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

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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.

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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.

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."

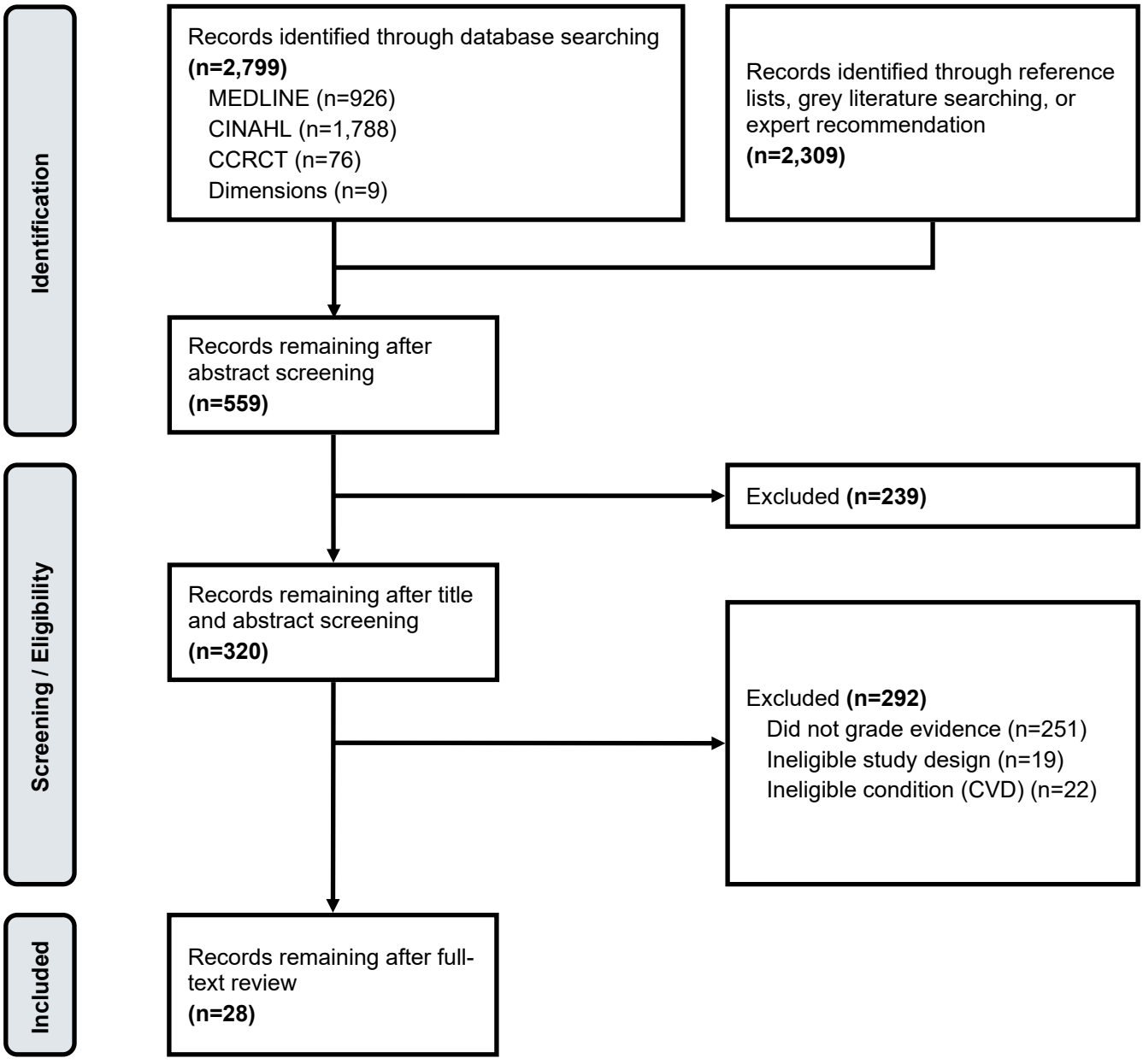
Dietary pattern or intervention (x-axis): Each conclusion is plotted as showing either "potential benefit" or "no benefit."

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

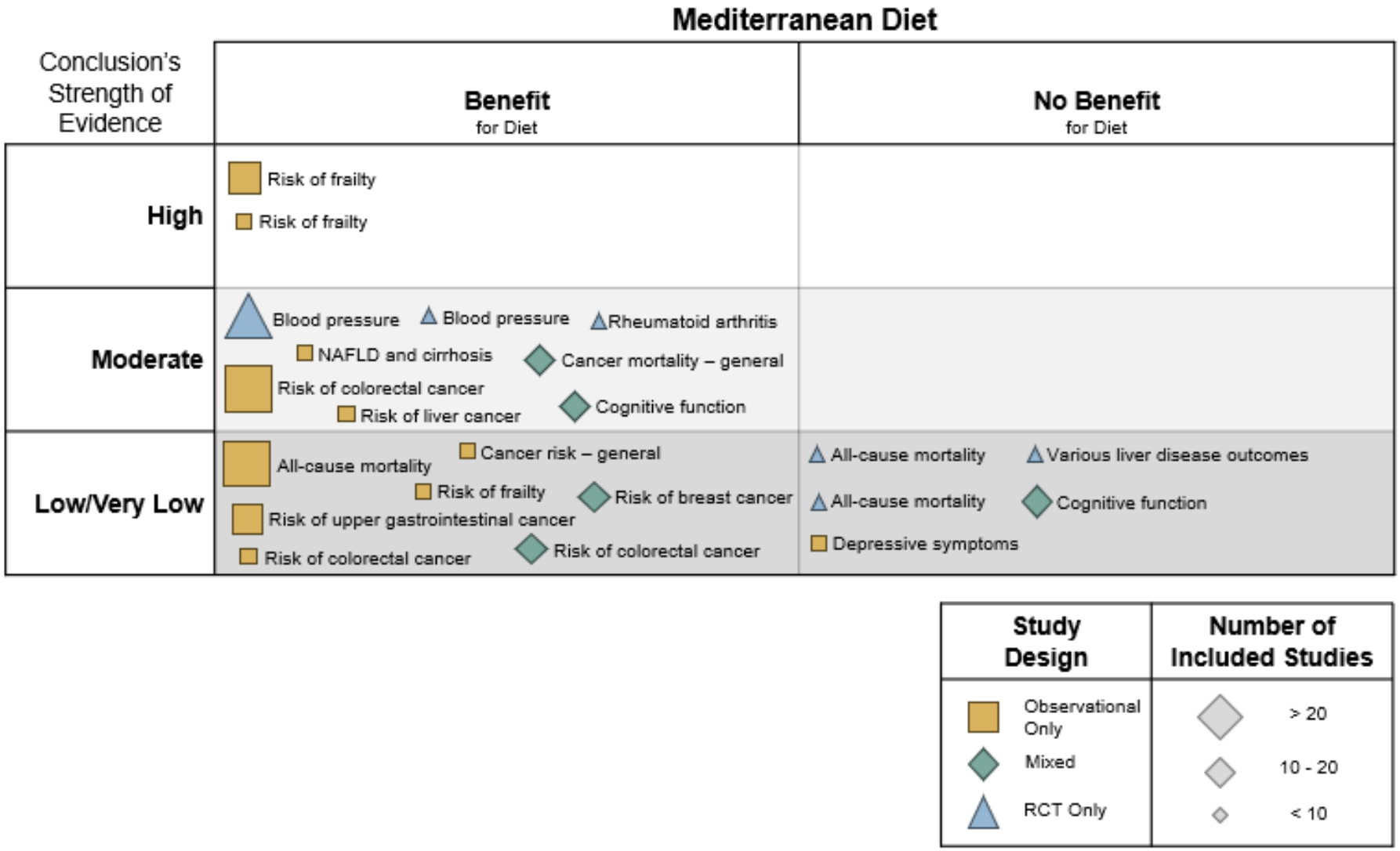


Table 2. Evidence Table of Mediterranean Diet Conclusions

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

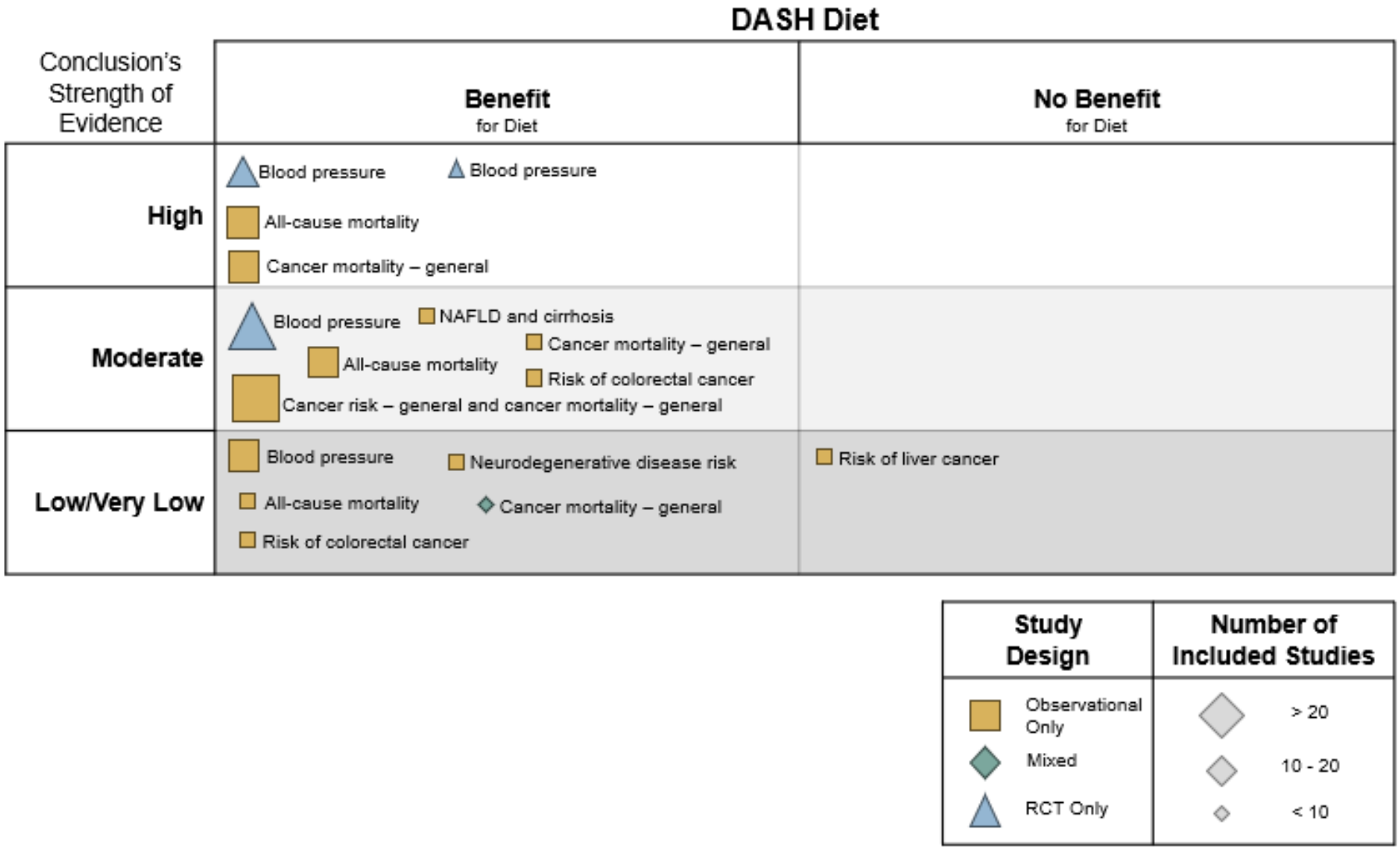


Table 3. Evidence Table of DASH Conclusions

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

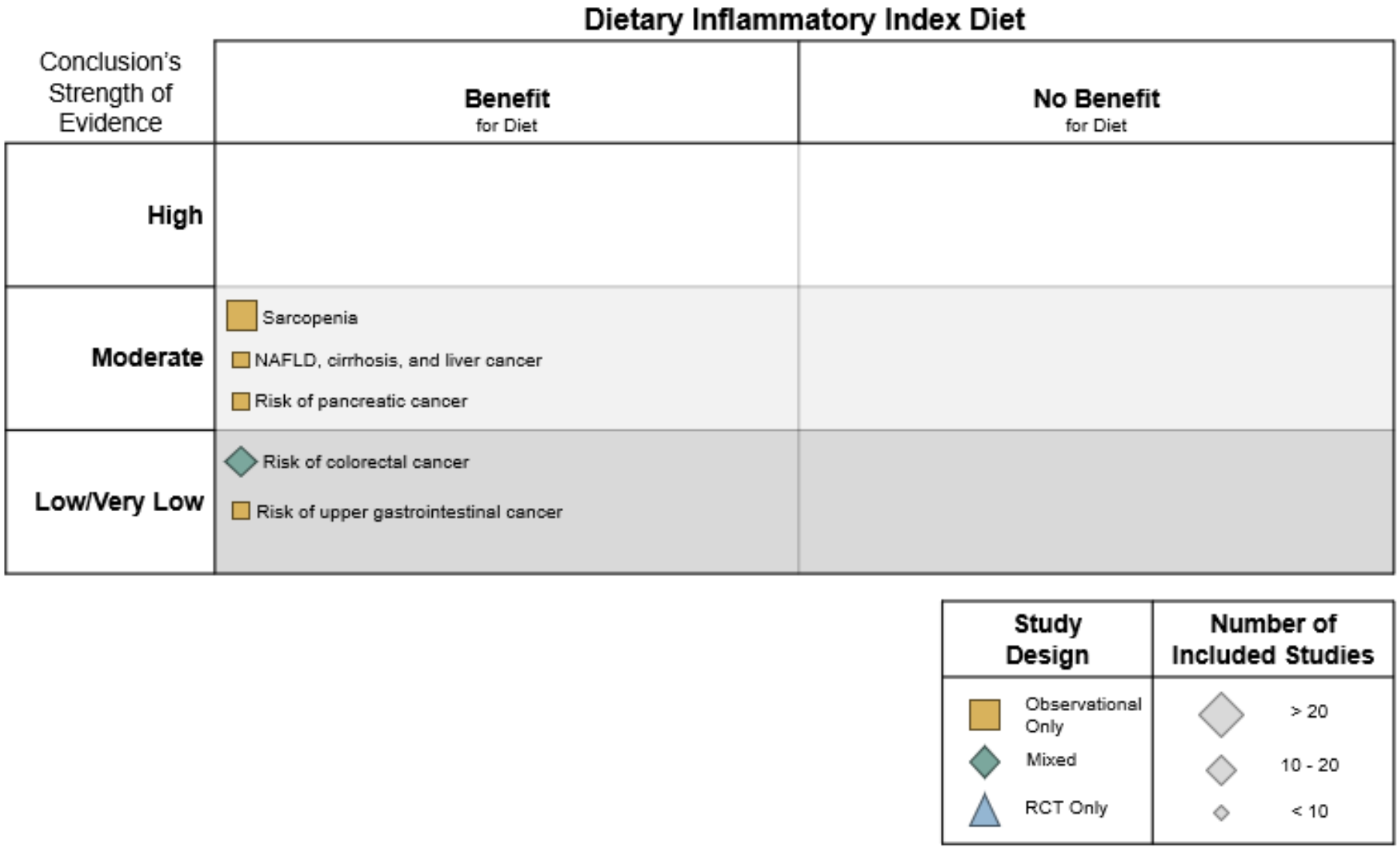


Table 4. Evidence Table of Dietary Inflammatory Index Conclusions

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

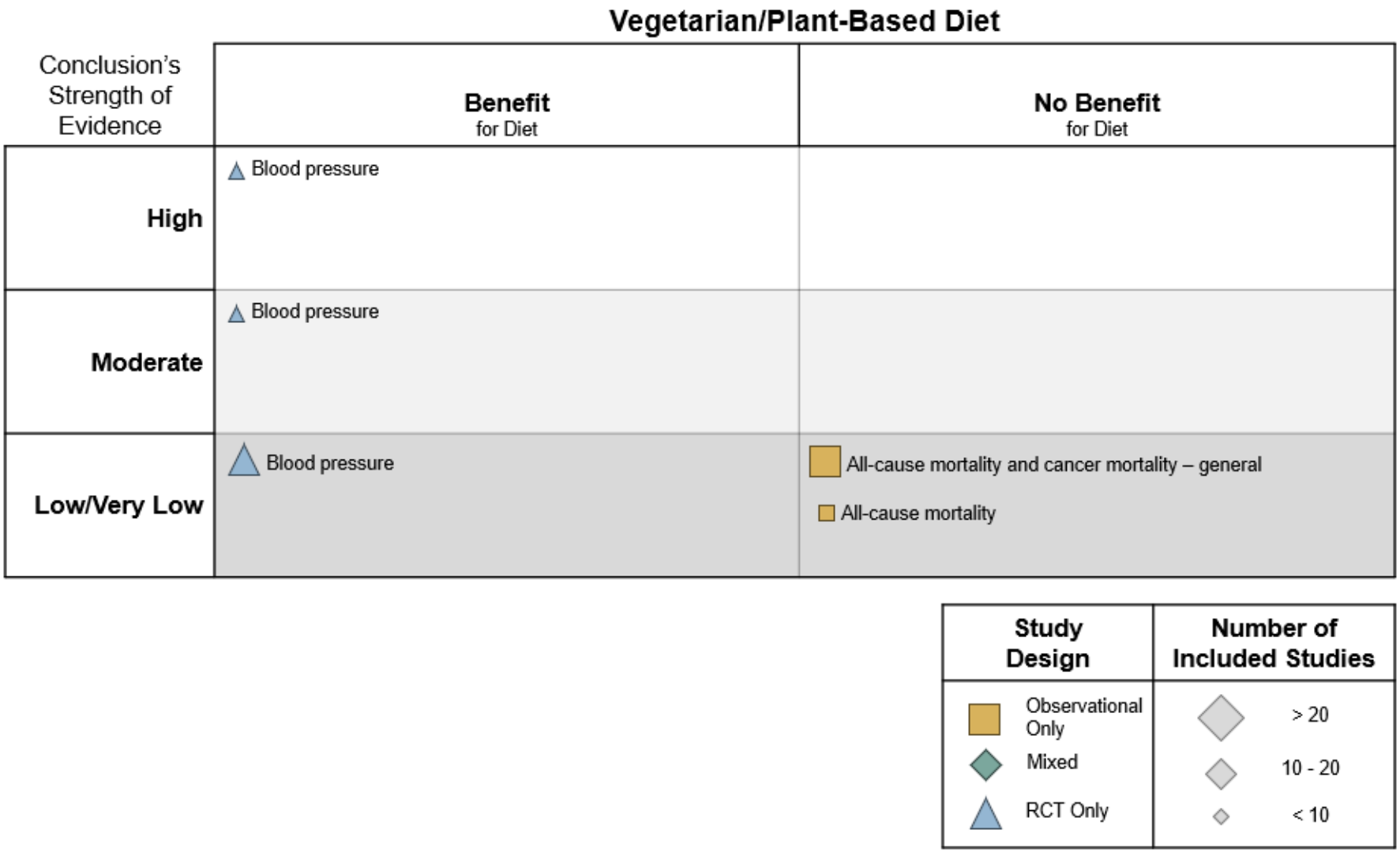


Table 5. Evidence Table of Vegetarian/Plant-Based Diet Conclusions

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

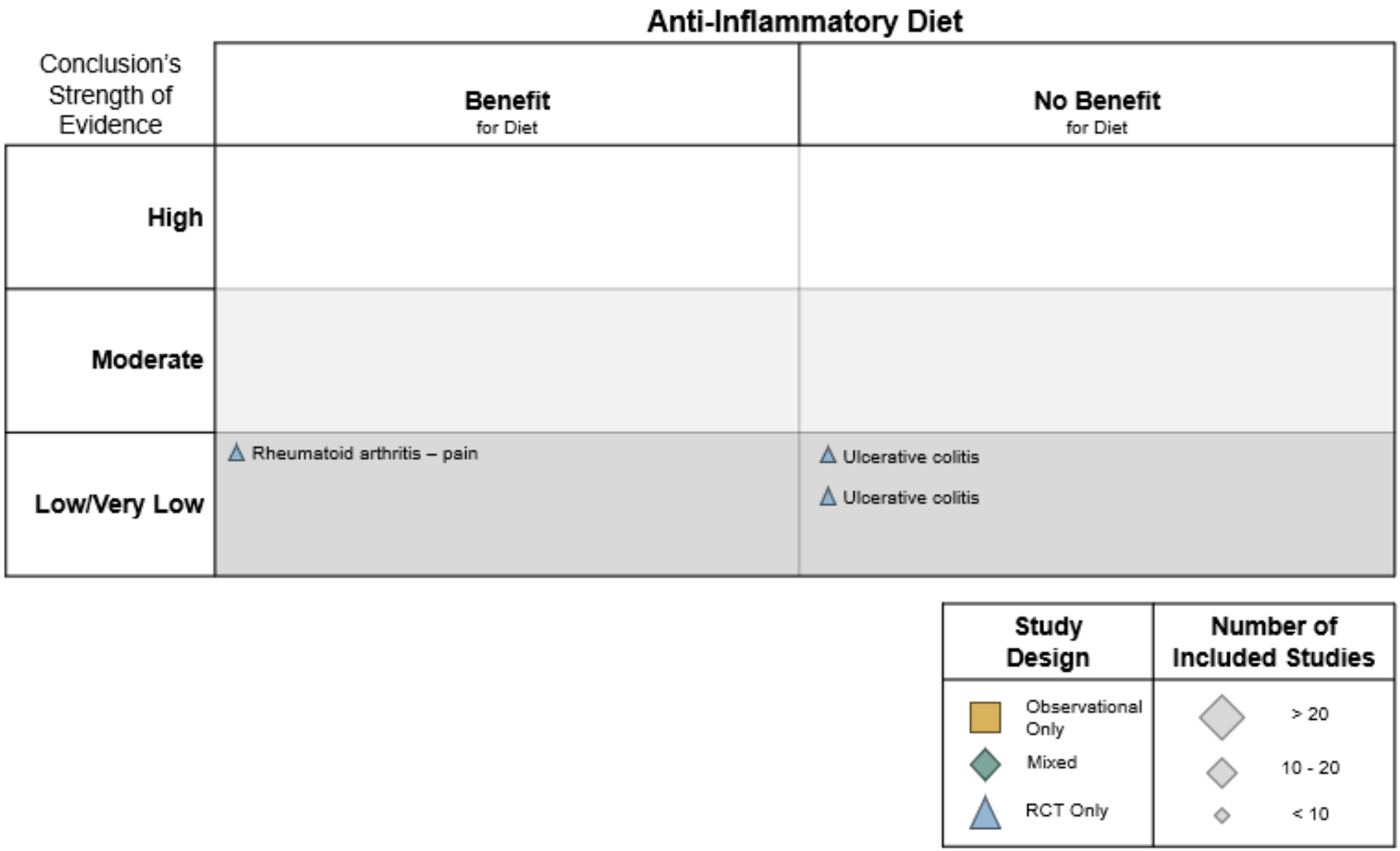


Table 6. Evidence Table of Anti-Inflammatory Diet Conclusions

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

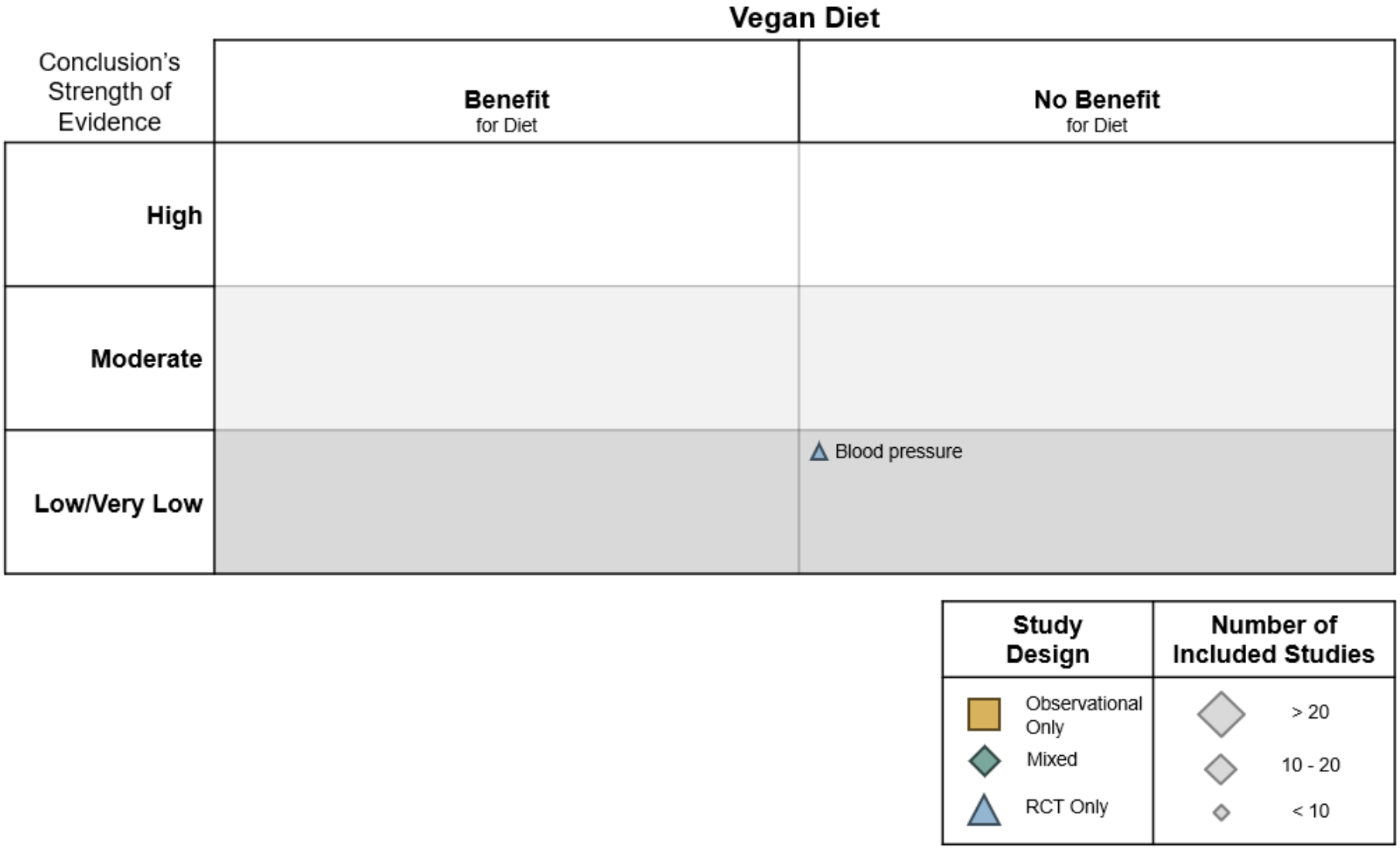


Table 7. Evidence Table of Vegan Diet Conclusions

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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