focus on these diets by the sponsor, with whom we worked to focus on the most relevant outcomes and dietary patterns.
55	2	Page 7, Lines 25-27: Recommend making note that only reviews that included formal evidence grading somewhere in the executive summary.	We have added that to the description of study selection.
56	8	13) Pg 8, first bullet– wondering why DASH low sodium was excluded?	DASH Low Sodium studies were excluded because studies of that diet combined the DASH diet (which is similar in important ways to other anti-inflammatory diets) with a low-sodium focused diet. Therefore, it would not be possible to attribute findings solely to the anti-inflammatory aspects of the eating pattern without

Comment #	Reviewer #	Comment	Author Response
			considering the possible synergism with lower sodium/higher potassium intake.
57	2	Page 8: While this is an evidence map, it seems the authors were interested in taking it a step further – and using the information gathered to provide practitioners with recommendations. Thus, it is not clear why the quality or risk of bias of the identified reviews was not assessed using AMSTAR or the ROBIS tool. This assessment would help in interpreting and describing the reviews in the maps and help better inform recommendations. However, if this remains an evidence map, and not an umbrella review, this assessment may not be needed.	The report was in fact intended to be an evidence map. Also, by imposing the inclusion criterion of GRADE or other certainty of evidence assessment, we assessed a higher quality subset of existing systematic reviews. Further, our intention was not to provide recommendations but to simply map the evidence and expose gaps.
58	2	Pg 9, Synthesis: Were any efforts made to evaluate the overlap in primary articles in reviews addressing the same dietary patterns and outcomes? Without this assessment, later in the paper, one cannot simply add the total included articles to estimate what evidence has been published on a topic. Also, without evaluating this overlap, its difficult to determine whether reviews on the same topic are based on the same or different bodies of evidence.	We now describe areas of overlap wherever possible. There were instances where we were unable to determine overlap based on the way included reviews reported on their data, but in all cases where there was overlap observed, we now include this in the text.
59	2	Pg 9, Synthesis, Line 1: Given that this is an evidence map, using the term “synthesis” to describe this step of the process may be inappropriate. Rather, the authors should describe this as “description of the evidence.”	The Synthesis section describes the approaches taken to understand the identified evidence. This general usage of “synthesis” is well established in the systematic review context, where the term encompasses quantitative pooling of studies as well as visualization and narrative synthesis methods like those used in the present review.
60	8	14) Pg 9, lines 5-6: says information is displayed on 4 dimensions but then names 5.	It is actually 5. Thank you.
Results			
61	2	Pg 11, Lines 6-7: use of the term “cardiovascular disease topic” is confusing here, given that reviews on CVD were excluded. Recommend changing this to more directly refer to BP?	This term is used to describe the number of studies excluded for covering that topic, but we have clarified that BP studies were included.
62	2	Pg 11, Characteristics of Included Reviews: Consider describing the outcomes addressed in the review first and the types of dietary patterns examined before describing the number of conclusions drawn. Also, does the number of conclusions matter as much as the nature or direction and strength of the	Because this is an evidence map, the numbers of conclusions per review and their crosswalk is simply an introduction to describing the landscape and mapping.

Comment #	Reviewer #	Comment	Author Response
		conclusions. That may not be a very useful metric to report. This is also where you can describe the 2 patterns – other than DASH and MD – that are covered in the evidence map.	
63	8	15) Pg 11, Characteristics of Included Reviews -- the number of reviews for each diet doesn't seem to match what is stated in the exec summary, pg vi, lines 39-40 & pg vii, lines 1-2	The information reported in the Executive Summary (numbers of reviews that reported on each dietary pattern) is different from the information reported in the main report. We have added the information from the Summary to the main report.
64	8	16) Pg 11 – delete "Error! Reference source not found."	We don't see that. It may have appeared in the pdf that was sent out for review. We apologize.
65	3	Pg 11, has the following sentence that needs to be removed. "Error! Reference source not found. "	We don't see that. It may have appeared in the pdf that was sent out for review. We apologize.
66	2	Pg 11, Lines 19-22: These sentences seem out of place, and would be better paired with the previous content about the number of conclusions drawn.	We have reorganized the sentences to clarify the descriptions.
67	5	I would also consider an evidence map for the anti-inflammatory research listed on page 12.	We are not sure what the reviewer is referring to. If the suggestion is to create an evidence map for the reviews of anti-inflammatory research identical to figure 4, the map in the Executive Summary is intended only as a sample.
68	2	Pg 13, Evidence Maps: A lot of the content in this section directly reports identical content to that in the actual figures or tables. In addition, throughout this section, the Tables are not internally referenced in the text. In all of the sections in this section, the information is not reported in a consistent format. It would be most useful to begin each section by orienting the reader the number of reviews identified, describing their findings, and sharing the conclusions and strength of evidence grades. In some cases, the grade or conclusion is mentioned before the reader has a sense for what was found in the literature.	We have reorganized the text to be more consistent across conditions and diets. We also added callouts for the figures and tables and information on the various ways of assessing the Med diet.
69	2	Pg 13, Evidence Maps: It would be very useful for the authors to provide a more thorough discussion and description of how the dietary patterns were defined in the literature – including how they were measured, the similar and dissimilar food and beverage components across papers, etc.	We have added a discussion of the definitions and the various measures used to assess the Mediterranean diet.

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70	2	Pg 13, Lines 11-12: Multiple measures of what? Multiple measures of dietary intake over time? Or multiple MD scoring indices?	The latter: we have completely revised the wording to clarify that multiple different tools were used to assess the MD.
71	2	Pg 13, Blood Pressure: This section is a good example of where one wonders how much overlap there is in the primary studies included in all of the reviews addressing the same topic.	We now report on the overlap between studies included in the two reviews of RCTs for MD and BP and discuss this in greater detail in our response to comment 58.
72	2	Pg 14, Lines 18-20: For a mapping activity, it seems highly useful to provide more documentation on these low and very low certainty reviews. I would suggest adding them into the main report, and not leaving them to a supplement only. This can be critical information for practitioners – who are likely interested in knowing where the evidence is strong, but also where there is no or very weak evidence.	A challenge is that for some conditions (*eg,* cancer and frailty for the Mediterranean Diet) some reviews reported moderate-to-high certainty conclusions while others reported low or very low certainly conclusions for the same conditions. We also have added an explanation regarding why we do not describe conclusions with low or very low certainty of evidence in the narrative.
73	2	Pg 15, Figure 2 (all figures): These are very helpful figures overall, but there is a lot of blank space – and some of the text is hard to read. The term “mixed” is also not clear – I presume this means both trials and observational studies? I would recommend just directly stating that in all places where “mixed” is used in this report. Also, these figures need to be able to standalone – and would benefit from more description labels/titles, keys, etc.	We have added the description of the symbols to the introductory text in the Results section. Since there were categories for which we found no studies, we are not sure how to rebalance the space.
74	2	Pg 16, Table 2: This table would be more useful to the reader if the studies were grouped by outcome, rather than alphabetical. The table would better support the text if re-organized in that way.	We agree and have done so.
75	2	Pg 23, DII & Pg 26 Vegetarian/Plantbased: These sections seems to be missing the same kind of introductory paragraph provided for MD and DASH. In addition, the term “plant-based” is problematic – while it commonly used by lay people, its really unclear from a scientific perspective, and it would be better to just use the term vegetarian, if that’s the case. (Most people consume a “plant-based” diet, given that the majority if the average person’s diet comes from plant foods, including grains.)	We have added explanatory paragraphs regarding the DII and vegetarian diets.
76	2	Pg 26: Consider describing the vegan dietary pattern evidence within this section.	We have re-organized the diet sections so that the vegan diet section immediately follows the vegetarian/plant-based diet section.
77	5	For the evidence maps, adding in the type of cancers would be helpful. For example, on page 24, Figure 4. Since these dietary	The tables of conclusions report the types of cancer and we have added that information to the text. We

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		approaches are similar, could we look at some of similarities and look at overall impact and build an evidence map off of those similarities?	believe adding that information to the evidence maps would make them unreadable.
78	2	Pg 34, Discussion: Did the authors consider including a more in-depth discussion of the commonalities between the DASH and MD dietary patterns, and how those relate or compare to current dietary guidance? Using only labels to describe dietary patterns is not always the most useful to practitioners or the public. It would be very useful to describe the common foods and beverages and highlight how much similarity there is between those patterns. When the commonalities are taken into account, it would seem that there is actually quite a bit of evidence, high and moderate strength, to support the recommendation of dietary patterns with fruits, vegetables, lean meats and seafood, low-fat dairy for a host of chronic conditions.	We have added this information to the introduction and we now briefly review it again in the Discussion.
79	2	Pg 34, Lines 17-18: Please see my previous comment about this not being an appropriate characterization of the key features of the DASH diet.	We have completely revised our description of the DASH diet.
80	8	17) Pg 34, lines 17-18 – again, reducing the DASH diet to “a diet low in saturated fat” misses the defining characteristics as mentioned in #12 above.	We have added detail regarding the DASH diet to the introduction as well as to the Discussion.
81	2	Pg 35, Table 8: This is a nice table, but it would be nice to see the same for the moderate reviews. Many are willing to base recommendations or guidance on high or moderate strength evidence, and highlighting all of that evidence would be useful to the end-user.	We have added a table with moderate reviews after table 8.
82	2	Pg 36: The number of search results is not an acceptable way to assess publication bias. Rather, you should focus on the comprehensive literature search that was done across multiple databases with no time restrictions.	Yes, we did not intend for these numbers to serve as evidence of the inclusiveness of our searches. We have omitted the statements
83	2	Pg 36: You cannot make a statement about the number of primary studies without evaluating overlap between reviews.	Yes, we have now assessed overlap of included studies where two or more reviews reported on the same intervention/exposure and outcomes, but we also deleted the comment regarding numbers of studies.
84	2	Pg 36, Lines 38-39: This limitation could easily be addressed by doing an AMSTAR assessment of each review.	We chose to use the criterion of conducting an assessment of the certainty of evidence in lieu of conducting AMSTAR or ROBINS.

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85	2	Pg 36, Line 30: Please provide more information about what criteria was used to determine what review was “the most informative.”	We now have listed our criteria.
86	2	Pg 36: Confounding is indeed an issue - but theoretically the grading accounted for this. So, while it is certainly a limitation of the primary literature - it seems unfair to make such a strong statement about it here, given that it is taken into consideration during the grading process, and the grades assigned account for it. In addition, the authors have not appropriately recognized the limitations of trials in this type of literature. Dietary patterns are intended to be consumed over time – and many of the outcomes are long-term – meaning that RCTs, especially short-term ones, cannot adequately capture the exposure and outcomes of interest.	We reframed the discussion of this limitation in light of your observations.
87	2	Pg 37, Conclusions: Based on the evidence identified, and the number of high and moderate reviews identified, I am not sure I would agree that the evidence is sparse? The evidence available was consistent, particularly when consider the commonalities between many of the patterns examined.	We have reframed this sentence.
88	8	Pg 38, line 4 – the Keys Seven Countries Study was not published in 2024, and the link listed is not a link to the actual study itself.	We thought it would be more helpful to cite a recent perspective on the importance of that study but have replaced it with one of the original references.