The Scientific Foundation For The Dietary Guidelines For Americans

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2025–2030

Ensuring a Rigorous, Independent Scientific Foundation for the *Dietary Guidelines for Americans, 2025–2030*

To establish a rigorous scientific foundation for the *Dietary Guidelines for Americans,* the Trump Administration implemented an independent evidence review process to address and correct deficiencies identified in the *Scientific Report of the 2025 Dietary Guidelines Advisory Committee* (DGAC Report), which framed its analysis through a health equity lens. In contrast, the Trump Administration believes that the central framework for the *Dietary Guidelines* should be the best available nutrition science centered around what humans should eat to prevent and reverse chronic disease and support optimal health. Accordingly, supplemental scientific work was undertaken.

To conduct this supplemental scientific analysis, nutrition scientists and subject matter experts were selected through a federal contracting process based on demonstrated expertise. All experts publicly disclosed any nutrition-related private interests, including those that could present an appearance or potential for private interests.

Prior to initiating the evidence review, a methodology expert established standardized protocols governing study inclusion and exclusion criteria, assessment of study quality and risk of bias, approaches to evidence synthesis, and criteria for grading the strength of evidence. These protocols were designed to ensure that conclusions were driven by the evidence itself rather than by predetermined interpretive frameworks.

Expert reviewers conducted rapid systematic reviews, umbrella reviews, and comprehensive literature syntheses. Evidence was evaluated based solely on scientific rigor, study design, consistency of findings, and biological plausibility. All reviews underwent internal quality checks to ensure accuracy, coherence, and methodological consistency.

The National Institutes of Health (NIH) Office of Nutrition Research coordinated an external peer review process, assigning two independent reviewers to each scientific review. Reviewers were selected based on relevant expertise and absence of conflicts of interest. Review authors addressed all peer reviewer comments and revised their analyses accordingly, and NIH confirmed completion of the peer review process.

Following incorporation of peer review feedback, the U.S. Department of Health and Human Services (HHS) and U.S. Department of Agriculture (USDA) Scientific Report—referred to here as the *Scientific Foundation for the Dietary Guidelines for Americans, 2025–2030*—was finalized as the evidentiary foundation for the 2025 *Dietary Guidelines for Americans.*

This document contains:

- An overview of concerns regarding the DGAC Report
- Overview of Evidence Accepted and Rejected from the DGAC Report
- *The Scientific Foundation for the Dietary Guidelines for Americans, 2025–2030*

The *Scientific Foundation for the Dietary Guidelines for Americans, 2025–2030,* appendices, including supplementary scientific reviews and the complete DGAC Report, are available online.

Concerns with the DGAC Report

The central concern with the DGAC Report was that all scientific questions were evaluated through a health equity lens, obligating reviewers to filter evidence through considerations of race, ethnicity, culture, and socioeconomic status. While these considerations are important for policy implementation, imposing them as interpretive filters during the evaluation of scientific evidence reverses the proper sequence of scientific inquiry.

The Biden Administration described "health equity" as the "central lens" for the DGAC's work, and the term appeared more than 170 times in the DGAC Report. Embedding an equity framework within a document intended to provide unbiased scientific assessment risks allowing existing policy challenges to shape scientific conclusions. Science should inform policy—not be constrained by it. As a scientific document, the DGAC Report should reflect the best available evidence, independent of current policy preferences or implementation concerns.

We recognize and share concerns regarding the affordability and accessibility of healthy food, particularly for disadvantaged populations. However, these challenges are best addressed by first establishing clear, unbiased scientific guidance on the optimal diet for Americans. That science can then serve as the foundation for effective downstream policy solutions.

The urgency of this distinction is underscored by the nation's worsening health outcomes. Today, the United States faces the highest chronic disease rates of any developed nation in the world. More than 70% of our nation's adults carry excess weight, over 40% meet the criteria for obesity, and more than half are diabetic or prediabetic. Our kids are not safe, either—over 35% of our nation's kids have excess body weight, more than 20% meet the criteria for obesity, 1 in 14 are severely obese, and 25% are prediabetic.

There is broad scientific consensus that the Standard American Diet—a typical U.S. diet high in processed foods, added sugars, unhealthy fats, and sodium, while being low in fruits, vegetables, and whole grains—is a major contributor to these skyrocketing chronic disease rates. Rigorous, policy-neutral science—untethered to concerns about equity and inclusion—is essential to enable policymakers to address issues of access and affordability of healthy food without compromising scientific integrity. Equity considerations and public policy preferences pervaded the DGAC Report. The Committee consistently advocated plant-based dietary patterns, deprioritized animal-sourced proteins, and favored high linoleic acid vegetable oils. For example, the DGAC proposed reorganizing protein food subgroups to prioritize beans, peas, and lentils while listing meats, poultry, and eggs last—a symbolic reordering lacking scientific justification. The Report recommended that fat replacements "focus on plant-based sources," encouraged dietary patterns that "increase plant-based and decrease animal-based protein foods," and continued longstanding recommendations for low-fat dairy and butter replacement, despite emerging evidence that calls these positions into question.

Additionally, despite substantial evidence linking highly processed foods to rising rates of chronic disease, the DGAC did not recommend clear limits on their consumption. Instead, the Report emphasized "cultural adaptation" and "flexibility" over clear, measurable guidance. It also failed to take a stronger position on limiting added sugars for children, despite epidemics of childhood obesity and prediabetes in the U.S.

For these reasons, the Trump Administration determined that adopting the DGAC Report would not meet the American public's need for objective, evidence-based nutrition guidance.

The American public deserves dietary guidance grounded in the best available science—free from ideological bias, institutional conflicts, or predetermined conclusions. The resulting *Dietary Guidelines for Americans, 2025–2030,* provide clear, evidence-based recommendations to help Americans make informed food choices that support health, prevent chronic disease, and improve quality of life.

The *Dietary Guidelines for Americans, 2025–2030*, are an invitation to all nutrition researchers to engage in continued scientific inquiry and dialogue to ensure the best possible diet is recommended for Americans. While further research and debate remain in nutrition science, there is broad agreement: The American diet should emphasize whole, minimally processed foods; prioritize high-quality protein, fruits, vegetables, healthy fats, and whole grains; and avoid highly processed foods.

Overview of Evidence Accepted and Rejected from the DGAC Report

	Implemented in the *Dietary Guidelines for Americans, 2025–2030*?		
Dietary Guideline Advisory Committee Recommendations	**Yes**	**Partial**	**No**
Dietary Patterns			
1. Develop a single, inclusive dietary pattern that offers flexibilities to support individual needs and preferences.	☐	☒	☐
2. The Departments conduct research with consumers and/or health professionals to finalize the dietary pattern name.	☐	☐	☒
3. Flexibilities within the core elements of the *Eat Healthy Your Way* Dietary Pattern are recommended.	☐	☒	☐
4. Along with the visual presentation of the *Eat Healthy Your Way* pattern, the Committee recommends narrative advice and tables around the flexibilities within the core elements.	☐	☐	☒
5. Emphasize consumption of vegetables, fruits, legumes (beans, peas, lentils), whole grains, nuts, and fish/seafood.	☐	☒	☐
6. Committee reaffirms current guidance in the *Dietary Guidelines for Americans, 2020–2025,* to limit foods and beverages higher in saturated fat and to limit total saturated fat intake to less than 10% of calories per day starting at age 2 by replacing it with unsaturated fat, particularly PUFA.	☐	☒	☐
7. Enhance the guidance (replace saturated fat with unsaturated fat, particularly PUFA) to indicate that replacement with MUFA and PUFA should focus on plant-based sources.	☐	☐	☒

	Implemented in the *Dietary Guidelines for Americans, 2025–2030*?		
Dietary Guideline Advisory Committee Recommendations	**Yes**	**Partial**	**No**
8. Modify the dietary pattern to emphasize dietary intakes of beans, peas, and lentils while reducing intakes of red and processed meats.	☐	☐	☒
9. Move Beans, Peas, and Lentils Subgroup from the Vegetables Food Group to the Protein Foods Group.	☒	☐	☐
10. Reorganize the order of the Protein Foods Subgroups to list Beans, Peas, and Lentils first, followed by Nuts, Seeds, and Soy Products, then Seafood, and finally Meats, Poultry, and Eggs.	☐	☐	☒
11. Continue to emphasize consumption of low-fat or nonfat dairy and unsaturated fats.	☐	☐	☒
12. Limit consumption of red and processed meats, foods high in saturated fat, and salty/savory snacks.	☐	☒	☐
13. When consuming grains, encourage mostly whole grains and limit refined grains. Intakes should be at least half Whole Grains but encourage shifts to even more Whole Grains.	☐	☒	☐
14. Continue to limit foods high in added sugars, including sweetened beverages and foods.	☒	☐	☐
15. Maintain existing guidance that emphasizes intakes of iron, folate/folic acid, iodine, and choline among pregnant and postpartum individuals.	☒	☐	☐
16. Include more nutrient-dense plant-based meal and dietary recommendation options.	☐	☐	☒
17. Remove the line in the 2020 Healthy U.S. Style Dietary Pattern that presents “Limits on Calories for Other Uses.”	☒	☐	☐
18. The *Eat Healthy Your Way* Dietary Pattern supports flexibility in the proportions of plant- to animal-based Protein Foods consumed that further increases plant-based and decreases animal-based Protein Foods.	☐	☐	☒
19. Highlight the diversity of options within each food group or subgroups that meet the *Eat Healthy Your Way* Dietary Pattern.	☐	☐	☒
20. Highlight the existing special considerations of nutrients and dietary components of public health concern. Calcium, potassium, vitamin D, and dietary fiber are underconsumed, and added sugars, saturated fat, and sodium are consumed in excess.	☐	☒	☐

	Implemented in the *Dietary Guidelines for Americans, 2025–2030*?		
Dietary Guideline Advisory Committee Recommendations	**Yes**	**Partial**	**No**
21. Retain the 2020 Healthy U.S. Style Diet for young children ages 12 through 23 months who are no longer receiving human milk or infant formula, except to change the name of the pattern to the Eat Healthy Your Way Dietary Pattern.	☐	☒	☐
22. Continue the use of inclusive language for feeding infants human milk or iron-fortified infant formula to reflect current practices, while continuing to recommend exclusive human milk feeding during the first 6 months of life when possible.	☒	☐	☐
Beverages and Food Sources of Saturated Fat			
23. Recommend plain drinking water as the primary beverage for people to consume. Water beverages flavored with a small amount of 100% fruit juice may also be suggested as a healthy option.	☒	☐	☐
24. Recommend intakes of sugar-sweetened beverages and other beverages that contain added sugars with minimal or no beneficial nutrients should be limited, rather than reduced/decreased.	☒	☐	☐
25. Reaffirm current guidance to lower consumption of butter and replace butter with vegetable oils that are higher in unsaturated fatty acids.	☐	☐	☒
26. Promote replacement of plant sources higher in saturated fat, such as coconut oil, cocoa butter, and palm oil, with vegetable oils higher in unsaturated fats.	☐	☐	☒
27. For the Dairy and Fortified Soy Alternatives food group, plain cow milk (whole milk) or fortified unsweetened soy beverage can be offered beginning around 12 months of age.	☐	☒	☐
28. Fat-free and low-fat dairy and fortified soy options are recommended for individuals ages 2 years and older.	☐	☐	☒
29. Products containing high amounts of calories and saturated fat and/or added sugars (such as half & half, cream, non-dairy creamers, and flavorings with added sugars such as syrups) should be replaced with versions lower in saturated fat and added sugars.	☐	☒	☐

	Implemented in the *Dietary Guidelines for Americans, 2025–2030*?		
Dietary Guideline Advisory Committee Recommendations	**Yes**	**Partial**	**No**
30. The next edition of the *Dietary Guidelines for Americans* should clearly state that water and nutrient-dense beverages should be the primary beverages consumed during pregnancy and lactation.	☒	☐	☐
Strategies for Individuals and Families Related to Diet Quality and Weight Management			
31. Continue to recommend regular breakfast consumption as part of a dietary pattern that is better aligned with the *Dietary Guidelines,* particularly for children and adolescents.	☐	☐	☒
32. State that recommendations for meals and snacks should focus on nutrient-dense foods and beverages and underconsumed food groups.	☐	☒	☐
33. Incorporate guidance about after dinner/evening snacking in the *Dietary Guidelines*.	☐	☐	☒
34. Use structured feeding practices to promote children's intake of vegetables and fruits, including making those foods available and accessible in the home, providing repeated exposure to new foods, and modeling healthy eating behaviors.	☒	☐	☐
35. Promote diets with a higher number of eating occasions in children, such as dividing nutrient-dense foods into smaller meals/snacks throughout the day.	☐	☐	☒
36. For children and adults, consume smaller portions of energy-dense foods to stay within energy requirements.	☒	☐	☐
37. For children, use portion size strategically to promote intake of vegetables and fruits.	☐	☐	☒
38. For adults, use pre-portioned foods to help reduce intake of energy-dense foods.	☐	☐	☒
39. For foods available in retail stores and food service establishments, offer choices so that energy-dense foods can be purchased in smaller, pre-portioned packages.	☐	☐	☒
40. Strategies to decrease packaging chemical exposures and increase sustainability should be considered, which can include repackaging bulk- or value-sized foods at home into smaller portions using sustainable options.	☐	☐	☒

	Implemented in the *Dietary Guidelines for Americans, 2025–2030*?		
Dietary Guideline Advisory Committee Recommendations	**Yes**	**Partial**	**No**
Lifespan			
41. Incorporate a lifespan perspective within a chronic disease prevention framework to promote growth and development and to improve the healthspan (i.e., the length of time that a person is in good health).	☒	☐	☐
42. Continue to report current dietary intakes by age and life stage—as done in the lifespan approach of the *Dietary Guidelines for Americans, 2020–2025*—while also expanding to consider other sociodemographic groups (age, sex, race and/or ethnicity, and food security status).	☐	☐	☒
43. Recommendations should continue to consider the poor health and high prevalence of nutrition-related chronic diseases among older adults, as well as the high prevalence of indicators of poor health among children, adolescents, and younger adults.	☒	☐	☐
44. The Committee envisions that the *Dietary Guidelines* could shift, through interactive technology, from a static presentation of healthy dietary patterns to provide consumers with more interactive guidance that introduces flexibilities and is more inclusive in its approach.	☐	☐	☒
45. Illustrate how the *Dietary Guidelines* can be adapted for different cultural diets.	☐	☒	☐
46. Provide guidance for adaptation of dietary patterns across different social, economic, geographic, and cultural contexts.	☐	☐	☒
47. Consider conducting more implementation science research to increase consumption of dietary patterns associated with decreased cardiovascular disease and type 2 diabetes, given the strength of the evidence.	☐	☐	☒
48. Consider more education and communication around cup and ounce equivalents and develop interactive tools to make conversions intuitive and easy.	☐	☐	☒
49. Consider directional language (e.g., “increase intake of”).	☒	☐	☐

	Implemented in the *Dietary Guidelines for Americans, 2025–2030*?		
Dietary Guideline Advisory Committee Recommendations	**Yes**	**Partial**	**No**
50. Conduct consumer research on the dietary pattern and food group and subgroup names: ◦ Recommend new consumer research regarding the food group name, "Protein Foods," because foods in other food groups also contain protein.	☐	☐	☒
51. Conduct consumer research on the dietary pattern and food group and subgroup names: ◦ For "Dairy and Fortified Soy Alternatives," suggest not referring to lactose-free options and fortified soy milk and yogurt as "alternatives" because they are part of the Dairy group. Determine if "Dairy and Fortified Soy Alternatives" is the best term to capture recommended foods within this food group (i.e., milk and soy milk, yogurt and soy yogurt, and cheese).	☐	☐	☒
52. Recommend exploring nomenclature for "Other Vegetables" to better reflect the foods in this food group (e.g., asparagus, avocado, bamboo shoots, beets, bitter melon, Brussels sprouts, cabbage [green, red, napa, savoy], cactus pads [nopales], cauliflower, celery, chayote [mirliton], cucumber, eggplant, green beans, kohlrabi, luffa, mushrooms, okra, onions, radish, rutabaga, seaweed, snow peas, summer squash, tomatillos, and turnips).	☐	☐	☒
53. Provide clear advice to consumers that alerts them to sodium levels in foods.	☒	☐	☐
54. Committee supports further reducing voluntary targets to further reduce sodium in the food supply.	☐	☐	☒
55. Consider the findings of 2 other expert committees that are addressing alcoholic beverages and health outcomes.	☐	☐	☒
56. Enhancements to current guidance should focus on feeding practices, which refer to specific goal-oriented behaviors used by caregivers to shape and/or guide children's eating behaviors. The Committee recommends describing feeding practices along higher-order conceptual dimensions of structure, autonomy, support, and control.	☐	☐	☒

Acknowledgements

The data for this report were compiled by Christopher Ramsden, MD, PhD, CAPT, U.S. Public Health Service Commissioned Corps, National Institute on Aging, National Institutes of Health. Input and revisions were provided by the U.S. Department of Health and Human Services and the U.S. Department of Agriculture.

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Disclosure of Nutrition-Related Private Interests

As part of the Trump Administration's commitment to radical transparency, all external nutrition experts conducting scientific reviews to support the *Dietary Guidelines for Americans, 2025–2030,* were asked to disclose any nutrition-related private interests, including those that present an *appearance of a private interest*, a *potential private interest*, or a *material private interest*. Because this request applies only to external experts, it does not follow federal disclosure requirements for federal employees. Instead, this is a streamlined disclosure focused solely on nutrition-related activities.

These disclosures are made publicly available alongside participant information to ensure clarity and trust in the scientific review process.

Experts were asked to provide the information below addressing any appearance, potential, or material private interests within the past 3 years.

Disclosure Categories

1. **Financial Relationships**
   Any current or recent funding, honoraria, consulting fees, or other financial support from food, beverage, supplement, or nutrition-related companies or organizations.
2. **Advisory or Leadership Roles**
   Any current or recent service on boards, committees, or advisory groups for nutrition-related entities.
3. **Intellectual Property**
   Any patents, royalties, or proprietary interests related to nutrition products or services.
4. **Other Relevant Interests**
   Any additional relationships or circumstances that could reasonably be perceived as influencing contributions to the *Dietary Guidelines* Scientific Review Group, including those that may present an appearance of a private interest or could be considered a potential or material private interest.

If no disclosures apply, subject matter experts (SMEs) were instructed to indicate: "No appearance, potential, or material private interests to disclose."

Summary of SME Disclosures

SME Name	Financial Relationships	Advisory or Leadership Roles	Intellectual Property	Other Relevant Interests
Ty Beal	N/A	2024–2026: Member, Guidelines Development Group for the World Health Organization's upcoming guidelines on optimal intake of animal-source foods. 2024–2025: Member, Technical Advisory Group for the Healthy Diets Monitoring Initiative on metrics for healthy diets for children aged 2–19 years. 2021–2024: Member, Scientific Advisory Committee for the Food and Agriculture Organization project, "Comprehensive and evidence-based global assessment of the contribution of livestock to food security, sustainable food systems, nutrition and healthy diets."	N/A	N/A
Benjamin Bikman	N/A	HLTH Code Unicity International.	N/A	Royalties from the sale of a book about insulin resistance.

SME Name	Financial Relationships	Advisory or Leadership Roles	Intellectual Property	Other Relevant Interests
J. Thomas Brenna	Global Dairy Platform (reimbursement for travel to a conference). Global Organization for EPA and DHA (GOED), Advisory panel to develop recommendations for intake of omega-3 DHA and EPA. Nutricia, a subsidiary of Danone (consulting). National Cattlemen's Beef Association/ Texas Beef Council. Consulting and research grant. General Mills and the Washington Grain Commission. Panel to review evidence on the healthfulness of grains in the U.S. diet. American Dairy Science Association. Travel reimbursement for an invited lecture at the annual meeting.	Adepa Life, Pty. Founder, Board member.	Patent US20160095833Al, Branched chain fatty acids for prevention or treatment of gastrointestinal disorders. Published 2008.	Seafood Nutrition Partnership: Board member. A personal financial contribution is made to this nonprofit organization (501(c)(3)), and no payment is received for advisory services. Partial travel reimbursements are received for attending Board meetings and advisory panels. Jiangnan University, Department of Food Science, Shanghai Institute for Biological Sciences: Reimbursement was provided for travel to lectures and meetings with collaborators in China. There is no appointment, laboratory, or staff affiliation, including graduate

SME Name	Financial Relationships	Advisory or Leadership Roles	Intellectual Property	Other Relevant Interests
				students, at any university in China. Danone: Participation on an expert panel that resulted in a publication in 2021 and was subsequently disbanded. Payment was made in 2023. The activity occurred more than 3 years ago, although payment was received at a later date.
Michael Goran	Scientific Advisor, Else Nutrition (infant formula company) for the period 2022–2024 (not currently active). Scientific Advisor, Bobbie Labs (infant formula company) for the period 2023–2024 (not currently active). Scientific Advisor, Begin Health (gut health supplements for infants and toddlers) for the period 2024–May 2025 (not currently active).	Scientific Advisory Board, Sansum Diabetes Research Institute (2021–2024). Medical Advisory Board for Eat Real (organization that promotes healthy school meals); 2024–current (unpaid). U.S. Food and Drug Administration (FDA) advisory committee for infant formula as part of Operation Stork Speed (June 2025; unpaid).	Author of *Sugarproof,* published by Avery/Penguin Random House in 2020; no new royalties received since 2021.	Endowed Chair and philanthropic research support from the Dr Robert C. and Veronica Atkins Foundation.

SME Name	Financial Relationships	Advisory or Leadership Roles	Intellectual Property	Other Relevant Interests
Donald Layman	National Cattlemen's Beef Association (honoraria, consulting fees). National Dairy Council (honoraria, consulting fees). Functional Medicine (consulting fees).	Nutrient Institute (advisory board).	N/A	Metabolic Designs, LLC (co-owner).
Heather Leidy	General Mills Bell Institute of Health and Nutrition (honoraria, research presentations). National Cattlemen's Beef Association (funding, research grant). National Pork Board (funding, research grant). General Mills Bell Institute of Health and Nutrition (funding, research grant). Novo Nordisk (funding, research grant).	General Mills Bell Institute of Health and Nutrition (advisory board). Rivalz™ (advisory board). National Pork Board (advisory board).	N/A	N/A
Ameer Taha	No consulting fees.	N/A	U.S. Nonprovisional Patent Application Title: *IN-SITU PRODUCTION OF ANTI-INFLAMMATORY LIPIDS USING*	Owner and founder of Certo Labs Inc., a company that makes and commercializes columns for lipid and antibiotic extractions.

SME Name	Financial Relationships	Advisory or Leadership Roles	Intellectual Property	Other Relevant Interests
	Received speaker's honoraria from the California Dairy Innovation Center for presenting at a Dairy Innovation Conference in February 2025. Research grants from non-federal sources are as follows: Funding Agency: Fonterra Limited Principal Investigator: Ameer Y. Taha Date: 05/01/2025–03/31/2026 Title: *Secondary analysis of data examining the effect of Milk Fat Globule membrane (MFGM) on cognition and other measures of well-being*. Goal: The major goal of this proposal is to understand the types of memory domains which may benefit from MFGM consumption. The project will involve secondary analysis of existing data. Funding Agency: California Dairy Research Foundation		*MILK FAT GLOBULES* Inventor(s): Nitin Nitin, Ameer Taha, Tana Hernández Barrueta, Sadia Sattar Sultani Filing Date: 10/22/2025 Applicant: The Regents of the University of California Application/Serial Number: 19/366,402 Status: Pending PCT International Patent Application Title: *Pharmaceutical Compositions of Bacterially Produced L-1,2-Propanediol and Uses Thereof.* Inventors: Carolyn Marie Slupsky, David A. Mills, Erkin Seker, Ameer Taha Filing Date: 10/27/2025 Applicant: The Regents of the University of California	Receives no payments and does not have an executive role.

SME Name	Financial Relationships	Advisory or Leadership Roles	Intellectual Property	Other Relevant Interests
	Principal Investigator: Ameer Y. Taha Date: 05/01/2024–03/31/2026 Title: *Examining the role of dairy co-products on brain function*. Goal: The major goal of this project is to determine the effects of dairy co-products such as whey protein phospholipid concentrate on cognitive function in rodents. Funding Agency: California Dairy Research Foundation Principal Investigator: Daniela Barile (Co-investigator on this grant) Date: 01/01/2026–12/31/2026 Title: *Dairy Co-Products for Brain Health: Quantifying Sialic Acid and Exploring Potential Mechanisms of Action Linking Dietary Sialic Acid to Cognitive Health.*		Application/Serial Number: PCT/US25/52703 Status: Pending	

SME Name	Financial Relationships	Advisory or Leadership Roles	Intellectual Property	Other Relevant Interests
	Goal: The major goal of this project is to determine whether sialic acid derived from milk fat globules in whey protein phospholipid concentrate contributes to brain myelination and behavioral changes in cognition in rodents. Funding Agency: Dairy Management Inc. Principal Investigator: Justin Seigel (Collaborator on this grant) Date: 07/01/2021–12/31/2025 Title: *Milk Molecules Initiative.* Goal: This project will utilize mass-spectrometry and NMR to comprehensively profile bioactives in bovine milk.			
Jeff Volek	Co-Founder with equity stake in Virta Health	Science Advisory Board for Simply Good Foods	Royalties from authoring educational nutrition books	N/A
Daisy Zamora	N/A	N/A	N/A	N/A

Table of Contents

Preface

The goal of the *Dietary Guidelines for Americans, 2025–2030,* is to provide clear, actionable, transparent, evidence-based guidance empowering Americans to select foods that support health and reduce chronic disease. This edition is organized around a simple principle: minimally processed, naturally nutrient-dense foods are the reference point for dietary guidance, and strong causal evidence is needed before recommending foods or ingredients that are highly processed. In practical terms, this means that minimally processed vegetables, fruits, meats, eggs, nuts, seeds, dairy, whole grains, beans, and seafood are the foundation for healthful diets. This report also emphasizes limitations of the existing body of evidence and identifies high-impact evidence gaps to guide future research. These steps are intended to strengthen the scientific basis of national nutrition policy and provide practical, trustworthy guidance to improve the metabolic health, healthspan, and lifespan of Americans.

Chapter 1. Introduction

Current State of Health in the U.S.

The U.S. is experiencing a largely preventable epidemic of chronic metabolic disease.[1-7] Currently, an estimated 72% of U.S. adults have excess body weight. Forty-one percent meet the criteria for obesity; 10% have severe obesity; 14% are diabetic, and 43% are prediabetic. Twenty-nine percent of U.S. seniors meet criteria for diabetes, and another 49% are prediabetic. Prevalence of these diet-associated metabolic diseases has increased markedly over the past 45 years (**Fig. 1.1A**) and has not spared our children (**Fig. 1.1B**). Thirty-six percent of U.S. youth and adolescents have excess body weight, and 21% meet the criteria for obesity. Severe obesity increased sevenfold since the 1970s and now affects about one in 14 youth and adolescents.

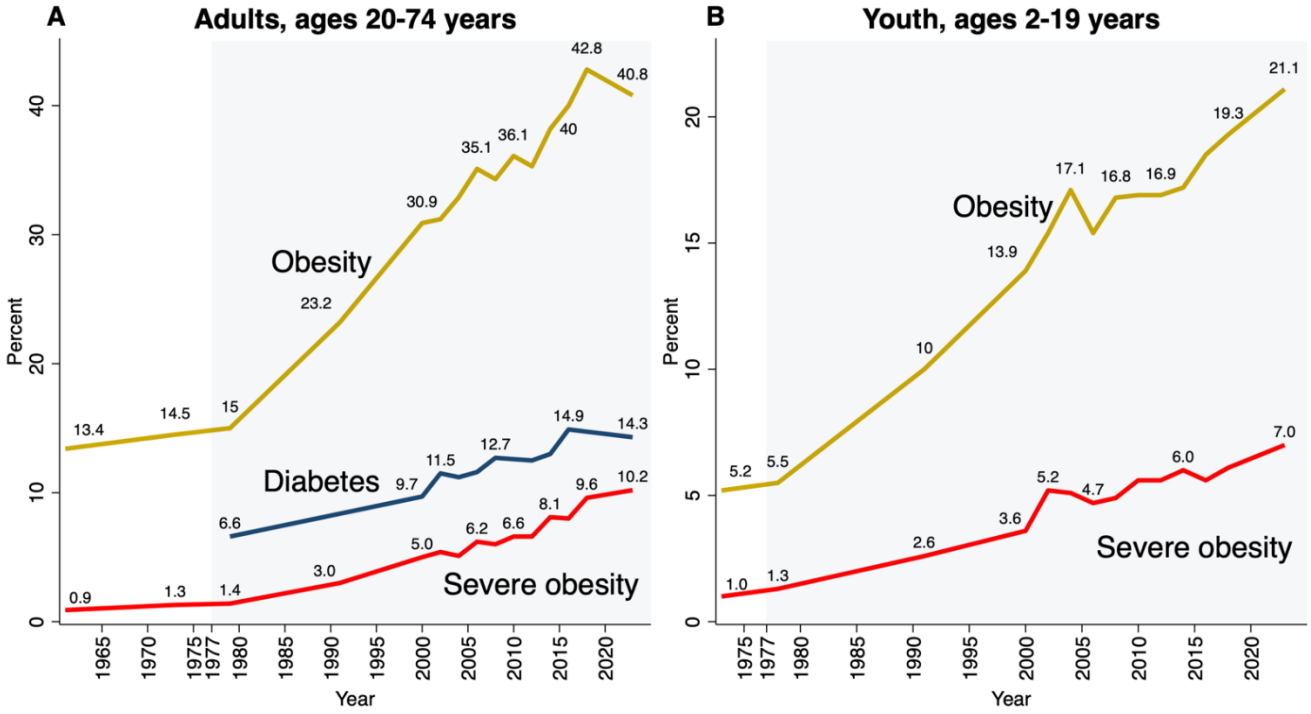

Figure 1.1. Rising prevalence of obesity, diabetes, and severe obesity among U.S. adults and youth, 1960–2023. (A) Prevalence estimates are shown for adults aged 20–74 years and (B) youth aged 2–19 years. Obesity (BMI ≥ 30.0 kg/m²) and severe obesity (BMI ≥ 40.0 kg/m²) have increased steadily over the years.[1-5] Diabetes prevalence has paralleled severe obesity rates in adults.[6-8] Shaded regions denote periods covered by U.S. Dietary Guidelines. Data are from the National Health Examination Survey (NHES) and the National Health and Nutrition Examination Survey (NHANES), National Center for Health Statistics (NCHS).[9] Each point reflects the representative year for earlier multi-year surveys and the ending year for continuous NHANES cycles (post-1999).

The growing prevalence of these conditions has profound economic consequences. U.S. health care spending accounts for a staggering 18% of gross domestic product, translating to approximately $15,000 per person per year.[10] This is twice the average of other industrialized peer countries and approximately 40% more than the next highest country.[11-13] Despite these enormous health expenditures, the U.S. is the outlier with the shortest life expectancy (**Fig. 1.2**), the highest rates of chronic metabolic diseases (**Figs. 1.1**), the shortest healthspan (defined as years of life without major chronic disease) (**Fig. 1.2**), and the largest healthspan-lifespan gap (**Fig. 1.2**).[14]

Not only does the U.S. face higher health care costs that burden many Americans, but families, the majority of seniors, and a growing number of youth and adolescents also contend with a disproportionate burden of disease-related loss of function and reduced quality of life.

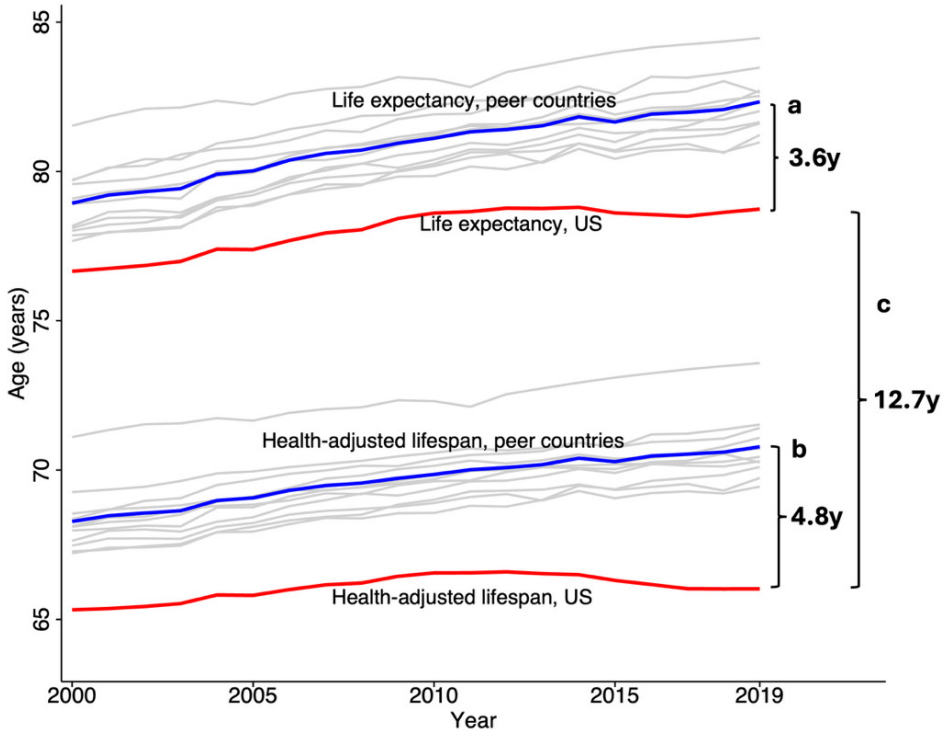

Figure 1.2. Life expectancy and healthy life expectancy at birth, 2000–2019. The U.S. has (a) the lowest life expectancy with 3.6 years below the peer average; (b) the lowest health-adjusted life expectancy, 4.8 years below average; and (c) the largest life expectancy–health-adjusted life expectancy gap, 12.7 years, relative to 11 high-income peers—Australia, Austria, Belgium, Canada, France, Germany, Japan, Netherlands, Sweden, Switzerland, and the United Kingdom. For each year, the peer average is the unweighted mean of the 11 countries. Lines: U.S. (red), individual peers (light gray), peer average (blue). Right-hand brackets show peer–U.S. differences in 2019. Data source: Global Health Observatory from the World Health Organization.[15]

Role of Food and Diet in Chronic Diseases, Lifespan, and Healthspan

Nutrition is one of the most significant factors influencing health. The nutrients that we eat each day as food provide energy and alter both the structure and metabolic functions of our bodies and brains. Depending on the food choices we make, these nutrients promote health or increase the risk of chronic disease (reviewed in Ramsden et al., 2016[16]). A large and convincing body of evidence has linked nutrients, foods, and dietary patterns to the development of cardiometabolic diseases, including insulin resistance, prediabetes, type 2 diabetes, obesity, fatty liver disease, and atherosclerotic cardiovascular disease.[16-23] Since dietary components also alter the structure and function of the brain and peripheral nervous system,[24-26] it is not surprising that emerging evidence also implicates suboptimal diets in development of common neurological diseases, including dementia and chronic pain.[27-30]

Modern U.S. Diets

Minimally processed, nutrient-dense foods are rich sources of nutrients—protein, fiber, fatty acids, vitamins, and minerals—without added sugars, refined starches, extracted oils, or chemical additives.

The diets consumed throughout most of human history consisted exclusively of minimally processed plant and animal foods—including fruits and berries, meats, eggs, vegetables, nuts, seeds, and seafood—that are naturally nutrient-dense.[31-37] Modern populations and individuals who continue to eat minimally processed, nutrient-dense foods have remarkably low rates of chronic diseases and longer lifespans.[38-43] However, over the past century, the U.S. food supply has undergone rapid industrialization. Many traditional American foods have been replaced by highly processed foods and engineered food-like items that combine ingredients extracted from foods such as refined oils, sugar, and starch, with chemical additives to enhance taste, texture, and shelf life.

Highly processed foods and beverages and engineered food-like items make up about two-thirds of the U.S. diet.

Highly processed foods and beverages currently account for about two-thirds of the energy consumed in the U.S. (**Fig. 1.3**). These substantial shifts have resulted in: (1) the consumption of certain nutrients in amounts that are significantly higher or lower than those achievable through natural diets and (2) exposure to hundreds of chemical additives with little knowledge of their long-term health effects (see **Appendix 1**). Together, these changes represent a massive, uncontrolled human experiment and appear to be a major driver of the current epidemic of diet-related chronic diseases (**Figs 1.1 and 1.2**).

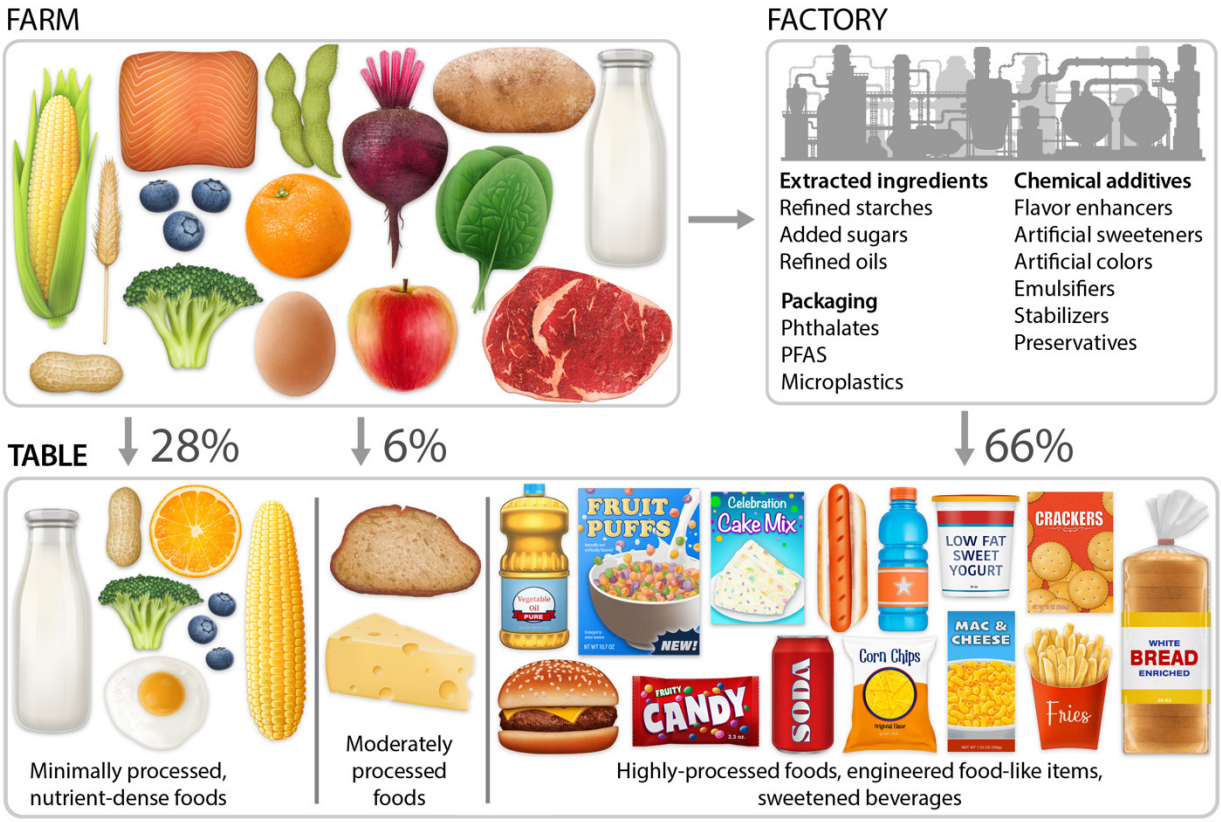

Figure 1.3. Highly processed and engineered foods and beverages make up the bulk of the U.S. diet. Highly processed foods and extracted ingredients account for about two-thirds of the energy consumed by U.S. youth and adolescents and 60% of the energy consumed by U.S. adults. Abbreviation: PFAS, per- and polyfluoroalkyl substances.

U.S. Dietary Guidelines and the Rising Tide of Chronic Diseases

In 1977, the U.S. Senate Select Committee on Nutrition and Human Needs released the Dietary Goals for the U.S. with the goal of combatting rising rates of chronic disease.[44] In 1980, the United States Department of Agriculture (USDA) and the U.S. Department of Health and Human Services (HHS) followed suit by issuing the first *Dietary Guidelines for Americans* (DGA) report.[45] Similar DGA reports were re-issued in 1985,[46] 1990,[47] 1995,[48] 2000,[49] 2005,[50] 2010,[51] 2015,[52] and 2020.[53] As shown in **Fig. 1.1**, these 10 sets of recommendations have failed to effectively counter the rising tide of chronic diseases. Although often presented as settled science, upon close inspection it becomes clear that several enduring tenets have been based on weak or contradictory evidence. Recommendations have relied primarily on findings from non-randomized and uncontrolled studies that are potentially subject to confounding due to healthy adherer bias and other factors (see **Chapter 2**), with comparatively little evidence from gold-standard randomized controlled trials (RCTs). Moreover, DGA reports have become increasingly lengthy and complex and consequently have not conveyed guidance in a way that is simple, focused, and actionable.

A New Beginning

> The guiding principles of the *Dietary Guidelines for Americans, 2025–2030,* are that minimally processed, naturally nutrient-dense foods are the standard for comparison and that high-quality, causal evidence is required before making recommendations that could favor consumption of highly processed foods.

The *Scientific Foundation for the Dietary Guidelines for Americans, 2025–2030,* provides a once-in-a-generation opportunity to start over. This report differs from previous U.S. guidelines in three crucial ways: First, guidance is centered on the principle of encouraging the consumption of minimally processed, naturally nutrient-dense foods and discouraging the consumption of highly processed foods across all food groups. This means that minimally processed vegetables, fruits, nuts, seeds, meats, eggs, whole grains, beans, dairy, and seafood are the starting point for all U.S. diets. Second, these guidelines raise the bar by requiring high-quality, causal evidence to stray from this principle of encouraging the consumption of minimally processed foods over highly processed foods or ingredients. Third, the *Scientific Foundation* report places a special emphasis on conveying limitations of the existing body of evidence and lack of consensus in a transparent manner. High-impact evidence gaps highlighted in this report will shape federal research priorities and inform the design of the RCTs that are needed to provide definitive answers to the most pressing questions linking modern U.S. diets to chronic disease (see **Appendix 2**). Together, these reformed guidelines and new emphasis on RCTs targeting our highest-impact evidence gaps will put the U.S. population on the path to halting and reversing the rising tide of chronic metabolic diseases and premature death.

Chapter 2. Strengthening the Evidence Base for Dietary Guidance

Background

Prior DGAs have not always made a clear distinction between causal evidence from RCTs and observational evidence from prospective cohort studies. The DGAs 2025–2030 begin a deliberate transition toward more explicit, structured evidence standards designed to clarify the strengths, limitations, and uncertainty of the current evidence base supporting dietary recommendations. The guiding principles of the DGAs 2025–2030 are that minimally processed, naturally nutrient-dense foods are the standard for comparison and that high-quality, causal evidence is required before making recommendations that could favor consumption of highly processed foods or ingredients. Observational and mechanistic evidence will continue to play an important role in supporting guidelines. However, any recommendation that could encourage consumption of highly processed foods over minimally processed foods must now be supported by robust causal evidence, ideally from RCTs. This chapter describes how these evidentiary principles are applied, including the respective roles of experimental and observational designs, clinical and surrogate endpoints, and approaches to grading the certainty of evidence.

The Complementary Roles of Experimental and Observational Evidence

Different study designs serve distinct purposes in nutrition science. High-quality RCTs can provide the most reliable evidence of true cause and effect relationships between nutrients and disease.[54-57] By randomly allocating participants to interventions, RCTs can balance both known and unknown confounders, minimizing bias and enabling direct inference about whether a dietary exposure changes health outcomes. When RCTs measure clinical endpoints—such as disease incidence and mortality—they provide the most reliable evidence for causal relationships.[58] While sometimes deemed infeasible due to costs, the reality is that RCTs are necessary to generate the causal evidence required for developing valid dietary recommendations.

Observational studies, including prospective cohort designs, are useful for identifying hypotheses and studying exposures that cannot feasibly or ethically be tested in randomized trials (i.e., exposures that are irreversible or potentially harmful). However, because people who choose certain diets often differ in other health behaviors or underlying conditions, observational findings

Why do we need randomized controlled trials?

Observational cohort studies can reveal patterns but cannot prove causation, no matter how large. People who follow diet guidelines often differ in other ways—such as health motivation, adherence to other healthy behaviors, avoidance of risky behaviors, stress levels, sleep, family support, and subclinical illness—that are difficult or impossible to measure and adjust for. Randomization balances these hidden factors, revealing cause and effect relationships between diet and disease.

remain subject to residual confounding. This is particularly true for nutrients that were the focus of dietary recommendations before the observational studies took place. Even after extensive statistical adjustment, unmeasured or mismeasured factors can still distort associations, making it difficult to determine whether the observed relationship reflects causation or underlying differences between groups.[54,59-61] Consequently, observational studies provide important insights for generating hypotheses and understanding real-world patterns, but they cannot by themselves determine whether a dietary exposure truly causes or prevents disease (see **Appendix 3**).

In nutrition research, results from non-randomized studies have often been overinterpreted. When national recommendations are based on indirect or non-causal evidence, even well-intentioned policies have the potential to cause population-level harm. Associations—no matter how consistent or plausible—cannot replace causal confirmation. Because dietary guidance can reshape food systems and individual behavior at scale, it should be grounded in evidence strong enough to justify that influence.

Distinguishing Clinical Outcomes from Biochemical Indicators

Distinguishing between clinical and surrogate endpoints is central to evaluating nutrition evidence.[58,62] Clinical endpoints—such as disease incidence and mortality—reflect outcomes that directly determine health and well-being. Evidence based on these outcomes provides the most dependable foundation for dietary policy. Surrogate endpoints, by contrast, are intermediate biochemical or physiological measures, including low-density lipoprotein (LDL) cholesterol, blood pressure, fasting glucose, or body weight. They are valuable for studying biological mechanisms and enable shorter or smaller trials, yet improvements in surrogate measures do not always correspond to better clinical outcomes. For example, agents that lowered LDL cholesterol in controlled studies have produced mixed results on coronary heart disease events and mortality: Some reduced risk,[63,64] others showed no effect,[65] and some increased deaths.[66,67] Similar patterns have been observed for agents that improve blood glucose or weight. These examples illustrate that surrogate markers can clarify pathways but cannot substitute for evidence showing that a dietary change improves health in measurable, clinically meaningful ways.

Transitioning Toward Structured Evidence Standards

To address several high-priority questions not encompassed within the charge of the *Scientific Report of the 2025 Dietary Guidelines Advisory Committee* (DGAC),[68] this edition of the *Scientific Foundation* report includes additional systematic evidence reviews on topics including health effects of saturated fat, highly processed foods, refined carbohydrates, and protein intake. This report also includes evidence reviews aimed at describing biological and metabolic mechanisms linking dietary exposures that are ubiquitous in the U.S. (e.g., refined carbohydrates and dietary oxidized lipids) to

health-related endpoints. These reviews were intended to speak directly to dietary exposures and conditions affecting most Americans and their families. Methodological details for each review are found in each individual review.

In conducting the new reviews and throughout this report, this edition incorporates elements of the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) framework,[69] including explicit certainty ratings and clearer differentiation between causal and associative evidence. GRADE provides transparent criteria for evaluating the certainty of evidence based on study design, risk of bias, confounding, consistency, precision, and directness. This edition also prioritized clinical outcomes—such as disease incidence and mortality—whenever possible and used surrogate or biochemical markers primarily when clinical endpoints were not available. This approach helps anchor dietary guidance in experimentally tested relationships whenever available, while still incorporating observational, mechanistic, and other supportive evidence to provide context.

Note: Guidance on alcoholic beverages and health in this report was informed by a study conducted by the National Academies of Sciences, Engineering, and Medicine. See the NASEM report for more information on this evidence base.[271]

Implications for Future Evidence Reviews

Future DGA evidence reviews could continue to build on the strengths of the existing Nutrition Evidence Systematic Review system—its transparency, methodological rigor, and consistency—while incorporating elements of internationally recognized frameworks such as GRADE to clarify how evidence strength and certainty are assessed. Over time, combining these complementary approaches will enhance reproducibility and make the evidentiary basis for recommendations more explicit, while highlighting limitations and identifying highest-impact research gaps and research priorities.

Summary and Outlook

The *Dietary Guidelines for Americans, 2025–2030,* represent a first, deliberate step toward modernizing national nutrition guidance—laying the groundwork for future cycles to implement more causal and transparent evidence standards. This report establishes the principles and structure needed to build credibility, clarify uncertainty, and move the DGA process toward reproducible science. Its long-term success will depend on collective effort: Researchers, funders, and policymakers are invited to collaborate in building the next generation of nutrition evidence so that future guidance rests on the strongest possible foundation and continues to earn the public's trust.

Chapter 3. Highly Processed Foods

Background

Minimally processed, naturally nutrient-dense foods consumed throughout human history have been largely replaced by highly processed foods and beverages. While there is currently no consensus definition for highly processed or ultra-processed foods, a joint USDA–U.S. Food and Drug Administration (FDA) effort to establish a uniform definition is underway.[70] For this report, highly processed foods are defined as any food, beverage, or engineered food-like item that is made primarily from substances extracted from foods (such as refined sugars, refined grains/starches, and refined oils) and/or containing industrially manufactured chemical additives. Using these criteria, highly processed foods and beverages account for approximately two-thirds and 60% of total energy consumed by youth and adults, respectively (**Fig. 3.1**).

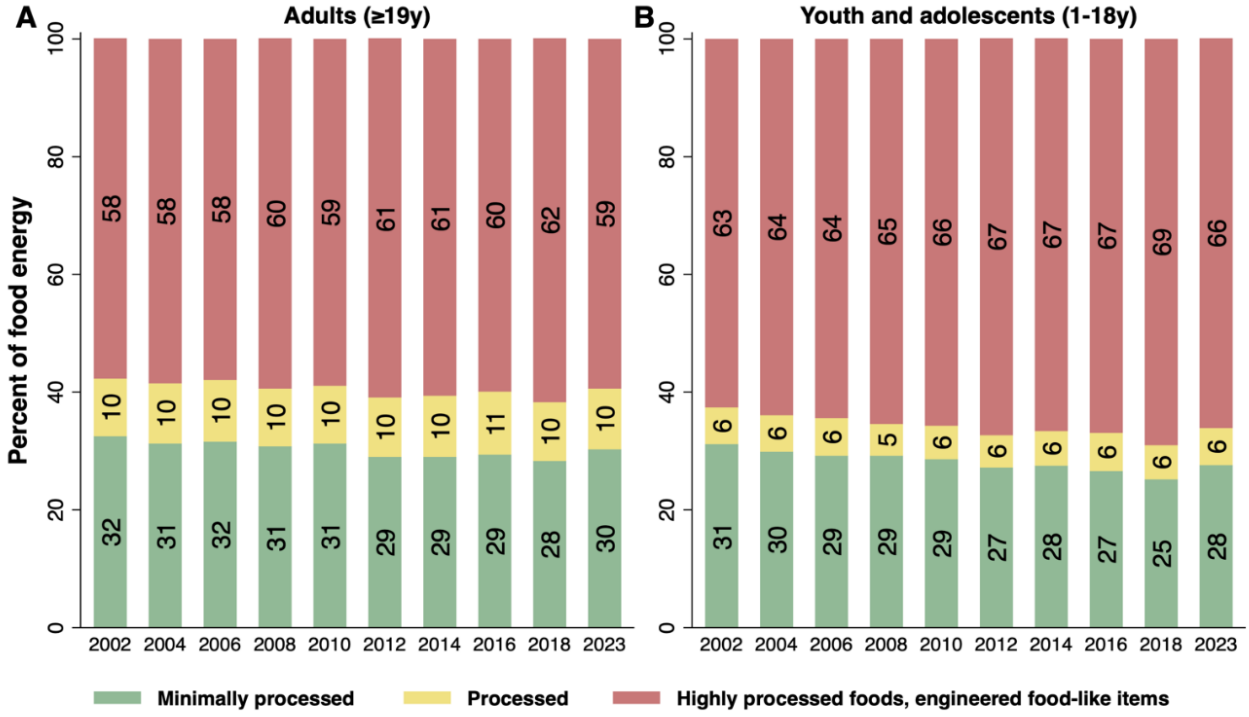

Figure 3.1. Trends in dietary energy contribution from processed foods among U.S. adults and youth, 2001–2023. Estimated percentage of total dietary energy derived from minimally processed (green), processed (yellow), and highly processed or engineered food-like products (red) among (A) adults (≥19 years) and (B) youth and adolescents (1–18 years). Food categories were classified according to the Nova food classification system.[71-73] The highly processed category combines Nova Group 2 (processed culinary ingredients such as refined starches, added sugars, and extracted oils) and Group 4 (ultra-processed foods). Data source: NHANES from NCHS.[9] Years shown are the last year of each cycle.

Evidence

Compared with minimally processed counterparts, highly processed and engineered foods tend to be hyper-palatable, less satiating, and more likely to induce a hyperglycemic response. Short-term RCTs have demonstrated that consumption of highly processed foods leads to increased caloric intake and adverse cardiometabolic effects,[74-77] including excess weight gain, increased adiposity,[75] insulin resistance, and increased blood levels of chemicals such as phthalates.[77] In population-based cohort studies, estimated intakes of highly processed foods are consistently associated with increased risk of cardiometabolic diseases, including obesity (incident obesity or weight gain), incident type 2 diabetes,[78] incident cardiovascular events and deaths, and all-cause mortality.[79] A research synthesis that systematically integrates findings from existing systematic reviews and meta-analyses—an umbrella review—was conducted to examine associations between highly processed foods and major chronic disease outcomes, including all-cause mortality, cardiovascular disease (CVD), cancer, obesity, and type 2 diabetes. The review integrated findings from 27 high-quality meta-analyses that were identified using search terms such as “junk food,” “industrial food,” “refined food,” “ultra processed foods,” and “highly processed foods” (see **Appendix 4.1** for a detailed review on highly processed foods, including full methods and findings). The evidence base consisted primarily of large prospective cohort studies with intake of highly processed foods consistently associated with increased risk across nearly all outcomes, with relative risks (RR) ranging from 1.12 for cancer to 1.55 for obesity. Moderate-certainty evidence linked highly processed foods to greater risk of all-cause mortality (RR 1.15), CVD (RR 1.35), and obesity (RR 1.55). Higher-certainty evidence linked highly processed foods to greater risk for type 2 diabetes (RR 1.48). These associations were consistent across outcomes and supported by clear dose-response relationships. For example, a 10% higher proportion of calories from highly processed foods was associated with a 14% higher risk of type 2 diabetes, 13% higher risk of cancer, 10% higher mortality risk, and 7% higher obesity risk, and each additional serving per day of highly processed foods increased CVD risk by 4%. No study demonstrated any protective effect of highly processed foods.

Importantly, in a nationally representative sample of U.S. adults with a median follow-up of 8 years, consumption of highly processed foods was associated with higher all-cause mortality,[80] even after adjusting for the Healthy Eating Index—a tool used to assess and score the quality of a person’s diet based on the existing DGAs. These findings indicate that existing U.S. dietary guidelines may not fully capture the adverse impact of highly processed foods.[81] As reviewed in the sections below, several subgroups of highly processed foods—including sugar-sweetened beverages; highly processed dairy products; and processed oils, fats, and condiments—were associated with higher all-cause mortality, suggesting that it is important to select minimally processed foods within each food group.

Highly processed foods are significant sources of added sugars, refined grains, and extracted oils, and they are the chief dietary source of industrially manufactured chemical additives. Given the large and growing number of chemical additives in the U.S. food supply (see **Appendix 1**) and historical context wherein it can take decades to attribute adverse health consequences to industrialized food ingredients,[82-84] we anticipate that it will take many decades to fully appreciate the deleterious consequences of highly processed foods and ingredients.

How can you identify highly processed foods?

Highly processed foods tend to have:

1. Refined grains and/or added sugars
2. Refined fats and oils
3. Long, complicated ingredient lists including chemical additives (e.g., artificial sweeteners, flavor enhancers, artificial colors, and emulsifiers).

Examples are provided in **Figures 4.3** and **5.8.**

Many processed convenience foods are packaged or heated in plastic packaging, films, and coatings that can migrate into foods prior to ingestion.[85-92] Emerging evidence indicates that chemicals derived from food packaging materials can accumulate in human tissues, including atherosclerotic lesions,[93,94] reproductive tissues,[95] and brains.[96] Additionally, an emerging but limited body of evidence links the accumulation of these compounds to adverse health consequences.[93,94,97]

Limitations and Evidence Gaps

The evidence linking highly processed foods to adverse cardiometabolic and clinical endpoints has several important limitations. First, a consensus definition for highly processed foods is not yet available. The most commonly used system for classifying processed food (Nova)[71,72,98,99] does not designate refined cooking ingredients such as refined starches, added sugars, or extracted oils as ultra-processed, and therefore may underestimate the percentage of highly processed items. The Nova system can also classify some nutrient-dense foods as ultra-processed foods.[100] Since there is an ongoing joint USDA-FDA federal effort to establish a uniform definition of ultra-processed foods,[70] definitions of highly processed foods used in this report can be considered provisional. Existing RCTs testing the effects of processed foods are of relatively short duration, include small to moderate sample sizes, and are limited to effects on metabolic markers, body weight, and adiposity (reviewed in **Appendix 4.1**). The majority of evidence linking highly processed foods to adverse health consequences is therefore derived from non-randomized, uncontrolled studies, which can be subject to confounding due to healthy adherer bias, reverse causation, and other factors (see **Chapter 2**). Another limitation is that there is a general lack of studies in children and other life-course stages.

Research Priorities

There is a pressing need for: (1) harmonized definitions of processed foods and a more accurate classification system that includes added sugars, refined oils, and refined starches under the umbrella of highly processed foods; (2) larger, longer randomized trials testing the effects of controlled alterations in different categories of processed foods, ingredients, and specific chemical additives on biochemical, toxicological, and clinical endpoints, including cardiometabolic and neurological diseases. RCTs are also needed to determine whether consumption of minimally processed foods and diets can reduce levels of food packaging contaminants (e.g., microplastics, phthalates) that have been shown to accumulate in human blood and tissues (see **Appendix 1**).[77,93,94,96]

Recommendation: Highly Processed Foods

- Avoid highly processed packaged, prepared, ready-to-eat, or other foods that are salty or sweet, such as chips, cookies, and candy that have added sugars and sodium (salt). Instead, prioritize nutrient-dense foods and home-prepared meals. When dining out, choose nutrient-dense options.

Chapter 4. Carbohydrates

Overview

Carbohydrates account for almost half of all energy consumed by Americans. Low-quality carbohydrate foods—including added sugars, artificial sweeteners, refined grains, and starches—account for more than 80% of total carbohydrates in U.S. diets.[101] High-quality carbohydrate foods include minimally processed vegetables, berries and other fruits, whole grains, and beans. This chapter evaluates the metabolic and health effects of refined, low-quality carbohydrate foods versus high-quality carbohydrate foods. The overarching goal of this chapter is to empower Americans to identify and select high-quality carbohydrate foods that optimize metabolism and support health and to discourage consumption of highly processed carbohydrates.

Concentrated Sources of Sugars and Chemical Sweeteners in U.S. Diets

The large-scale addition of refined sugar to foods and beverages is a recent nutritional phenomenon.[102,103] Prior to the industrial age, concentrated sugar was not available. The majority of sugar came from intact fruits (fruits that are in their natural state) that are rich in fiber and other nutrients. Industrialization enabled mass production of refined sucrose extracted from sugarcane and sugar beets and, more recently, high fructose corn syrup (HFCS) manufactured industrially from corn starch (**Fig. 4.1A**). Loss-adjusted per capita availability of added sugars, which was already high in 1970, increased to 27 teaspoons per day in 1999 (**Fig. 4.1B**), before declining slowly to current levels of about 22 teaspoons per day, or approximately 14% of total food energy.[104] This modest decline in added sugars since 1999 has been accompanied by a corresponding increase in the consumption of industrially manufactured chemical sweeteners[105,106] added to soft drinks, candies, baked goods, and other highly processed foods and beverages. Fruit juices, which are produced by removing the fiber naturally present in whole fruits (**Fig. 4.1A-B**), provide another concentrated source of sugar in U.S. diets. Together, added sugars and fruit juices currently provide about 16% of total energy in U.S. diets.[104,107]

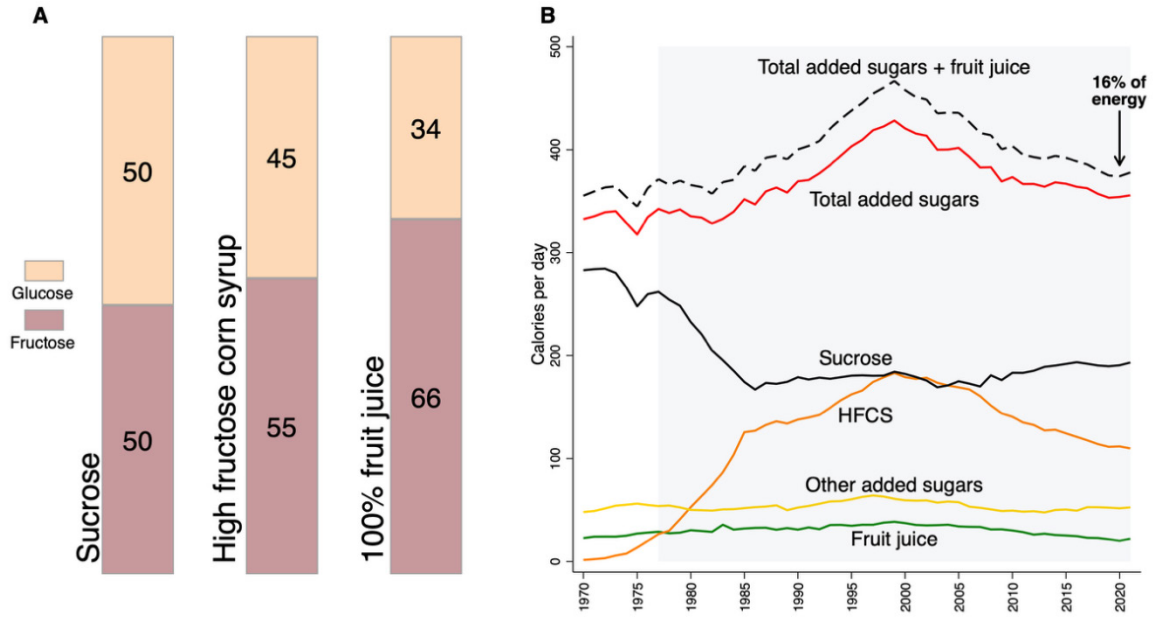

Figure 4.1. Composition and trends in fructose- and glucose-containing sweeteners in the U.S., 1970–2021. (A) Relative proportions of glucose and fructose in three concentrated sources of sugar: sucrose (table sugar), high-fructose corn syrup (HFCS), and 100% fruit juice. Values represent approximate monosaccharide contributions by weight. Source: FoodData Central from USDA Agricultural Research Service (ARS).[108] (B) Per capita daily availability (loss-adjusted) of total added sugars, sucrose, HFCS, other added sugars, and fruit juice in the U.S. food supply from 1970 to 2021. Total added sugars and fruit juice together account for roughly 16% of total daily energy intake in recent years. Source: Food Availability (Per Capita) Data System from USDA Economic Research Service (ERS).[104]

Evidence

Published RCTs and observational studies have provided concordant evidence implicating sugar-sweetened beverages, such as soft drinks, with adverse metabolic and health effects including dental caries,[109] increased body weight, visceral adiposity, insulin resistance, type 2 diabetes, and high blood triglycerides in children and adults.[110-114] An umbrella review on added sugars, sugar-sweetened beverages, and 100% fruit juice synthesized 54 meta-analyses of prospective cohorts and RCTs (see **Appendix 4.2** for full methods and results). Briefly, across outcomes, sugar-sweetened beverages showed consistent associations with increased risk of chronic diseases, including higher risk of type 2 diabetes (39%; Moderate certainty evidence), CVD (20%; Low certainty evidence), adult obesity (17%; Moderate certainty evidence), all-cause mortality (10%; Low certainty evidence), depression (25%; Moderate certainty evidence), and dental caries (57%; High certainty evidence). Each 12-ounce can of sugar-sweetened beverage per day was associated with 10% increased risk for all-cause mortality, 14% for CVD, and ~20% for type 2 diabetes (see **Appendix 4.2**). Fruit

juice (100%) consumption is linked to significant weight gain in children with high certainty (see **Appendix 4.2**), but not in adults. The evidence linking fruit juice (100%) consumption to metabolic and clinical endpoints other than obesity is limited and less conclusive than that for sugar-sweetened beverages (see **Appendix 4.2**). While other sources of added sugar may also negatively impact cardiometabolic health and fatty liver disease, the evidence for these effects is not as strong.

Replacing added sugars with industrially manufactured chemical sweeteners, such as sugar alcohols, aspartame, and sucralose, is hypothesized to decrease energy intake and thus benefit body composition and health. However, evidence from animal models and human non-randomized studies suggests that chronic consumption of artificial sweeteners may paradoxically increase energy intake or disrupt metabolism[114] and therefore increase cardiometabolic disease. An umbrella review synthesized findings from 19 meta-analysis on the effects of alternative sweeteners on adverse health outcomes (see **Appendix 4.2** for full methods and results). Alternative sweeteners were associated with increased risks of all-cause mortality (13%, Moderate certainty evidence), CVD (17%, Low certainty evidence), and type 2 diabetes (8%, Low certainty evidence). Emerging evidence from non-randomized and mechanistic studies suggests that the sugar alcohols xylitol and erythritol may be linked to thrombotic CVD events,[115-117] warranting further investigation.

Limitations and Research Needs

The evidence linking concentrated sources of sugar and artificial sweeteners to adverse cardiometabolic and health endpoints has several important limitations (see **Appendix 4.2**). First, added sugars and artificial sweeteners are mostly consumed in highly processed and engineered foods and beverages that contain many other chemical additives. It is therefore not possible to definitively disentangle adverse health consequences due to sugars or artificial sweeteners from other chemicals that are often consumed together. Existing RCTs are relatively short, small to moderate size, and limited to metabolic effects rather than hard clinical endpoints. The majority of evidence linking sugars and artificial sweeteners to adverse health consequences is therefore derived from non-randomized studies. Although directionally concordant, there is potential for confounding due to healthy adherer bias and reverse causation (see **Chapter 2**). Future RCTs are needed to definitively determine whether replacement of sugars with artificial sweeteners has beneficial, harmful, or neutral metabolic and health effects.

Recommendations: Added Sugars

- Limit foods and beverages that include artificial flavors, petroleum-based dyes, artificial preservatives, and low-calorie non-nutritive sweeteners.
- Avoid sugar-sweetened beverages, such as sodas, fruit drinks, and energy drinks.

- While no amount of added sugars or non-nutritive sweeteners is recommended or considered part of a healthy or nutritious diet, one meal should contain no more than 10 grams of added sugars.
- To help identify sources of added sugars, look for ingredients that include the word “sugar” or “syrup” or end in “-ose.”
- Added sugars may appear on ingredient labels under many different names, including high-fructose corn syrup, agave syrup, corn syrup, rice syrup, fructose, glucose, dextrose, sucrose, cane sugar, beet sugar, turbinado sugar, maltose, lactose, fruit juice concentrate, honey, and molasses. Examples of non-nutritive sweeteners include aspartame, sucralose, saccharin, xylitol, and acesulfame K.
- Some foods and drinks, such as fruits and plain milk, have naturally occurring sugars. The sugars in these foods are not considered added sugars.
- When selecting snack foods, added sugar limits should follow FDA “Healthy” claim limits. For example, grain snacks (e.g., crackers) should not exceed 5 grams of added sugar per ¾ ounce whole-grain equivalent, and dairy snacks (e.g., yogurt) should not exceed 2.5 grams of added sugar per ⅔ cup equivalent.

Refined Grains and Starches in the U.S. Food Supply

Refined Grains and Starches are Sugar

- Refined grains are highly purified sources of starch.
- Starches are long chains of glucose—a form of sugar.
- During chewing and digestion, enzymes rapidly break down starch into glucose, raising blood sugar much like table sugar does.
- Refined grain foods—white bread, crackers, breakfast cereals, chips, pastries, and pasta—can therefore act metabolically like sugar, delivering fast-absorbing carbohydrates with few nutrients or fiber to slow absorption.

Take-home message: Refined grains are sugar in disguise. Choose whole grains, beans, or vegetables instead.

The large-scale consumption of refined grains and starches is a recent and atypical nutritional phenomenon. Prior to the industrial age, humans consumed minimally processed whole grains without removing the nutrient-dense grain kernel (bran, germ, and endosperm). As shown in **Fig. 4.2A**, these whole grains are rich in fiber and protein. Industrialization enabled mass production of refined grains that are rich sources of starch but largely devoid of fiber and protein. Following well-intentioned 1977–2000 U.S. guidance to decrease fat and increase consumption of complex carbohydrates and fiber,[44-49] loss-adjusted availability of grains—especially wheat and corn—increased markedly in the U.S. (**Fig. 4.2B**). Remarkably, despite an emphasis on promoting consumption of whole grains, refined grains currently account for 86–87% of total grains consumed by U.S. youth and adults (**Fig. 4.2C-D**). When considered together with added sugars, fruit

juices, and processed potato products (e.g., French fries, potato chips, and hash browns), low-quality carbohydrates account for more than 80% of all carbohydrates consumed in the U.S.[101]

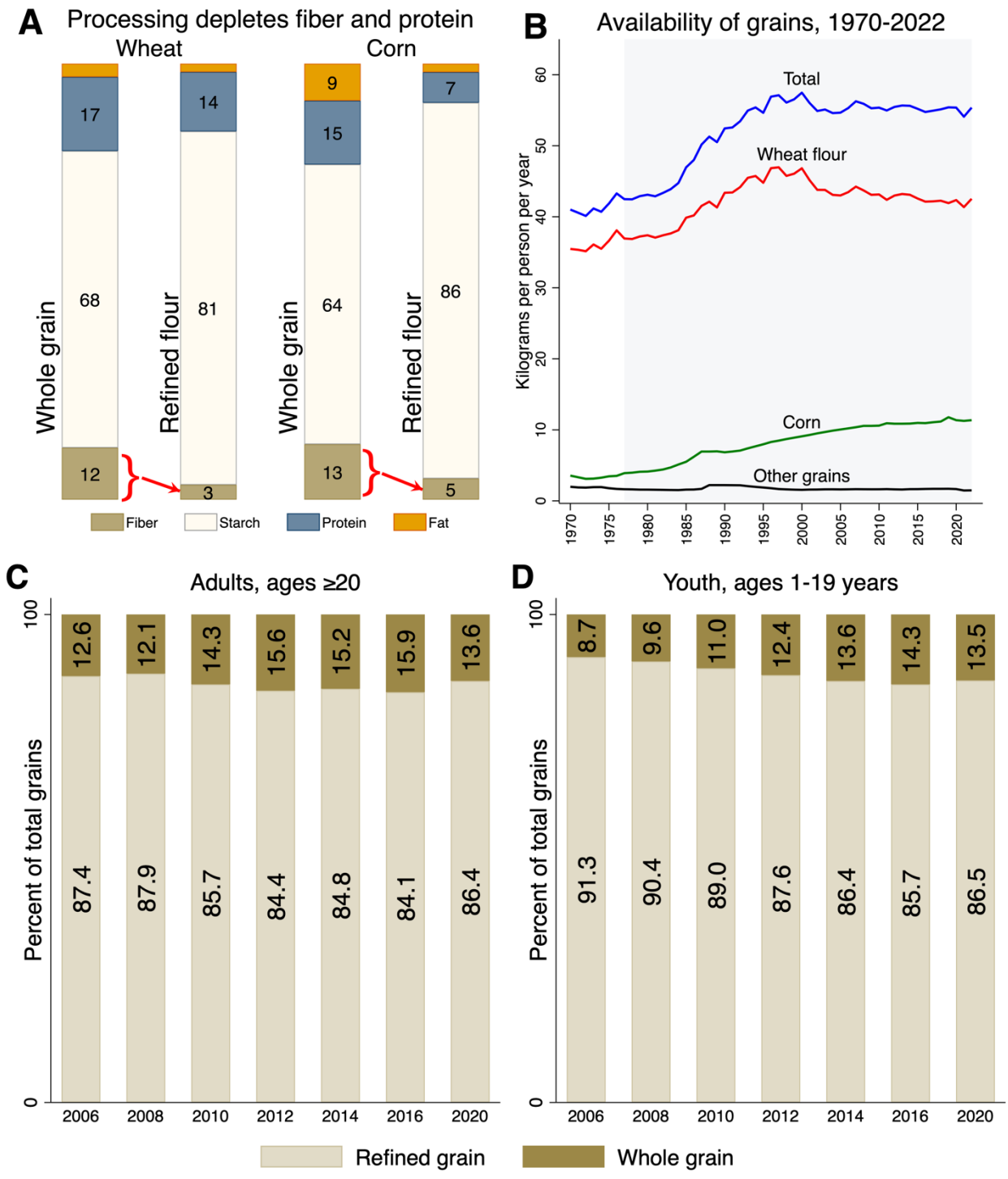

Figure 4.2. Nutrient depletion and consumption trends for refined and whole grains in the U.S. (A) Nutrient composition of whole versus refined wheat and corn. Refined grains contain 60–80% less fiber and 20–50% less protein than whole grains. Source: FoodData Central from USDA ARS.[108] (B) Loss-adjusted per-capita grain availability in the United States increased substantially between 1970 and 2000 as indicated by the gray box, driven primarily by wheat flour, with smaller contributions from corn and other grains. Data source: Food Availability (Per Capita) Data System from USDA ERS.[104] (C–D) The large majority of grains consumed by U.S. adults and youth are refined; whole grains account for only about 13% of total grain intake. Data source: NHANES from NCHS.[9] Years presented are the last year of each cycle.

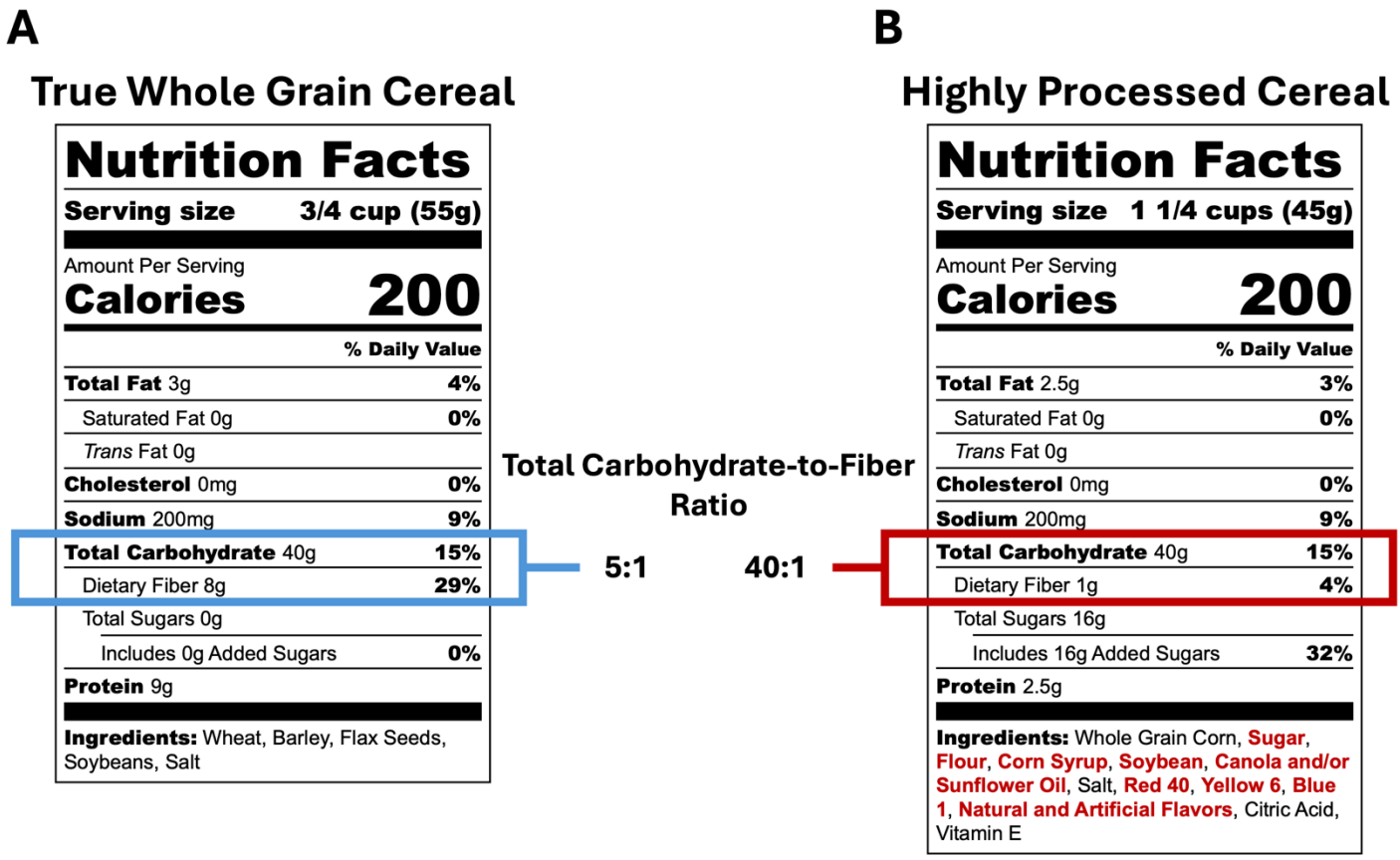

Figure 4.3. How to distinguish between true whole-grain cereals and highly processed cereals. (A) An example of a true whole-grain cereal with four whole-grain ingredients, providing 8 grams of dietary fiber and 9 grams of protein per serving. Its carbohydrate-to-fiber ratio of 5:1 is consistent with a minimally processed whole-grain food, containing no added sugar or chemical additives. (B) An example of a highly processed cereal that lists whole-grain corn as the first ingredient but includes refined starches (flour), two added sugars (sugar, corn syrup), and artificial colors and flavors. It provides 90% less fiber and 70% less protein than the whole-grain cereal, yielding a total carbohydrate-to-fiber ratio of 40:1—indicative of a refined, low-quality grain product.

Evidence

Separating the Wheat from the Chaff

- Many processed foods labeled as "Made with Whole Grain"' or "Multigrain" contain mostly refined grains.
- Most true whole-grain foods have ≥1 gram of fiber for every 8 grams of carbohydrate.

RCTs demonstrate beneficial cardiometabolic effects of minimally processed carbohydrate-rich foods, such as intact fruits, vegetables, and whole grains, and adverse cardiometabolic effects of highly processed carbohydrate-rich foods, such as refined grains, refined potatoes, and added sugars (see **Appendix 4.3** for a detailed review on refined grains and carbohydrates and insulin resistance). In non-randomized studies, associations between intakes of minimally processed carbohydrate-rich foods and fiber show consistent directionality toward decreased risk of cardiometabolic diseases, including obesity; cardiovascular events and deaths; diabetes; and all-cause mortality.[118] In addition to fiber, vegetables and fruits are rich sources of phytonutrients with beneficial effects on metabolism and health, such as polyphenols, carotenoids, and glucosinolates. RCTs in generally healthy and at-risk adults show that increasing intake of vegetables and whole fruits (typically from 2–3 to 5–8 servings/day) improves blood pressure, microvascular function, and cardiometabolic risk markers,[119-122] while increasing circulating antioxidants and decreasing inflammatory markers.[122-124]

Replacement of refined grains and other low-quality carbohydrate foods with fruits, vegetables, and whole grains shows directionally concordant evidence of benefit. An umbrella review of 19 high-quality meta-analyses evaluated carbohydrate quality—whole grains, refined carbohydrates, total dietary fiber, and glycemic index—in relation to all-cause mortality, CVD, type 2 diabetes, colorectal cancer, and obesity (see **Appendix 4.4** for a detailed review on refined grains and carbohydrates). Higher whole-grain intake was associated with lower risk of all-cause mortality (7%, High certainty evidence), CVD (15%, High certainty evidence), colorectal cancer (13%, Moderate certainty evidence), obesity (15%, Low certainty evidence), and type 2 diabetes (33%, Low certainty evidence). Higher dietary fiber was associated with lower risk of all-cause mortality (17%, Moderate certainty evidence), colorectal cancer (16%, Moderate certainty evidence), type 2 diabetes (8%, Moderate certainty evidence), and coronary heart disease (20%, Low certainty evidence). Dose-response analysis identified significant risk reductions per 30 g/day of whole grain consumption (ranging between 6% reduction for all-cause mortality and colorectal cancer to 24% for type 2 diabetes) and an optimal intake of 25–29 g/day for total fiber.

A growing body of evidence from RCTs indicates that low-carbohydrate diets (<130 grams per day) can decrease triglyceride levels, increase high-density lipoprotein (HDL) cholesterol, and improve glycemic control, particularly among individuals with type 2

diabetes (see **Appendix 4.5** for a detailed review on low-carbohydrate diets), with no evidence of serious adverse events or nutrient deficiencies.

Microbiome

Emerging evidence indicates that carbohydrate quality influences the composition and activity of the gut microbiome. Diets centered on minimally processed, fiber-rich plant foods—including vegetables, fruits, beans, nuts, and whole grains—provide fermentable fibers and other substrates that support microbial diversity and the production of short-chain fatty acids.[125-128] In contrast, highly processed foods that are low in fiber and high in refined grains, added sugars, and chemical additives are associated with less favorable microbial profiles in controlled feeding studies.[129-131] Although the field is still developing and causal pathways are not fully defined, randomized and controlled feeding trials show that increasing intake of minimally processed and fermented plant foods modulates the microbiome and microbial metabolites in directions generally considered more favorable for gut and metabolic health.[125,128]

Limitations and Research Needs

Although the evidence linking carbohydrate quality to cardiometabolic outcomes is extensive, several methodological and translational limitations remain. First, surrogate endpoints such as blood triglycerides, LDL and HDL cholesterol, and glycemic control are imperfect markers for clinical disease. Second, existing RCTs have small to moderate sample sizes and shorter duration than non-randomized studies, which limits estimates of the long-term effects of exposures. Larger, longer RCTs are needed to determine the cardiometabolic and clinical benefits of replacing low-quality carbohydrates with vegetables, fruits, whole grains, and minimally processed meats. Finally, most data for refined and whole grains are derived from prospective cohorts rather than randomized trials, limiting causal inference and leaving potential residual confounding due to healthy adherer bias, reverse causation, and other factors (see **Chapter 2**).

Recommendations: Whole Grains and Refined Carbohydrates

- Prioritize fiber-rich whole grains.
- Significantly reduce the consumption of highly processed, refined carbohydrates, such as white bread, ready-to-eat or packaged breakfast options, flour tortillas, and crackers.
- Whole grains serving goals: 2–4 servings per day, adjusting as needed based on your individual caloric requirements.
- Individuals with certain chronic diseases may experience improved health outcomes when following a lower carbohydrate diet. Work with your health care professional to identify and adopt a diet that is appropriate for you and your health condition.

Recommendations: Vegetables and Fruits

- Eat a variety of colorful, nutrient-dense vegetables and fruits.
- Eat whole vegetables and fruits in their original form. Wash thoroughly prior to eating raw or cooking.
- Frozen, dried, or canned vegetables or fruits with no or very limited added sugars can also be good options.
- If preferred, flavor with salt, spices, and herbs.
- 100% fruit or vegetable juice should be consumed in limited portions or diluted with water.
- Vegetables and fruits serving goals for a 2,000-calorie dietary pattern, adjusting as needed based on your individual caloric requirements:
    - Vegetables: 3 servings per day
    - Fruits: 2 servings per day

Chapter 5. Fats and Oils

Introduction

Fat is an essential macronutrient. It provides energy, regulates metabolism, forms cell membranes, and supports hormonal and signaling functions vital for human health. The three principal fatty acid classes—saturated, monounsaturated (MUFA), and polyunsaturated (PUFA) (**Fig. 5.1**)—occur naturally in a variety of foods such as meat, dairy, nuts, and fish and appear in more concentrated forms when refined into cooking oils, frying oils, salad dressings, and other processed food ingredients.

Over the past century, industrial food production and evolving nutrition policy have fundamentally altered the sources, composition, and understanding of dietary fats in the U.S. Once the primary contributors of saturated fat and MUFA, traditional animal fats have been progressively displaced by manufactured fats and oils rich in the omega-6 PUFA linoleic acid (e.g., soybean oil, corn oil, cottonseed oil, safflower oil, and sunflower oil). These changes were accelerated by early public-health efforts to reduce the risk of heart disease through broad recommendations to lower total and saturated fat and replace them with “unsaturated” or “polyunsaturated” fats. While grounded in the best evidence available at the time, these initiatives created large-scale shifts in both the U.S. food supply and population exposure to specific fatty acids—particularly linoleic acid, which is now consumed in amounts that are higher than can be achieved by natural diets without the addition of extracted oils.[35,132]

This chapter re-examines the scientific and policy foundations of current dietary-fat guidance in light of modern standards for causal evidence. It opens by tracing how industrial innovation and public-health recommendations together transformed the U.S. fat supply over four distinct phases, setting the stage for the present landscape—an unprecedented fatty acid profile dominated by linoleic acid. The chapter then reviews causal evidence from randomized trials testing whether reducing saturated fat or replacing it with linoleic acid–rich oils lowers coronary heart disease or mortality risk. It then reviews how selective publication, reliance on observational associations, and surrogate markers such as LDL cholesterol sustained confidence in the diet-heart hypothesis despite neutral or unfavorable trial results. Finally, it discusses potential unintended consequences of legacy nutrient-based fat guidance and proposes updated, food-based recommendations emphasizing minimally processed, nutrient-dense foods and dietary patterns.

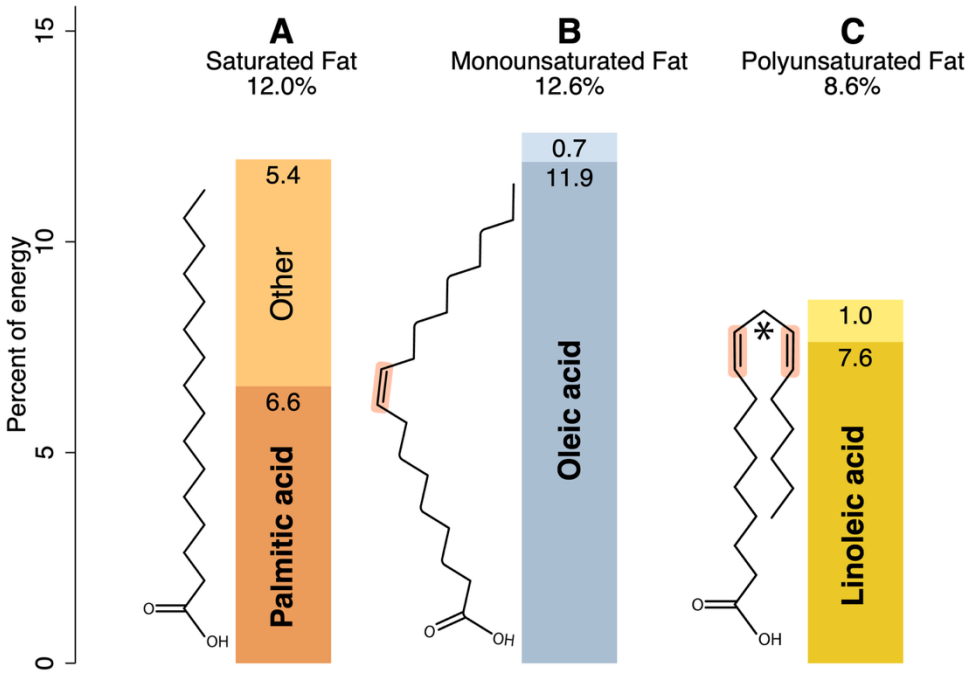

Figure 5.1. Saturated, monounsaturated, and polyunsaturated fats in the U.S. food supply. (A) Saturated, (B) monounsaturated (MUFA), and (C) polyunsaturated (PUFA) fatty acids differ in the number of double bonds in their carbon chains (designated by orange shading). Saturated fatty acids have no double bonds; MUFA have one; PUFA have two or more. The carbon atom between two double bonds in PUFA (see asterisk in linoleic acid) is susceptible to peroxidation, which can generate toxic lipid hydroperoxides and reactive lipid aldehydes. Palmitic acid is the most abundant saturated fatty acid (A); oleic acid is the primary MUFA (B); and linoleic acid is the primary PUFA (C), accounting for about 88% of total PUFA and 7.6% of total energy in U.S. diets. Data source: NHANES 2021–2023, dietary recall (2-day average).[133]

A Century of Change: From Animal Fats to Industrial Fats and Oils

Over the past century, the composition of dietary fat in the United States has undergone one of the most extensive nutrient shifts in human history. Industrial processing, wartime supply pressures, and public-health policy together reshaped the fat sources in the national food supply (**Fig. 5.2**). Four distinct phases mark this transformation—from locally produced animal fats to partially hydrogenated and then refined linoleic acid–rich oils (**Fig. 5.2**).

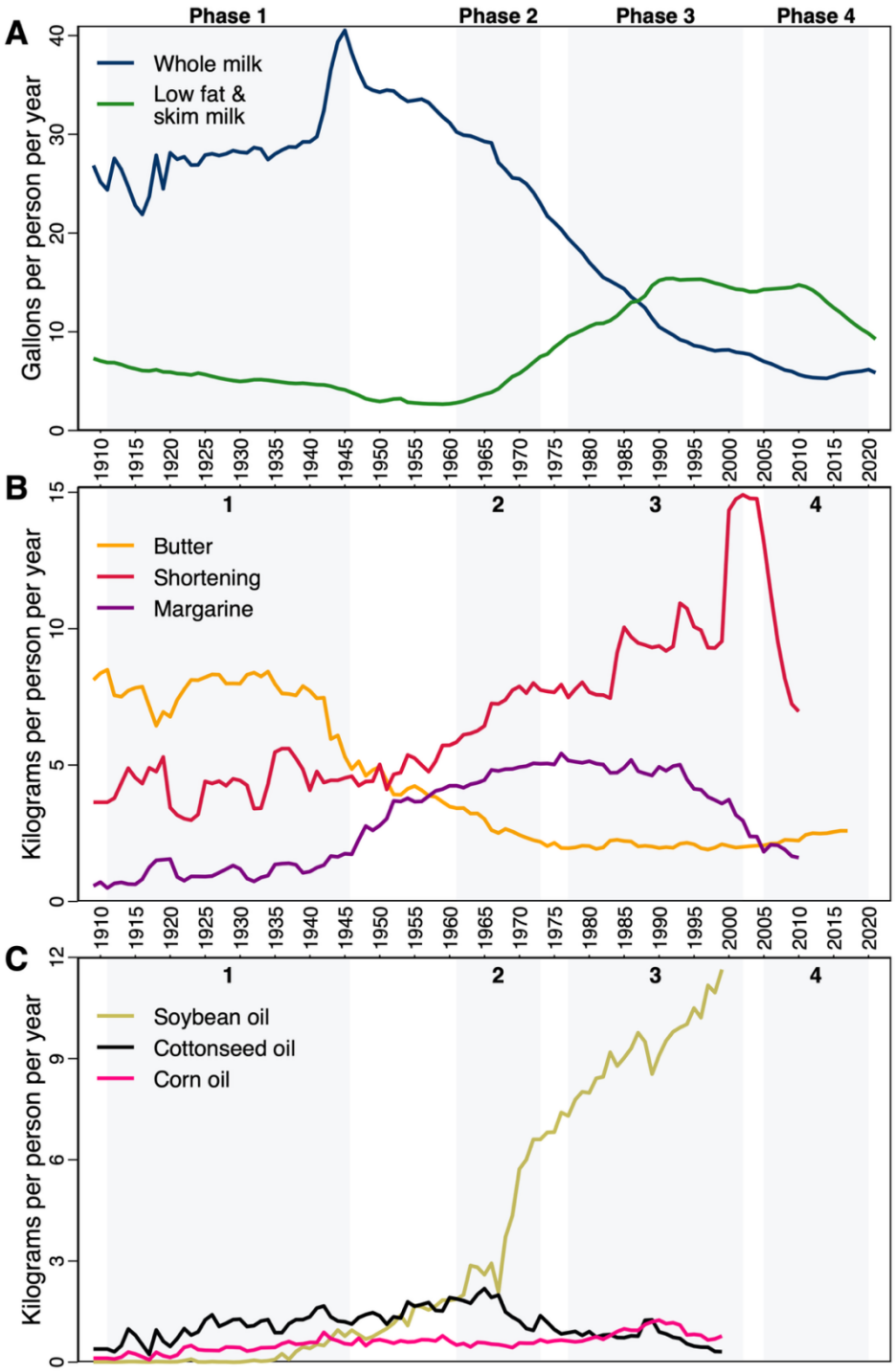

Figure 5.2. Radical transformation of dietary fats in the U.S. in four phases, 1911–2025. The combination of industrially manufactured foods, dietary guidelines, and authorized health claims contributed to: (A) reduced consumption of whole-fat milk with partial replacement by low-fat and skim milk; (B) reduced intake of butter and increased partially hydrogenated vegetable oil (PHVO) margarines and shortenings; and (C) major increases in linoleic acid–rich oils, especially soybean oil. Graph A is food availability for 1909–2021, and Graph B is loss-

adjusted food availability for 1909–2017, both from the U.S. Department of Agriculture (USDA) Economic Research Service.[104] Graph C data provided by USDA Center for Nutrition Policy and Promotion (data for 2000–2010 are not available); methods as described in Blasbalg et al., 2011[132]. As of 2010, data for many fats and oils are not available due to termination of the Current Industrial Reports by the Census Bureau.

Phase 1: The first major change began in 1911, when industrially manufactured shortenings and margarines made with partially hydrogenated vegetable oils (PHVO) entered the food supply. Partial hydrogenation transforms linoleic acid–rich oils—which are naturally less stable—into more shelf-stable mixtures containing saturated fat, trans fat, linoleic acid, and MUFA. Estimated percentages of these fatty acids in common PHVO margarines and shortenings are shown in **Fig. 5.3**.[134,135] Over the next four decades, PHVO shortenings and margarines (**Fig. 5.2B**) replaced a small, yet substantial, amount of traditional fats typically consumed in the U.S. diet.

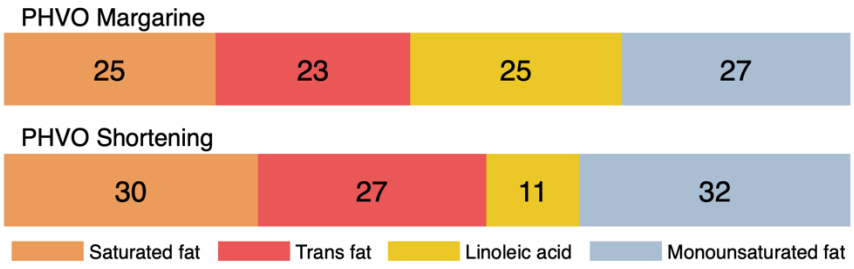

Figure 5.3. PHVOs are rich sources of saturated fat, trans fat, and linoleic acid. Although the terms "trans fat" and "PHVO" are often used interchangeably, PHVO products also contain substantial amounts of saturated fatty acids and linoleic acid.

Phase 2: The second and perhaps most radical phase was triggered by widely publicized American Heart Association (AHA) recommendations in 1961, 1965, 1968, and 1973 to decrease total fat, saturated fat, and dietary cholesterol and to replace animal fats with PUFA-rich oils.[136-138] The 1968 AHA guidelines raised the cap for total fat to 40% of energy to accommodate further increases in PUFA-rich oils.[139] Importantly, since linoleic acid accounts for about 90% of total PUFA intake, the terms "PUFA" and "linoleic acid" were often used interchangeably at the time. As shown in **Fig. 5.2**, these recommendations: (1) triggered a remarkable decline in consumption of whole-fat milk, with partial replacement by low-fat and skim milk (**Fig. 5.2A**); (2) amplified the existing declines in butter consumption, with corresponding increases in PHVO shortenings and margarines (**Fig. 5.2B**); and (3) heralded remarkable increases in extracted linoleic acid–rich oils (**Fig. 5.2C**).[132]

Phase 3: The third major change occurred when the U.S. government adopted AHA-like guidelines to reduce total fat, saturated fats, and dietary cholesterol from 1977 to 2000. Food companies promoted processed foods made with PHVO shortenings and margarines as "healthy alternatives" to traditional fats. In 1993,[140,141] the FDA authorized food claims that aligned with the U.S. dietary guideline goals of decreasing saturated fat and dietary cholesterol. Whole milk, whole-fat yogurt, and butter were not eligible for health claims. By contrast, PHVO margarines, refined oils, and processed foods made with PHVO shortenings qualified for "Cholesterol Free" claims. Fat-free yogurts with added sugar or artificial sweeteners and other chemical additives qualified for "Low Fat" and "Low Saturated Fat" claims (see **Fig. 5.8**). Similarly, processed snack foods combining refined carbohydrates and extracted oils (e.g., crackers, chips, cookies) were eligible for "Low Saturated Fat" claims.

Emphasis on limiting saturated fat may have inadvertently promoted the selection of highly processed foods and culinary ingredients.

These guidelines and authorized health claims accelerated: (1) declines in whole-fat milk (**Fig. 5.2A**); (2) massive increases in engineered food items containing industrialized PHVO shortenings and linoleic acid–rich oils (**Fig. 5.2B**), and (3) marked increases in use of PHVOs and linoleic acid–rich oils for cooking, for frying, and in dressings (**Fig. 5.2C**). By 1981, substantial amounts of trans fats of industrial origin were already present in the blood and tissues of Americans.[142-145] By 1990, PHVOs and PHVO-derived saturated fats and trans fats accounted for about 10%, 2–3%, and 2.6% of total food energy, respectively, in U.S. diets.[134,135,146] Use of PHVO shortenings and margarines continued to rise further before peaking in 2001 (**Fig. 5.2B**). Similarly, the rapid rise in the use of extracted, high-linoleic-acid oils for cooking, frying, salad dressings, and processed foods (**Fig. 5.2C**) increased the amount of linoleic acid in human tissues to levels that are higher than can be achieved by historical diets.[147]

Phase 4: The fourth major change was triggered by a 2002 National Academies report,[148] which concluded that intake of trans fats of industrial origin should be as low as possible. This guidance, which was reinforced in the 2005 DGAs[50] and FDA-mandated trans fats labeling,[82] triggered a precipitous decline in PHVO consumption (**Fig. 5.2B**). The processed food industry replaced PHVO shortenings—a key ingredient in most manufactured foods—with newer shelf-stable chemical additives such as inter-esterified fats,[149] mono- and diglycerides,[150] and blends of fully hydrogenated fats with non-hydrogenated, liquid oils.

Modern Fat Sources and the Linoleic Acid Dominant Profile

Today's U.S. fat supply is the cumulative result of a century of industrial processing and decades of dietary guidance and food-labeling policies. Although PHVOs have been banned and quantitative limits on total fat and dietary cholesterol repealed, legacy nutrient targets—limiting saturated fat and promoting linoleic acid–rich oils—continue to

shape both the food industry and national consumption patterns. The result is a narrow set of industrially refined oils that are unusually enriched in linoleic acid (**Fig. 5.4**). Linoleic acid now contributes an estimated 7.6% of food energy[133]—several times higher than estimated for pre-industrial or traditional diets, in which most linoleic acid was derived naturally from nuts and seeds.[35,132] In modern diets, however, the majority of linoleic acid comes from refined oils extracted from sources like soybean, corn, and canola. This large-scale consumption of linoleic acid–rich oils is a recent and atypical nutritional phenomenon.[16] Studies show that such exposure markedly increases the linoleic acid concentrations across multiple organs,[24,147,151-153] suggesting that these linoleic acid–rich levels could affect the function of many tissues. However, the effects of these changes in humans are understudied and incompletely understood.

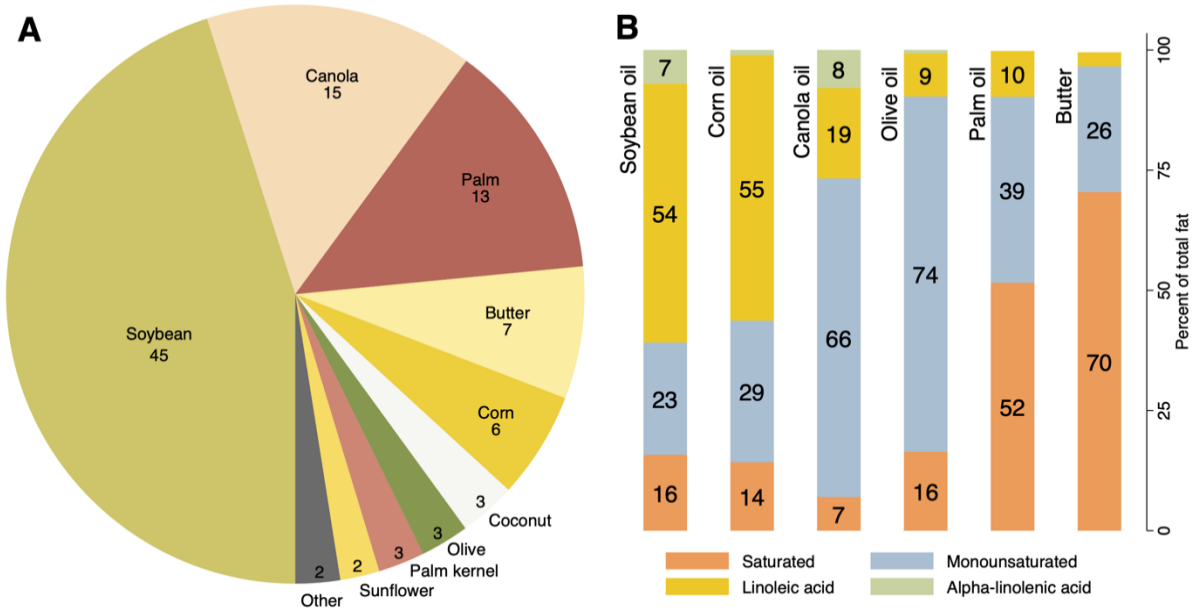

Figure 5.4. Domestic disappearance of edible fats and oils in the U.S. food supply, 2024. (A) Soybean and corn oils together account for about half of the added fats and oils in the U.S.; chart excludes biofuel uses of soybean, corn, and canola oils. Source: Oil Crops Yearbook.[154] (B) Profiles of commercially available fats showing their relative fatty-acid composition, highlighting that soybean and corn oils are concentrated sources of linoleic acid. Source: FoodData Central. Note: "Domestic disappearance" is the quantity of a commodity available for U.S. use (total supply minus exports and ending stocks). It approximates but does not equal actual consumption.[108]

Omega-3 Fatty Acids

Americans consume an estimated 0.8% of energy from the plant-derived omega-3 alpha-linolenic acid (ALA).[133] Rich sources of ALA include flax seed, chia seed, walnuts, soy products, and soybean and canola oils. Seafood, which includes fish and shellfish, provides preformed long chain omega-3 fatty acids (eicosapentaenoic acid [EPA] and

docosahexaenoic acid [DHA]) that are incorporated into cell membranes throughout the body and support cardiometabolic and neurological health. Americans consume an average of about 110 mg per day of EPA and DHA.[133] Emerging evidence from RCTs suggests that higher intakes of EPA and DHA (1 to 1.5 grams per day) from seafood may decrease physical pain.[27,28,30] DHA consumption may be particularly important for neurodevelopment (see **Chapter 7**). Seafood varieties higher in EPA and DHA and lower in methylmercury include salmon, sardines, anchovies, and trout (see **Chapter 6**).[155,156]

Evaluating the Evidence for Saturated-Fat Reduction and Replacement

Initial recommendations to reduce saturated fat intake and substitute it with linoleic acid–rich oils emerged in the 1960s[44,136,157,158] and were subsequently incorporated into successive editions of the DGAs. In the 2020–2025 DGAs, the guidance states: "For those two years and older, intake of saturated fat should be limited to less than 10% of calories per day by replacing them with unsaturated fats, particularly polyunsaturated fats."[53] The persistence of the recommendation to reduce saturated fat intake and replace it with linoleic acid–rich oils over several decades reflects enduring confidence in the traditional diet-heart hypothesis, which holds that lowering serum cholesterol by replacing saturated fat with linoleic acid can slow atherosclerotic progression, reduce coronary heart disease (CHD) events, and improve survival.[16]

Several moderate to large dietary RCTs conducted between the 1960s and 1980s tested this hypothesis by providing linoleic acid–rich oils and reducing saturated fats by restricting intake of dairy fats, meats, and PHVO-derived "common" margarines and shortenings (see **Appendices 4.6 and 4.7**). Although interventions effectively lowered blood cholesterol, none of the individual RCTs demonstrated the anticipated benefit, and a couple suggested potential for increased risk in some populations despite greater cholesterol lowering (see **Appendix 4.6**).

As reviewed in **Appendix 4.6**, several older reviews of diet-heart RCTs included non-randomized studies —like the Finnish Mental Hospital Study[159]—and multi-component RCTs that reduced saturated fat along with multiple healthy dietary changes. These reviews suggested modest benefits and attributed them to high-linoleic-acid oils.[160,161] Importantly, however, several of these RCTs included confounding factors that likely had a much greater impact than decreasing saturated fat or increasing linoleic acid–rich oils. The Oslo Diet Heart Study (ODHS)[162] is a clear example: Often cited as evidence for cardiovascular benefit of linoleic acid–rich oils, it markedly reduced partially hydrogenated fish oil (PHFO) and PHVO margarines (**Fig. 5.5A**), markedly increased fish-derived omega-3 fatty acids via provision of sardines and cod liver oil (**Fig. 5.5B**), and improved overall dietary quality (**Fig. 5.5B**)—changes that make it impossible to isolate the effects of high-linoleic-acid oils. When RCTs with dominant confounders such as ODHS are appropriately excluded, there is no indication of benefit. Systematic reviews and meta-analyses of the remaining RCTs report that replacing saturated fat

with linoleic acid–rich oils does not reduce CHD events, CHD mortality, or all-cause mortality (see **Appendix 4.6**).[16,163] Applying the GRADE certainty framework,[164] certainty of evidence is moderate for no effect on mortality and very low for CHD events because of inconsistency and imprecision (see **Appendix 4.6**).

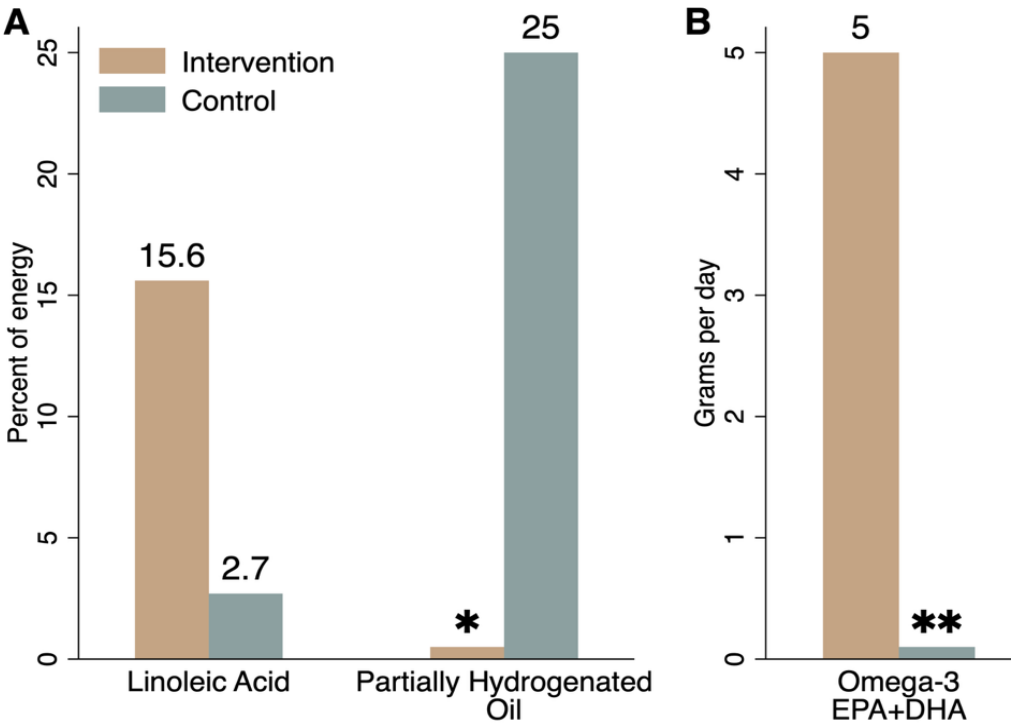

Figure 5.5. Three dominant confounders in the Oslo Diet Heart Study (ODHS).
(A) The control group consumed a staggering 25% of energy from PHFO and PHVO margarines.[162] (B) The experimental group replaced these PHFOs and PHVOs with Norwegian sardines canned in cod liver oil, which provided a massive dose of marine omega-3 fatty acids (about 5 grams per day or ≈40 times average U.S. intake). The ODHS experimental group was also instructed to eat more fruits, vegetables, and nuts and to restrict intake of refined grains and sugar. All three confounders are expected to favor the experimental group (reviewed in Appendix 4.6). *hydrogenated oils "entirely restricted" in the experimental group; **seafood not provided to control group.

There are not enough RCTs measuring actual disease outcomes to draw conclusions about whether replacing saturated fat with MUFA or carbohydrates affects the risk of coronary events or deaths. Overall, the RCT evidence does not provide causal support for reducing saturated fat below 10% of energy or replacing saturated fat with linoleic acid–rich oils to prevent CHD or death (see **Appendix 4.6**).

How the Diet-Heart Hypothesis Persisted Without Causal Evidence

Although causal testing in randomized trials failed to confirm benefit (see **Appendix 4.6**), the recommendation to replace saturated fat with linoleic acid–rich oils remains central to U.S. dietary recommendations. Its persistence reflects how early

interpretations of the evidence were shaped by selective reporting and reliance on surrogate markers (reviewed in Ramsden et al, 2016[16]). Together, these factors fostered enduring confidence in the saturated fat to PUFA substitution hypothesis, despite the absence of verified clinical benefit.

Publication bias and selective reporting of RCTs

For most of the history of the DGAs, interpretation of the evidence was distorted by publication bias. Early meta-analyses supporting replacement of saturated fat with linoleic acid–rich oils were based on incomplete datasets, as RCTs with null or unfavorable outcomes were not fully published for decades.[16] Recovery and inclusion of data from these trials fundamentally altered the evidence base, revealing that the anticipated reductions in CHD mortality failed to occur despite substantial cholesterol lowering. This incomplete and selective record created an enduring perception of benefit that continues to influence dietary policy despite the absence of confirmed clinical efficacy. Recovery of the full Sydney Diet Heart Study dataset showed that replacing saturated fat with safflower oil (concentrated source of linoleic acid) increased all-cause, cardiovascular, and CHD mortality, and an updated meta-analysis found no cardiovascular benefit of linoleic acid substitution (see **Appendices 4.6 and 4.7**).[165] Moreover, reevaluation of classic diet-heart trials indicates that lowering serum cholesterol by replacing saturated fat with linoleic acid–rich oils does not translate into reduced CHD mortality.[16]

In contrast, smaller multi-component RCTs and non-randomized studies that appeared favorable—most notably the ODHS and the Finnish Mental Hospital Study—were widely cited and became the foundation for early meta-analyses. As a result, pooled estimates in the 1970s–2000s overstated benefit by relying on an incomplete dataset.

Limitations of non-randomized studies

1. Observational confounding in dietary fat research

In contrast to RCTs,[69] cohort studies can only observe associations that may be distorted by unmeasured or residual confounding, selection bias, or correlated health behaviors. Several large prospective cohorts that were included in saturated fat to linoleic acid substitution meta-analyses were launched after widespread public health campaigns to reduce saturated fat and increase use of high-linoleic acid oils. Thus, higher linoleic intake may indicate adherence to prevailing advice and correlated health behaviors rather than an independent biological effect of linoleic acid (see **Chapter 2**). Although statistical models in these cohorts adjust for multiple variables, residual confounding is inevitable (see **Appendix 4.6**). As a result, higher linoleic acid intake and modeled substitution for saturated fat may partly reflect healthy user/adherer bias despite multivariable adjustment.[60] Even if perfectly measured, observational estimates are indirect with respect to the specific intervention tested in RCTs.[166,167] Moreover, the statistical constructs used in cohort substitution models infer hypothetical nutrient exchanges that did not actually occur in a person's diet.[168] Because participants' diets

include correlated behaviors and complex nutrient mixtures, these models are descriptive, not experimental.

2. Limitations of linoleic acid biomarkers as dietary indicators

The idea that linoleic acid is beneficial for health has been sustained by findings from observational studies showing that—when expressed as a percentage of total fatty acids—low levels of linoleic acid in plasma (blood) are associated with slightly higher risk of cardiometabolic diseases and premature death.[169] These findings have been widely interpreted as causal evidence that higher dietary linoleic acid intake is protective. However, the percentage of linoleic acid is a relative measure that can be distorted by metabolic factors that are known risk factors for chronic disease and premature death (see **Appendix 3**). Most notably, high blood triglycerides can decrease the *relative* amount of linoleic acid in blood. This is because linoleic acid is highly enriched within a special type of lipid known as a cholesteryl ester[151,170-172] and is much less abundant in triglycerides, which consist mostly of saturated fatty acids and MUFA (**Fig. 5.6**).

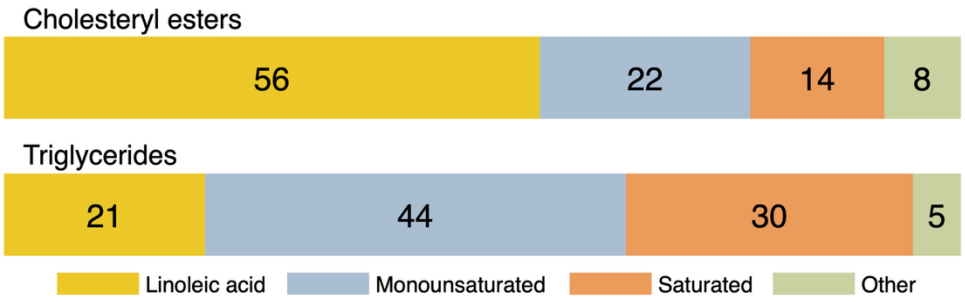

Figure 5.6. Linoleic acid is enriched in cholesteryl esters but less abundant in triglycerides. High blood triglycerides can dilute the relative amount of linoleic acid in plasma.

Because high blood triglycerides and other metabolic factors that dilute linoleic acid in plasma are known risk factors for multiple chronic diseases and premature death,[173-182] low levels of linoleic acid (expressed as a percentage of total fatty acids) can appear harmful (see **Appendix 3**). Such findings could partly reflect reverse causation or residual confounding by underlying health status rather than direct dietary effects, illustrating the inherent limitations of observational evidence (see **Appendix 3**).

Linoleic Acid Peroxidation and Health Implications of Heated Oils

Linoleic acid is unique among the major dietary fatty acids because it contains a structure known as a bis-allylic carbon that is highly vulnerable to peroxidation (**Fig. 5.7**),[183,184] which in turn generates toxic lipid hydroperoxide radicals and reactive lipid aldehydes (reviewed in **Appendix 4.8**).

Cooking and frying with linoleic acid–rich oils generates lipid hydroperoxides and reactive lipid aldehydes.

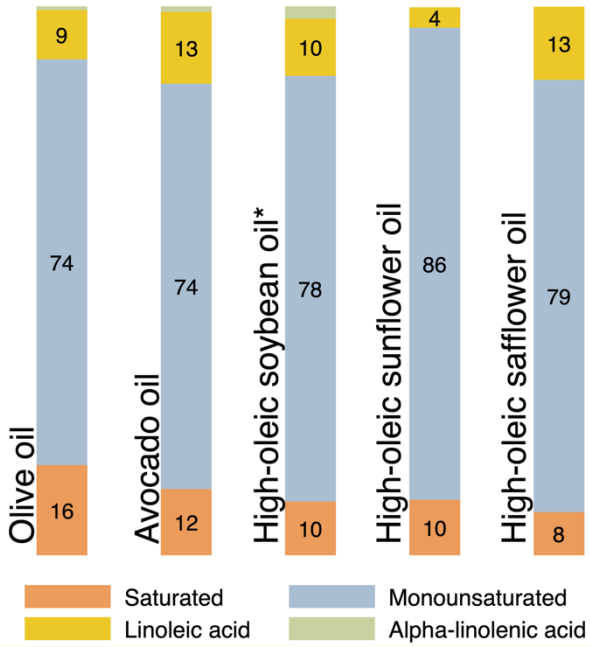

Figure 5.7. Peroxidation-resistant high-oleic oils in the U.S. High-oleic oils have fatty acid profiles that match olive oil. *Indicates mean of three high-oleic soybean oils available in the U.S.

Published evidence shows that cooking or frying with linoleic acid–rich oils produces much larger amounts of lipid hydroperoxides and aldehydes than oleic acid or saturated fat containing oils and fats.[185-199] Linoleic acid oxidation products and aldehydes present in foods are absorbed and incorporated into plasma lipoproteins and tissues (reviewed in **Appendix 4.8**).[200-204] Hydroperoxide radicals and aldehydes have been implicated in the etiology of many chronic diseases,[205-214] including CVD (reviewed in [215,216]).

These collective observations—which suggest potential harm from chronic consumption of heated, linoleic acid–rich oils—may help explain the neutral or unfavorable outcomes seen in diet-heart RCTs (see **Appendix 4.6**). Despite the ubiquitous use of linoleic acid–rich oils for cooking, frying, and industrial food manufacturing in the U.S., the clinical consequences of chronic consumption of lipid hydroperoxides and aldehydes are understudied. Given the availability of peroxidation-resistant oils such as olive oil and avocado oil in the U.S. (**Fig. 5.7**), there is an urgent need to determine whether cooking or frying with peroxidation-resistant oils can improve the health of Americans (see **Appendix 2**). Findings from such studies may be especially valuable to inform guidance for populations that are reported to be vulnerable to adverse effects of lipid hydroperoxides and aldehydes, such as pregnant women and older adults.[217-222]

Potential Unintended Consequences of Legacy Nutrient-Based Guidance

The historical emphasis on reducing total fat, saturated fat, and dietary cholesterol, combined with early emphasis on lowering serum cholesterol as a primary marker of health, contributed to major changes in the U.S. food supply. Although well-intentioned, these nutrient-specific targets encouraged food reformulation strategies that replaced natural fats first with PHVOs then later with refined oils, starches, sugars, and chemical additives. The result was a generation of “Cholesterol Free,” “‘Low-Fat,” and “‘Heart-Healthy” foods that met labeling criteria but did not necessarily improve diet quality or population health.

Dairy as a Case Example

Dairy products illustrate how this nutrient-centered approach contributed to product reformulation. The fat that is naturally present in whole-fat yogurts and other dairy foods prevents separation of components and imparts a creamy texture and satisfying flavor. As shown in **Fig. 5.8**, a suite of processed ingredients and manufactured chemicals are needed to compensate for the loss of natural dairy fat in low-fat and fat-free products. Refined sugars and artificial sweeteners enhance taste; modified corn starch and xanthan gum thicken and stabilize; carrageenan, polysorbate (Tween) 80, methylcellulose, and other emulsifiers mimic the creaminess of dairy fat and prevent separation of components. Consequently, emphasis on restricting saturated fat in dietary guidelines and authorized health claims may have inadvertently encouraged selection of processed products, such as low- and nonfat yogurts with added sugars, artificial sweeteners, emulsifiers, thickeners, and other chemical additives.

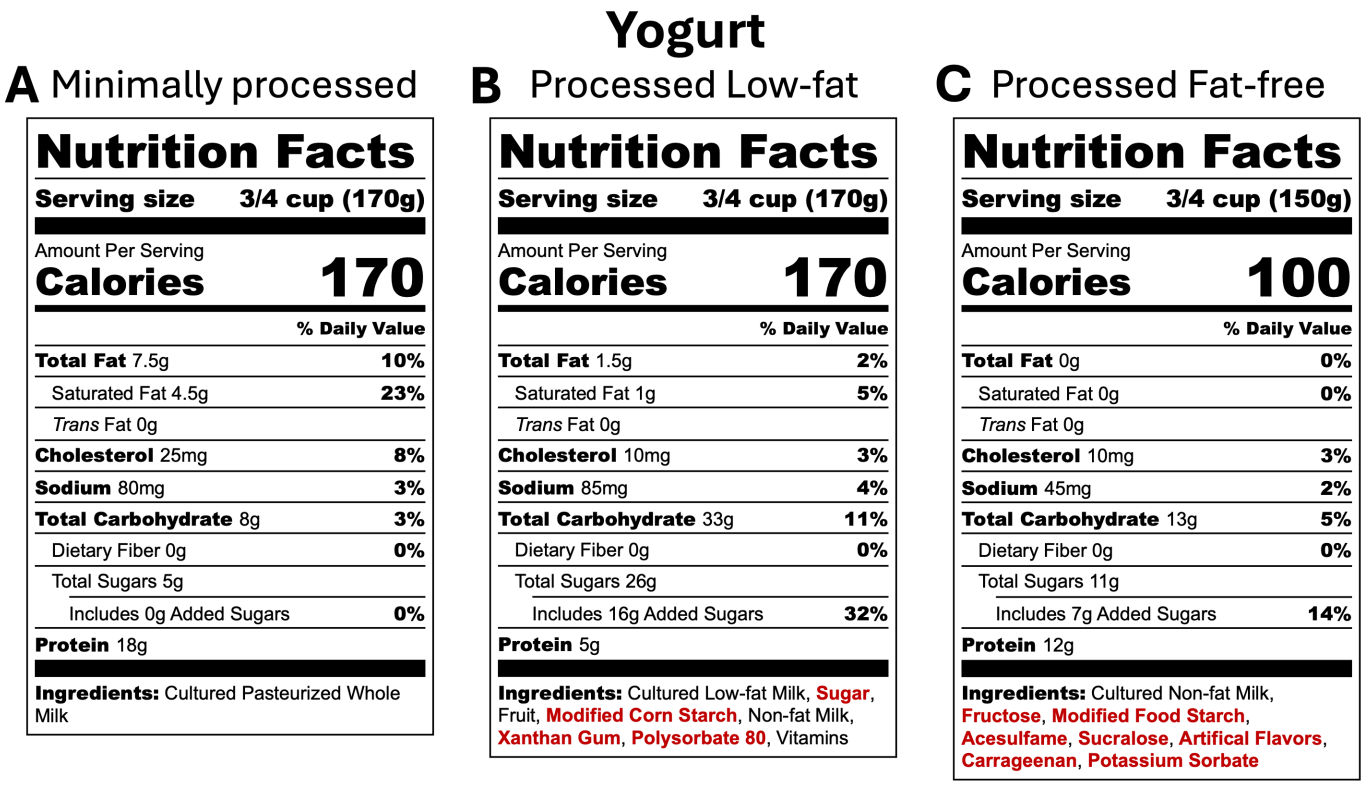

Figure 5.8. Legacy guidelines and health claims inadvertently favor highly processed dairy products. Yogurt A—which has one ingredient (whole milk) and is a rich source of protein (18g/serving)—is ineligible for health claims due to the presence of saturated fat. The more-processed low-fat and fat-free yogurts in B and C, which are eligible for the "Low saturated fat" health claim, have eight ingredients, 30–70% less protein, and large amounts of added sugar, starch, and chemical additives. Legacy guidelines and health claims create the illusion that processed Yogurts B and C are healthier choices than Yogurt A.

Emerging Evidence of Adverse Effects

Despite enduring guidance to replace whole-fat dairy with low-fat products, there is a remarkable lack of evidence from RCTs and observational studies[223-226] demonstrating adverse clinical consequences of whole-fat dairy in adults or children. The large-scale replacement of whole-fat dairy with highly processed dairy products may have had unintended consequences. In a nationally representative sample of U.S. adults with a median follow-up of 8 years, consumption of ultra-processed dairy products was associated with higher all-cause mortality.[80] Moreover, in a large observational cohort of French adults,[227] cumulative exposures to emulsifiers commonly added to low- or nonfat dairy foods was associated with increased risk of incident type 2 diabetes,[228] cancer,[228] and CVD.[229] While these associations do not establish causation, they highlight the need to re-evaluate whether nutrient-based labeling and health-claim criteria align with modern evidence on food processing and chronic-disease risk.

Policy Implications and Recommendations

A half century of research has not confirmed that lowering saturated fat below 10% of energy—or substituting it with linoleic acid–rich oils—reduces coronary heart disease or mortality risk. Overall, causal evidence does not demonstrate cardiovascular or mortality benefit from lowering saturated fat below current population averages. Within typical intake ranges, saturated fat appears neither uniquely harmful nor protective. The evidence therefore supports a neutral stance: Foods containing saturated fat can be part of healthy dietary patterns when consumed in reasonable amounts and within minimally processed contexts (see **Appendices 4.6 and 4.7**). Continued emphasis on numeric nutrient targets and surrogate biomarkers may have diverted attention from food quality and degree of processing—factors that increasingly appear more relevant to population health.

Linoleic acid is an essential nutrient required in small amounts for normal growth, skin integrity, and other physiological functions. However, modern intake levels from refined oils now exceed physiological requirements severalfold. The concern is not the presence of linoleic acid in the diet but its concentration and source. High exposure to industrially refined oils is a historically novel condition whose long-term effects remain insufficiently studied for adverse events, particularly in children, adolescents, and pregnant or breastfeeding women. Research is needed to determine the optimal range of linoleic acid intake and to distinguish health effects of whole-food sources—such as nuts and seeds—from those of refined and thermally stressed oils.

Moreover, high-quality RCTs are urgently needed to clarify which dietary fats and oils are most compatible with long-term health (see **Appendix 4.8**). For example, substituting peroxidation-resistant high-oleic oils in place of linoleic acid–rich oils when frying or cooking may improve health by reducing dietary exposures to lipid hydroperoxides and aldehydes. However, rigorous RCTs are needed to definitively determine whether reduced dietary exposures translate to improved clinical outcomes.

Recommendations: Healthy Fats

- Healthy fats are plentiful in many whole foods, such as meats, poultry, eggs, omega-3–rich seafood, nuts, seeds, full-fat dairy, olives, and avocados.
- When cooking with or adding fats to meals, prioritize oils with essential fatty acids, such as olive oil. Other options can include butter or beef tallow.
- In general, saturated fat consumption should not exceed 10% of total daily calories. Significantly limiting highly processed foods will help meet this goal. More high-quality research is needed to determine which types of dietary fats best support long-term health.

Recommendations: Dairy

- When consuming dairy, include full-fat dairy with no added sugars. Dairy is an excellent source of protein, healthy fats, vitamins, and minerals.
- Dairy serving goals: 3 servings per day as part of a 2,000-calorie dietary pattern, adjusting as needed based on your individual caloric requirements.

Chapter 6. Dietary Protein

Background

Protein is an essential nutrient that supports structural, enzymatic, and regulatory functions throughout the body.[230] It provides the nine essential amino acids required for synthesis of enzymes, hormones, and neurotransmitters;[231] for immune defense;[232] and for the continual renewal of muscle, bone, and other tissues.[233] Because there is no dedicated storage pool for amino acids, regular dietary intake is necessary to sustain tissue repair and metabolic balance.[231] Adequate protein intake may help preserve lean mass, regulate appetite, and maintain metabolic health—factors that influence long-term well-being, weight management, and physical function.[234-236] Requirements increase during periods of growth, pregnancy, lactation, and aging, when the efficiency of protein utilization declines (see **Chapter 8**).

The current Recommended Dietary Allowance (RDA) for protein—0.8 grams per kilogram of body weight per day—was established to prevent deficiency based on nitrogen-balance data. It represents the lowest intake that maintains equilibrium in most healthy adults but does not reflect the intake required to maintain optimal muscle mass or metabolic function under all conditions.[237] The Acceptable Macronutrient Distribution Range (AMDR) defines the proportion of total energy that can be derived from protein while supporting nutrient adequacy and reducing chronic-disease risk. For adults, the AMDR is 10–35% of total energy. In practice, the RDA and AMDR serve complementary purposes: The RDA prevents deficiency (e.g., preventing loss of lean body mass or negative nitrogen balance), while the AMDR identifies a range of intakes compatible with health and nutrient adequacy.[237]

U.S. adults consume on average about 1 g/kg/day,[133] or roughly 15% of total energy, placing the average intake near the midpoint of the AMDR—suggesting that deficiency is rare.[238] The remaining question is whether protein intakes moderately above the RDA offer measurable advantages for body composition or metabolic health. The following section summarizes evidence from randomized controlled feeding trials addressing this question.

Effect of Protein Intake of 1.2 to 1.6 g/kg/day on Body Composition

A systematic review of 30 randomized controlled trials examined the effects of higher-protein diets on weight management and nutrient adequacy in adults (see **Appendix 4.9** for detailed methods and results). Higher-protein diets were defined as providing 1.2–1.6 g/kg body weight from protein, compared with control diets providing 0.8–1.0 g/kg. Most trials were conducted in adults with overweight or obesity during calorie restriction, with several smaller studies in weight-stable adults. Across trials lasting 12 weeks to 2 years, 67% reported significant improvements in at least one weight-related outcome—typically greater fat loss, preservation of lean mass, or improved weight-loss maintenance—while none showed adverse weight effects. The standardized mean

difference in fat mass loss was −1.31 kg, and lean mass preservation was +0.81 kg, both rated moderate-to-high certainty. Most interventions increased protein through nutrient-dense animal source protein. No evidence of adverse effects on kidney function, bone health, or metabolic markers has been observed within this tested range (see **Appendix 4.9**), and currently no upper limit for dietary protein has been established due to a lack of high-quality studies.[239] The AMDR upper range for adults of 35% would correspond to roughly 2.5 g/kg body weight per day.

Overall, the evidence supports that protein intakes well above the RDA are safe and compatible with good health and may confer functional advantages for preserving muscle and metabolic resilience, particularly in individuals who are physically active or undergoing weight loss. For individuals engaged in regular resistance or endurance training, RCTs show enhanced muscle hypertrophy, strength gains, and preservation of lean mass with increasing daily protein intake up to approximately 1.6 g/kg body weight.[240] These findings complement existing population recommendations, reinforcing the adequacy of the AMDR framework as the policy basis for protein guidance. **Appendix 4.9** describes practical ways to achieve this intake pattern while improving nutrient adequacy and remaining well within the AMDR macronutrient ranges.

Protein Sources and Nutrient Quality

Both animal-source and plant-source proteins contribute uniquely to nutrient adequacy. Animal-source foods—meat, poultry, seafood, eggs, and dairy—supply high-density essential amino acids and bioavailable nutrients such as vitamin B_{12}, iron, zinc, calcium, and choline. Plant-source foods—pulses, soy, nuts, and seeds—supply complementary nutrients, including fiber, folate, magnesium, and phytonutrients, but have lower essential-amino-acid density and reduced mineral bioavailability.

Animal-Source Protein Foods

Meat, poultry, seafood, eggs, and dairy are concentrated sources of high-quality protein with complete essential-amino-acid profiles and high digestibility. These foods provide substantial shares of nutrients often underconsumed in U.S. diets, including vitamin B_{12}, vitamin D, calcium, heme iron, zinc, and choline. Evidence from randomized trials indicates neutral to beneficial effects of minimally processed animal-protein foods on body composition, glycemia, and lipid profiles. Observational associations linking meat intake with chronic disease risk are inconsistent and may be largely driven by processed-meat subtypes (see **Appendix 4.10**).[241-243] Processed meats—such as sausages, hot dogs, and deli meats—contain added sodium, nitrates/nitrites, and lipid oxidation products generated during curing or high-temperature cooking. Because evidence for harm derives primarily from non-randomized data, its certainty is low; however, limiting heavily processed forms is prudent for alignment with Chapter 3's broader guidance on processed foods.

Seafood, which includes fish and shellfish, provides high-quality protein and long-chain omega-3 fatty acids—EPA and DHA—that support cardiometabolic and neurocognitive health. Because mercury, in the form of methylmercury, is present in varying amounts among species, the FDA and the Environmental Protection Agency provide joint advice to help limit exposure, particularly for women who are or may become pregnant, those who are lactating, and young children.[155,156] Seafood varieties higher in EPA and DHA and lower in methylmercury—such as salmon, anchovies, sardines, Pacific oysters, and trout—are encouraged. Tilapia, shrimp, catfish, crab, and flounder are also commonly consumed species that are lower in methylmercury.

Eggs supply complete protein and choline, an essential nutrient for brain and liver function. Dairy foods provide protein together with calcium, potassium, and vitamin D. Whole-fat and low-fat dairy forms are acceptable within nutrient-dense diets (see **Chapter 5** on saturated fat).

Plant-Source Protein Foods

Legumes, pulses, nuts, seeds, and soy products provide plant-based pathways to meet protein needs while increasing fiber and phytochemical intake. Compared with animal sources, plant proteins have lower essential-amino-acid density but provide other benefits, such as higher magnesium and folate. Short-term RCTs show improved insulin sensitivity when plant proteins, particularly soy, replace refined carbohydrates or added sugars. Nutrient gaps can occur in fully plant-exclusive diets (notably vitamin B_{12}, iron, zinc, iodine, and calcium) and should be addressed through fortified foods or supplementation (see **Chapter 8** for vegetarian diets).

Processing and Preparation

Processing alters protein quality and introduces additives and oxidized lipids that can diminish health value. Cooking methods also matter: Charring and high-temperature frying generate advanced-glycation end products, nitrates, and lipid-peroxidation products (see **Chapters 3 and 5**).

Policy Implications and Recommendations

Protein remains a cornerstone of dietary adequacy and long-term health. The DGAs 2025–2030 reaffirm the AMDR for protein (10–35% of total energy) as a broad and flexible framework. Historically, the lower end of this range has been emphasized, but evidence indicates that higher intakes within the AMDR (e.g., approximately 1.2–1.6 g/kg of body weight) can support maintenance of lean mass and metabolic health. For those who are physically active (e.g., weight training), it is recommended to aim for an upper limit of 1.4–1.6 g/kg of body weight. Both animal- and plant-source protein foods contribute essential nutrients and can form part of healthy dietary patterns when consumed in minimally processed forms.

Recommendations: Protein

- Prioritize high-quality, nutrient-dense protein foods as part of a healthy dietary pattern.
- Consume a variety of protein foods from animal sources, including eggs, poultry, seafood, and red meat, as well as a variety of plant-sourced protein foods, including beans, peas, lentils, legumes, nuts, seeds, and soy.
- Swap deep-fried cooking methods with baked, broiled, roasted, stir-fried, or grilled cooking methods.
- Consume meat with no or limited added sugars, refined carbohydrates or starches, or chemical additives. If preferred, flavor with salt, spices, and herbs.
- Protein serving goals: 1.2–1.6 grams of protein per kilogram of body weight per day, adjusting as needed based on your individual caloric requirements.

Chapter 7. Sodium and Other Micronutrients

Vitamins and Minerals

Vitamins A, C, D, E, B_{12}, and niacin, and minerals including potassium, magnesium, iron, calcium, and zinc, must be obtained through diet or supplementation for normal growth and metabolism and to prevent deficiency-related diseases. Minimally processed foods tend to have higher amounts of vitamins and minerals than highly processed counterparts.[244-246] Healthy individuals eating omnivorous diets can generally meet their nutritional needs by selecting a variety of nutrient-dense foods and limiting highly processed foods.[245] Additional considerations for optimizing micronutrient intake throughout the life stages and in vegan and vegetarian diets are discussed in **Chapter 8** and **Appendices 4.11 and 4.12**.

Sodium

Sodium is an essential mineral that regulates extracellular fluid balance, blood pressure, and neuromuscular function. It is naturally present in small amounts in foods and added as salt (sodium chloride) for preservation and flavor. The majority of persons in the U.S. exceed current recommendations for dietary sodium,[247] in part due to consumption of highly processed and prepared/restaurant foods. Healthy eating patterns limit sodium to the Chronic Disease Risk Reduction (CDRR) levels defined by the National Academies: 1,200 mg/day (ages 1–3), 1,500 mg/day (ages 4–8), 1,800 mg/day (ages 9–13), and 2,300 mg/day (ages ≥14).[53,248] Highly active individuals or those with heavy sweat losses may require an additional intake to maintain hydration and prevent hyponatremia.[249]

Recommendations: Sodium

- Sodium and electrolytes are essential for hydration. The general population, ages 14 and above, should consume less than 2,300 mg per day of sodium. Highly active individuals may benefit from increased sodium intake to offset sweat losses.
- For children, the recommendations vary by age:
    - Ages 1–3: less than 1,200 mg per day
    - Ages 4–8: less than 1,500 mg per day
    - Ages 9–13: less than 1,800 mg per day
- Highly processed foods that are high in sodium should be avoided.

Chapter 8. Special Considerations for Life Stages and Vegetarians & Vegans

Introduction

Nutrient-dense, whole foods play a vital role in improving overall diet quality and reducing nutrient gaps.[250]

While these principles apply to everyone, certain life stages—such as infancy, childhood, adolescence, pregnancy, lactation, and older adulthood—come with unique nutritional needs that require special attention. This chapter highlights key nutrition priorities and considerations for these populations.

Infancy and Early Childhood (Birth–4 Years)

For about the first 6 months of life, exclusive breastfeeding is optimal. When breast milk is not available, infants should be fed iron-fortified infant formula. Breastfeeding should continue for as long as it is mutually desired by the mother and child, for 2 years or beyond. If feeding or supplementing with formula, discontinue infant formula at 12 months of age and transition to whole milk.

All infants, whether breastfed or formula-fed, should receive 400 International Units (IU) of vitamin D daily, starting shortly after birth. After about 6 months of age, infants may begin to eat solid foods. It is crucial to continue breastfeeding or formula feeding alongside the introduction of solids, as breast milk or infant formula remains the main source of nutrition for infants from 6 to 12 months.

From birth to 4 years of age, children have high nutrient needs to support brain development, overall growth, and bone health. These include iron, zinc, copper, choline, omega-3 fatty acids, fats, protein, calcium, and vitamin D. Poor nutrition during this period can cause lifelong health issues. Infants and toddlers should receive a diverse range of minimally processed, nutrient-dense foods in appropriate textures, including animal-source foods and iron-rich plants, while limiting nutrient-poor and highly processed foods.[251] Where access to nutrient-dense foods is limited, fortified products or supplements—such as iron—may be necessary under professional guidance.

Infants and toddlers should avoid added sugars and highly processed foods. By 7 to 8 months of age, infants can eat a variety of foods from different food groups, including meats or other proteins such as fish and poultry, vegetables and fruits, yogurt and cheese, and whole grains. Potentially allergenic foods—including nut butters, eggs, shellfish, and wheat—should be introduced along with other complementary foods. If an infant is at high risk for peanut allergy (due to the presence of severe eczema and/or egg allergy), caregivers should talk with a health care professional about peanut introduction as early as 4 to 6 months of age. For infants with mild to moderate eczema, peanut-containing foods can be introduced at around 6 months of age.[253]

At 12 months, introduce whole cow's milk, as dietary fats are important for growth and brain development. Whole cow's milk continues to play an important role in supporting these functions. Limited literature in this field does not support restricting dairy intake to only reduced-fat products.[224,254] Observational data, supported by limited RCTs, suggest that consuming whole cow's milk instead of reduced-fat milk is associated with lower odds of being overweight or obese.[252,254]

Recommendations: Infancy and Early Childhood (Birth–4 Years)

- For about the first 6 months of life, feed your baby only breast milk. When breast milk is not available, feed your baby iron-fortified infant formula.
- Continue breastfeeding as long as mutually desired by mother and child for 2 years or beyond. If feeding or supplementing your baby with infant formula, stop feeding your baby infant formula at 12 months of age and give them whole milk.
- All breastfed infants, as well as infants who consume less than 32 ounces of infant formula per day, should receive a daily oral vitamin D supplement of 400 IU starting shortly after birth. Consult your health care professional about vitamin D supplementation.
- Some infants require iron supplementation. Talk with your health care professional about iron supplementation.
- At about 6 months of age, infants may begin to have solid foods. It is crucial to continue breastfeeding or formula feeding while solids are introduced. Breast milk or infant formula continues to be the main source of nutrition for your infant up to 12 months of age.
    - If your infant is at high risk for peanut allergy (due to the presence of severe eczema and/or egg allergy), talk with your health care professional about peanut introduction as early as 4 to 6 months. This can be done by mixing a small amount of peanut butter with breast milk or formula, thinning it to a safe consistency, and feeding it by spoon. For infants with mild to moderate eczema, introduce peanut-containing foods at around 6 months of age.
- Introduce potentially allergenic foods—including nut butters, eggs, shellfish, and wheat—with other complementary foods at about 6 months. Ask your infant's health care professional about their risk for food allergies and safe ways to introduce these foods.
- Infants should receive a diverse range of nutrient-dense foods in appropriate textures, while avoiding nutrient-poor and highly processed foods.
- Examples of nutrient-dense foods to introduce during the complementary feeding period include:
    - Meat, poultry, and seafood
    - Vegetables and fruits

    - Full-fat yogurt and cheese
    - Whole grains
    - Legumes and nut- or seed-containing foods prepared in a safe, infant-appropriate form
- Avoid added sugars during infancy and early childhood.

Middle Childhood (5–10 Years)

Young children continue to have high nutrient needs to support brain development, overall growth, and bone health. Their diets should align with established dietary guidelines and emphasize whole, nutrient-dense foods, including protein sources, dairy, vegetables, fruits, healthy fats, and whole grains.

As noted in the infant and early childhood section, observational data with limited RCTs suggest that consuming whole-fat cow's milk rather than reduced-fat milk is associated with lower odds of being overweight or obese.[224,254]

Water should be the preferred beverage instead of sugar-sweetened beverages (SSBs). Intake of 100% fruit juice should be limited to small portions, or the juice should be diluted with water to reduce sweetness and overall sugar exposure. See **Appendix 4.2** for a detailed review on added sugars**.**

Recommendations: Middle Childhood (5–10 Years)

- Focus on whole, nutrient-dense foods such as protein foods, dairy, vegetables, fruits, healthy fats, and whole grains.
- Full-fat dairy products are important for children to help meet energy needs and support brain development.
- Avoid caffeinated beverages.
- No amount of added sugars is recommended.
- Make cooking meals fun and a regular part of the household's routine.

Adolescents (11–18 Years)

Adolescence is a period of rapid growth and continued brain development. During this stage, energy, protein, calcium, and iron needs increase[255]—particularly for girls due to menstruation, with nearly 40% of U.S. adolescent girls being iron deficient.[256] Increased calcium[257] and adequate vitamin D intake are essential for achieving peak bone mass.[258] Adolescents should focus on consuming nutrient-dense foods such as dairy products, leafy greens, and iron-rich animal foods, while limiting sugary drinks, energy drinks, and highly processed snacks.[251] When access to nutrient-dense foods is limited, fortified foods or supplements may be necessary under medical guidance.

Recommendations: Adolescence (11–18 Years)

- Adolescence is a rapid growth period with increased needs for energy, protein, calcium, and iron—especially for girls due to menstruation. Adequate calcium and vitamin D are vital for peak bone mass.
- Adolescents should eat nutrient-dense foods such as dairy, leafy greens, and iron-rich animal foods, while significantly limiting sugary drinks and energy drinks and avoiding highly processed foods. When access to nutrient-rich foods is limited, fortified foods or supplements may be needed under medical guidance.
- Encourage adolescents to become active participants in food shopping and cooking so they learn how to make healthy food choices for life.

Young Adulthood

During young adulthood, the brain continues to mature.[259] Young adults' diets should align with established dietary guidelines and emphasize whole, nutrient-dense foods, including protein sources, dairy, vegetables, fruits, healthy fats, and whole grains.

Non-pregnant, non-lactating women of reproductive age

Women of reproductive age have higher iron needs due to menstrual blood loss, making iron-deficiency anemia common.[260] Adequate iron intake from animal sources, fortified foods, and vitamin C–rich plant foods is essential to prevent deficiency. Women planning pregnancy should ensure sufficient folate intake through diet or supplements to reduce the risk of neural tube defects. Those with limited intake of animal foods—such as vegetarians and vegans—may require fortified foods or supplements for iron, folate, iodine, and vitamin B_{12} under medical guidance.

Supporting testosterone health in men

Men seeking to maintain healthy testosterone levels should focus on a balanced diet that includes foods rich in healthy fats. Avoiding strict low-fat diets is important, as research consistently shows that very low fat intake is associated with modest reductions in serum testosterone.[261-265] Conversely, weight loss in overweight or obese men—regardless of dietary composition—typically results in increased testosterone concentrations.[266] Evidence also suggests that DHA-rich fish oil supplementation may further support testosterone production in this population.[267] While adequate protein intake is beneficial, very high-protein diets exceeding 3.4 g/kg/day should be avoided, as they may suppress testosterone levels.[268] Certain supplements, such as zinc and vitamin D (particularly when deficient), may offer modest benefits but are best used as supportive measures rather than primary interventions.[266] Finally, maintaining regular physical activity and a healthy body weight is strongly associated with higher testosterone levels in men.[269] Overall, dietary and lifestyle strategies should be personalized, emphasizing overall health, nutritional balance, and long-term sustainability.

Recommendation: Young Adulthood

- Following the *Dietary Guidelines* will support optimal health during this period, including reducing risk of the onset or progression of chronic disease and supporting other aspects of health. The brain continues to mature during young adulthood. While the most significant increases in bone density occur during adolescence, optimizing bone health to achieve peak bone mass and peak bone strength is essential. Additionally, following the *Dietary Guidelines* can support reproductive health for both women and men—with special emphasis on healthy fats, iron, and folate for women and healthy fats and protein for men.

Pregnant Women

Pregnancy significantly increases nutrient needs to support both maternal health and fetal growth. Iron, folate, and iodine are top priorities—iron needs rise by about 50% to prevent anemia, adequate iodine intake during pregnancy is critical for normal fetal brain development,[270] and folate is essential before and during early pregnancy to prevent neural tube defects. Protein, choline, vitamin B_{12}, and omega-3 DHA are also vital for fetal brain development. Pregnant women should consume a variety of nutrient-dense foods, including iron-rich meats; folate-rich greens and legumes; choline-rich eggs; calcium-rich dairy; and low-mercury, DHA-rich seafood. Prenatal supplements, taken under medical guidance, are recommended. Pregnant women should completely avoid alcohol.[271]

Recommendations: Pregnant Women

- Pregnancy increases nutrient needs to support maternal health and fetal growth, with iron, folate, and iodine as top priorities.
- Pregnant women should consume diverse nutrient-dense foods, including iron-rich meats, folate-rich greens and legumes, choline-rich eggs, calcium-rich dairy, and low-mercury omega-3–rich seafood (e.g., salmon, sardines, trout).
- Women should talk to their health care professional about taking a daily prenatal vitamin during pregnancy.

Lactating Women

Lactation increases energy and nutrient requirements to support milk production and maternal health. Key nutrients such as vitamin B_{12}, iodine, vitamins D and A, DHA, and choline depend on the mother's diet and are essential for infant brain development.[272] Breastfeeding women should consume a diverse range of nutrient-dense foods, particularly animal-source foods rich in these nutrients, along with folate-rich legumes and vitamin A–rich vegetables. When dietary variety is limited, supplements or fortified foods under medical guidance may be necessary.

Recommendations: Lactating Women

- Lactation increases energy and nutrient needs to support milk production and maternal health. Breastfeeding women should consume a wide variety of nutrient-dense foods, including vitamin B_{12}–rich protein sources such as meats, poultry, eggs, and dairy; omega-3–rich seafood; folate-rich legumes; and vitamin A–rich vegetables.
- Women should talk to their health care professional about whether dietary supplements may be needed while breastfeeding.

Older Adults

Older adults require fewer calories but equal or greater amounts of key nutrients such as protein, vitamin B_{12}, vitamin D, and calcium.[234] Aging can impair nutrient absorption—especially of vitamin B_{12}—while adequate vitamin D and calcium are crucial for bone health, and protein supports muscle maintenance. Nutrient-dense foods such as fortified dairy, lean meats, seafood, eggs, legumes, and whole plant foods should be emphasized. When dietary intake or absorption is insufficient, fortified foods or supplements may be necessary under medical supervision. For individuals at risk of calcium oxalate kidney stones, dietary oxalate should be monitored by avoiding foods such as spinach, chard, and rhubarb; limiting intake of potatoes, chocolate, nuts, beets, and bran; and ensuring adequate calcium consumption with meals.[273]

See **Appendix 4.11** for a detailed review on life stages with special considerations.

Recommendation: Older Adults

- Some older adults need fewer calories but still require equal or greater amounts of key nutrients such as protein, vitamin B_{12}, vitamin D, and calcium. To meet these needs, they should prioritize nutrient-dense foods such as dairy, meats, seafood, eggs, legumes, and whole plant foods (vegetables and fruits, whole grains, nuts, and seeds). When dietary intake or absorption is insufficient, fortified foods or supplements may be needed under medical supervision.

Vegetarian and Vegan Diets

Vegetarian and vegan diets can support health across the life course but bring distinct micronutrient and protein challenges that warrant targeted guidance. Modeled vegetarian patterns generally meet most nutrient goals, whereas modeled vegan patterns often fall short for several vitamins (A, D, E, B_6, B_{12}) and minerals (calcium, iron, zinc, iodine), choline, long-chain omega-3s (EPA/DHA), and, in some age–sex groups, protein. These limitations reflect both intake and bioavailability constraints (e.g., non-heme iron, phytate-bound zinc, provitamin A carotenoids, ALA to EPA/DHA conversion).[274,275]

Observational and trial data align with these modeling signals. Vitamin B_{12} deficiency is common without fortification or supplements, with substantially higher prevalence in vegans than omnivores. Studies show that B_{12} status can decline within weeks of adopting a vegan diet and necessitate routine daily supplementation to mitigate the loss of this essential vitamin.[276-278]

Iron stores tend to be lower in vegetarians and vegans than in omnivores. Women of reproductive age, who already face a high risk of iron deficiency, should focus on iron-rich foods paired with vitamin C; limit inhibitors such as tea, coffee, and calcium around meals; and monitor ferritin levels if they follow a vegetarian or vegan diet. Iron supplements should be used only when deficiency is confirmed.[260,279]

Zinc status is also frequently low in vegans. Techniques like soaking, sprouting, or fermenting legumes and grains can improve zinc absorption, and supplementation is effective when deficiency is present.[280] Vitamin D and calcium intakes are consistently lower in vegan diets. Using fortified foods or supplements for both nutrients can reduce fracture risk and support overall bone health.[281-283]

Iodine intake can be unreliable without dairy or iodized salt. A modest daily iodine supplement of about 150 micrograms, or consistent use of iodized salt, helps maintain adequacy in a vegan or vegetarian diet. Seaweed should be consumed cautiously, since iodine content varies widely, and excess intake can harm thyroid function.[284] Choline intake may be suboptimal in many Americans,[285,286] especially when eggs are not included in the diet.[287] As mentioned above, supplementation may be needed during pregnancy and lactation to support fetal and infant brain development.

Because plant-based ALA is converted to EPA and DHA inefficiently, vegans and vegetarians may not achieve adequate long-chain omega-3 levels from food alone. An algal DHA/EPA supplement is an effective way to meet these omega-3 needs.[288,289]

In practical terms, vegetarians benefit from regularly including eggs and dairy. Vegans should rely on fortified foods; varied protein sources such as soy or mycoprotein; complementary plant proteins; and a focused supplement bundle that typically includes vitamin B_{12}, vitamin D, iodine, algal DHA, and calcium or iron when indicated. Closer monitoring is especially important during pregnancy, infancy and early childhood, adolescence, and older adulthood.

See **Appendix 4.12** for a detailed review on vegetarian and vegan diets.

Recommendations: Vegetarians and Vegans

- Consume a variety of whole foods, especially protein-rich foods, such as dairy, eggs, beans, peas, lentils, legumes, nuts, seeds, tofu, or tempeh.
- Significantly limit highly processed vegan or vegetarian foods that can include added fats, sugars, and salt.

- Pay careful attention to potential nutrient gaps when consuming a vegetarian or vegan diet. Vegetarian diets often fall short in vitamins D and E, choline, and iron, whereas vegan diets show broader shortfalls in vitamins A, D, E, B_6, and B_{12}; riboflavin; niacin; choline; calcium; iron; magnesium; phosphorus; potassium; zinc; and protein. Monitor nutrient status periodically, especially for iron, vitamin B_{12}, vitamin D, calcium, and iodine.
- To avoid nutrient gaps, prioritize targeted supplementation, diversify plant protein sources for amino acid balance, and enhance mineral bioavailability through food preparation techniques.

References

1. Emmerich SD, Ogden CL. QuickStats: Prevalence of obesity and severe obesity among persons aged 2–19 years — United States, 1999–2000 through 2021–2023. MMWR Morb Mortal Wkly Rep. Oct 17 2024;73(41):936. doi:10.15585/mmwr.mm7341a5
2. Fryar CD, Carroll MD, Afful J. Prevalence of overweight, obesity, and severe obesity among children and adolescents aged 2–19 years: United States, 1963–1965 through 2017–2018. NCHS Health E-Stats. 2020. https://www.cdc.gov/nchs/data/hestat/obesity-child-17-18/obesity-child.htm
3. Fryar CD, Carroll MD, Afful J. Prevalence of overweight, obesity, and severe obesity among adults aged 20 and over: United States, 1960–1962 through 2017–2018. NCHS Health E-Stats. 2020. https://www.cdc.gov/nchs/data/hestat/obesity-adult-17-18/obesity-adult.htm
4. Emmerich SD, Fryar CD, Stierman B, Gu Q, Afful J, Ogden CL. Trends in obesity-related measures among US children, adolescents, and adults. JAMA. Mar 25 2025;333(12):1082–1084. doi:10.1001/jama.2024.27676
5. Emmerich SD, Fryar CD, Stierman B, Ogden CL. Obesity and severe obesity prevalence in adults: United States, August 2021–August 2023. NCHS Data Brief. Sep 2024;(508). doi:10.15620/cdc/159281
6. Centers for Disease Control and Prevention. National Diabetes Statistics Report: At a Glance. Centers for Disease Control and Prevention. Updated May 15 2024. https://www.cdc.gov/diabetes/php/data-research/index.html
7. Gwira JA, Fryar CD, Gu Q. Prevalence of total, diagnosed, and undiagnosed diabetes in adults: United States, August 2021–August 2023. NCHS Data Brief. Nov 2024;(516). doi:10.15620/cdc/165794
8. Hadden WC, Harris MI. Prevalence of diagnosed diabetes, undiagnosed diabetes, and impaired glucose tolerance in adults 20-74 years of age. Vital Health Stat 11. Feb 1987;(237):1–55.
9. Centers for Disease Control and Prevention, National Center for Health Statistics. National Health and Nutrition Examination Survey (NHANES). U.S. Department of Health and Human Services, Centers for Disease Control and Prevention. https://wwwn.cdc.gov/nchs/nhanes/
10. U.S. Centers for Medicare and Medicaid Services. NHE Fact Sheet. U.S. Centers for Medicare & Medicaid Services. Updated Jun 24 2025. https://www.cms.gov/data-research/statistics-trends-and-reports/national-health-expenditure-data/nhe-fact-sheet
11. OECD. Understanding differences in health expenditure between the United States and OECD countries. 2022. https://www.oecd.org/en/publications/understanding-differences-in-health-expenditure-between-the-united-states-and-oecd-countries_6f24c128-en.html
12. Papanicolas I, Marino A, Lorenzoni L, Jha A. Comparison of health care spending by age in 8 high-income countries. JAMA Netw Open. Aug 3 2020;3(8):e2014688. doi:10.1001/jamanetworkopen.2020.14688

13. Papanicolas I, Woskie LR, Jha AK. Health care spending in the United States and other high-income countries. JAMA. Mar 13 2018;319(10):1024–1039. doi:10.1001/jama.2018.1150
14. Garmany A, Terzic A. Global healthspan-lifespan gaps among 183 World Health Organization member states. JAMA Netw Open. Dec 2 2024;7(12):e2450241. doi:10.1001/jamanetworkopen.2024.50241
15. World Health Organization. Data from: Global Health Observatory (GHO) OData API: Life expectancy at birth (WHOSIS_000001) and Healthy life expectancy (HALE) at birth (WHOSIS_000002). Geneva, Switzerland.
16. Ramsden CE, Zamora D, Majchrzak-Hong S, et al. Re-evaluation of the traditional diet-heart hypothesis: Analysis of recovered data from Minnesota Coronary Experiment (1968-73). BMJ. Apr 12 2016;353:i1246. doi:10.1136/bmj.i1246
17. Cueto-Galan R, Fontalba-Navas A, Gutierrez-Bedmar M, et al. Adherence to the Mediterranean diet to prevent or delay hepatic steatosis: A longitudinal analysis within the PREDIMED study. Front Nutr. 2025;12:1518082. doi:10.3389/fnut.2025.1518082
18. Martinez-Gonzalez MA, Sayon-Orea C, Bullon-Vela V, et al. Effect of olive oil consumption on cardiovascular disease, cancer, type 2 diabetes, and all-cause mortality: A systematic review and meta-analysis. Clin Nutr. Dec 2022;41(12):2659–2682. doi:10.1016/j.clnu.2022.10.001
19. Jensen T, Abdelmalek MF, Sullivan S, et al. Fructose and sugar: A major mediator of non-alcoholic fatty liver disease. J Hepatol. May 2018;68(5):1063–1075. doi:10.1016/j.jhep.2018.01.019
20. Vancells Lujan P, Vinas Esmel E, Sacanella Meseguer E. Overview of non-alcoholic fatty liver disease (NAFLD) and the role of sugary food consumption and other dietary components in its development. Nutrients. Apr 24 2021;13(5). doi:10.3390/nu13051442
21. Hassani Zadeh S, Mansoori A, Hosseinzadeh M. Relationship between dietary patterns and non-alcoholic fatty liver disease: A systematic review and meta-analysis. J Gastroenterol Hepatol. Jun 2021;36(6):1470–1478. doi:10.1111/jgh.15363
22. Ruanpeng D, Thongprayoon C, Cheungpasitporn W, Harindhanavudhi T. Sugar and artificially sweetened beverages linked to obesity: A systematic review and meta-analysis. QJM. Aug 1 2017;110(8):513–520. doi:10.1093/qjmed/hcx068
23. Nguyen M, Jarvis SE, Tinajero MG, et al. Sugar-sweetened beverage consumption and weight gain in children and adults: A systematic review and meta-analysis of prospective cohort studies and randomized controlled trials. Am J Clin Nutr. Jan 2023;117(1):160–174. doi:10.1016/j.ajcnut.2022.11.008
24. Ramsden CE, Ringel A, Majchrzak-Hong SF, et al. Dietary linoleic acid-induced alterations in pro- and anti-nociceptive lipid autacoids: Implications for idiopathic pain syndromes? Mol Pain. 2016;12. doi:10.1177/1744806916636386
25. Sastry PS. Lipids of nervous tissue: Composition and metabolism. Prog Lipid Res. 1985;24(2):69–176. doi:10.1016/0163-7827(85)90011-6

26. Bazinet RP, Laye S. Polyunsaturated fatty acids and their metabolites in brain function and disease. Nat Rev Neurosci. Dec 2014;15(12):771–785. doi:10.1038/nrn3820

27. Ramsden CE, Zamora D, Faurot KR, et al. Dietary alteration of n-3 and n-6 fatty acids for headache reduction in adults with migraine: Randomized controlled trial. BMJ. Jun 30 2021;374:n1448. doi:10.1136/bmj.n1448

28. Ramsden CE, Faurot KR, Zamora D, et al. Targeted alteration of dietary n-3 and n-6 fatty acids for the treatment of chronic headaches: A randomized trial. Pain. Nov 2013;154(11):2441–2451. doi:10.1016/j.pain.2013.07.028

29. van Soest AP, Beers S, van de Rest O, de Groot LC. The Mediterranean-Dietary Approaches to Stop Hypertension Intervention for Neurodegenerative Delay (MIND) diet for the aging brain: A systematic review. Adv Nutr. Mar 2024;15(3):100184. doi:10.1016/j.advnut.2024.100184

30. Zamora D, Kenney K, Horowitz M, et al. A high omega-3, low omega-6 diet reduces headache frequency and intensity in persistent post-traumatic headache: A randomized trial. J Neurotrauma. Oct 2025;42(19–20):1719–1731. doi:10.1089/neu.2025.0126

31. Broadhurst CL, Cunnane SC, Crawford MA. Rift Valley lake fish and shellfish provided brain-specific nutrition for early Homo. Br J Nutr. Jan 1998;79(1):3–21. doi:10.1079/bjn19980004

32. Cordain L, Eaton SB, Miller JB, Mann N, Hill K. The paradoxical nature of hunter-gatherer diets: Meat-based, yet non-atherogenic. Eur J Clin Nutr. Mar 2002;56 Suppl 1:S42–52. doi:10.1038/sj.ejcn.1601353

33. Eaton SB, Eaton SB, 3rd. Paleolithic vs. modern diets – selected pathophysiological implications. Eur J Nutr. Apr 2000;39(2):67–70. doi:10.1007/s003940070032

34. Eaton SB, Eaton SB, 3rd, Sinclair AJ, Cordain L, Mann NJ. Dietary intake of long-chain polyunsaturated fatty acids during the paleolithic. World Rev Nutr Diet. 1998;83:12–23. doi:10.1159/000059672

35. Kuipers RS, Luxwolda MF, Dijck-Brouwer DA, et al. Estimated macronutrient and fatty acid intakes from an East African Paleolithic diet. Br J Nutr. Dec 2010;104(11):1666–1687. doi:10.1017/S0007114510002679

36. O'Keefe JH, Jr., Cordain L. Cardiovascular disease resulting from a diet and lifestyle at odds with our Paleolithic genome: How to become a 21st-century hunter-gatherer. Mayo Clin Proc. Jan 2004;79(1):101–108. doi:10.4065/79.1.101

37. Zohar I, Alperson-Afil N, Goren-Inbar N, et al. Evidence for the cooking of fish 780,000 years ago at Gesher Benot Ya'aqov, Israel. Nat Ecol Evol. Dec 2022;6(12):2016–2028. doi:10.1038/s41559-022-01910-z

38. Dominguez LJ, Di Bella G, Veronese N, Barbagallo M. Impact of Mediterranean diet on chronic non-communicable diseases and longevity. Nutrients. Jun 12 2021;13(6). doi:10.3390/nu13062028

39. Sofi F, Cesari F, Abbate R, Gensini GF, Casini A. Adherence to Mediterranean diet and health status: Meta-analysis. BMJ. Sep 11 2008;337:a1344. doi:10.1136/bmj.a1344

40. Trichopoulou A, Costacou T, Bamia C, Trichopoulos D. Adherence to a Mediterranean diet and survival in a Greek population. N Engl J Med. Jun 26 2003;348(26):2599–2608. doi:10.1056/NEJMoa025039

41. Jalilpiran Y, Jayedi A, Djafarian K, Shab-Bidar S. The Nordic diet and the risk of non-communicable chronic disease and mortality: A systematic review and dose-response meta-analysis of prospective cohort studies. Crit Rev Food Sci Nutr. 2022;62(11):3124–3136. doi:10.1080/10408398.2020.1863906

42. Olsen A, Egeberg R, Halkjaer J, Christensen J, Overvad K, Tjonneland A. Healthy aspects of the Nordic diet are related to lower total mortality. J Nutr. Apr 1 2011;141(4):639–644. doi:10.3945/jn.110.131375

43. Willcox DC, Scapagnini G, Willcox BJ. Healthy aging diets other than the Mediterranean: A focus on the Okinawan diet. Mech Ageing Dev. Mar–Apr 2014;136–137:148–162. doi:10.1016/j.mad.2014.01.002

44. U.S. Senate Select Committee on Nutrition and Human Needs. Dietary Goals for the United States: Second Edition. U.S. Government Printing Office; 1977.

45. U.S. Department of Agriculture and U.S. Department of Health and Human Services. Nutrition and Your Health: Dietary Guidelines for Americans. U.S. Government Printing Office. Updated Feb 1 1980. https://www.dietaryguidelines.gov/about-dietary-guidelines/previous-editions/1980-dietary-guidelines-americans

46. U.S. Department of Agriculture and U.S. Department of Health and Human Services. Nutrition and Your Health: Dietary Guidelines for Americans. U.S. Government Printing Office. Updated Aug 1 1985. https://www.dietaryguidelines.gov/about-dietary-guidelines/previous-editions/1985-dietary-guidelines-americans

47. U.S. Department of Agriculture and U.S. Department of Health and Human Services. Nutrition and Your Health: Dietary Guidelines for Americans. U.S. Government Printing Office. Updated Nov 1 1990. https://www.dietaryguidelines.gov/about-dietary-guidelines/previous-editions/1990-dietary-guidelines-americans

48. U.S. Department of Agriculture and U.S. Department of Health and Human Services. Nutrition and Your Health: Dietary Guidelines for Americans. U.S. Government Printing Office. Updated Dec 1 1995. https://www.dietaryguidelines.gov/about-dietary-guidelines/previous-editions/1995-dietary-guidelines

49. U.S. Department of Agriculture and U.S. Department of Health and Human Services. Nutrition and Your Health: Dietary Guidelines for Americans. U.S. Government Printing Office. Updated May 27 2000. https://www.dietaryguidelines.gov/about-dietary-guidelines/previous-editions/2000-dietary-guidelines-americans

50. U.S. Department of Agriculture and U.S. Department of Health and Human Services. Dietary Guidelines for Americans. U.S. Government Printing Office. Updated Jan 12 2005. https://www.dietaryguidelines.gov/about-dietary-guidelines/previous-editions/2005-dietary-guidelines-americans

51. U.S. Department of Agriculture and U.S. Department of Health and Human Services. Dietary Guidelines for Americans. U.S. Government Printing Office. Updated Jan 31 2011.

https://www.dietaryguidelines.gov/about-dietary-guidelines/previous-editions/2010-dietary-guidelines

52. U.S. Department of Agriculture and U.S. Department of Health and Human Services. 2015–2020 Dietary Guidelines for Americans. U.S. Government Printing Office. Updated Jan 7 2016. https://www.dietaryguidelines.gov/about-dietary-guidelines/previous-editions/2015-dietary-guidelines
53. U.S. Department of Agriculture and U.S. Department of Health and Human Services. Dietary Guidelines for Americans, 2020–2025. 9th Edition. U.S. Government Printing Office. https://www.dietaryguidelines.gov/sites/default/files/2021-03/Dietary_Guidelines_for_Americans-2020-2025.pdf
54. D'Amico F, Marmiere M, Fonti M, Battaglia M, Belletti A. Association does not mean causation, when observational data were misinterpreted as causal: The observational interpretation fallacy. J Eval Clin Pract. Feb 2025;31(1):e14288. doi:10.1111/jep.14288
55. Balshem H, Helfand M, Schunemann HJ, et al. GRADE guidelines: 3. Rating the quality of evidence. J Clin Epidemiol. Apr 2011;64(4):401–406. doi:10.1016/j.jclinepi.2010.07.015
56. Hariton E, Locascio JJ. Randomised controlled trials - the gold standard for effectiveness research: Study design: randomised controlled trials. BJOG. Dec 2018;125(13):1716. doi:10.1111/1471-0528.15199
57. Higgins JP, Altman DG, Gotzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. Oct 18 2011;343:d5928. doi:10.1136/bmj.d5928
58. Fleming TR, Powers JH. Biomarkers and surrogate endpoints in clinical trials. Stat Med. Nov 10 2012;31(25):2973–2984. doi:10.1002/sim.5403
59. Fewell Z, Davey Smith G, Sterne JA. The impact of residual and unmeasured confounding in epidemiologic studies: A simulation study. Am J Epidemiol. Sep 15 2007;166(6):646–655. doi:10.1093/aje/kwm165
60. Shrank WH, Patrick AR, Brookhart MA. Healthy user and related biases in observational studies of preventive interventions: A primer for physicians. J Gen Intern Med. May 2011;26(5):546–550. doi:10.1007/s11606-010-1609-1
61. VanderWeele TJ, Ding P. Sensitivity analysis in observational research: Introducing the E-value. Ann Intern Med. Aug 15 2017;167(4):268–274. doi:10.7326/M16-2607
62. IOM (Institute of Medicine). Evaluation of biomarkers and surrogate endpoints in chronic disease. The National Academies Press; 2010.
63. Buchwald H, Varco RL, Matts JP, et al. Effect of partial ileal bypass surgery on mortality and morbidity from coronary heart disease in patients with hypercholesterolemia. Report of the Program on the Surgical Control of the Hyperlipidemias (POSCH). N Engl J Med. Oct 4 1990;323(14):946–955. doi:10.1056/NEJM199010043231404
64. Naci H, Brugts JJ, Fleurence R, Tsoi B, Toor H, Ades AE. Comparative benefits of statins in the primary and secondary prevention of major coronary events and all-cause mortality: A network meta-analysis of placebo-controlled and active-comparator trials. Eur J Prev Cardiol. Aug 2013;20(4):641–657. doi:10.1177/2047487313480435

65. The Coronary Drug Project. Findings leading to discontinuation of the 2.5-mg day estrogen group. The Coronary Drug Project Research Group. JAMA. Nov 5 1973;226(6):652–657.

66. The Coronary Drug Project. Findings leading to further modifications of its protocol with respect to dextrothyroxine. The Coronary Drug Project Research Group. JAMA. May 15 1972;220(7):996–1008.

67. The Coronary Drug Project. Initial findings leading to modifications of its research protocol. JAMA. Nov 16 1970;214(7):1303–1313.

68. Dietary Guidelines Advisory Committee. Scientific Report of the 2025 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Health and Human Services and Secretary of Agriculture. 2024. https://www.dietaryguidelines.gov/2025-advisory-committee-report

69. Guyatt GH, Oxman AD, Vist GE, et al. GRADE: An emerging consensus on rating quality of evidence and strength of recommendations. BMJ. Apr 26 2008;336(7650):924–926. doi:10.1136/bmj.39489.470347.AD

70. Assistant Secretary for Public Affairs (ASPA), U.S. Department of Health and Human Services. HHS, FDA and USDA Address the Health Risks of Ultra-Processed Foods. Updated Jul 23 2025. https://www.hhs.gov/press-room/hhs-fda-usda-ultra-processed-foods-definition-rfi.html

71. Monteiro CA, Cannon G, Levy RB, et al. Ultra-processed foods: What they are and how to identify them. Public Health Nutr. Apr 2019;22(5):936–941. doi:10.1017/S1368980018003762

72. Steele EM, O'Connor LE, Juul F, et al. Identifying and estimating ultraprocessed food intake in the US NHANES according to the Nova classification system of food processing. J Nutr. Jan 2023;153(1):225–241. doi:10.1016/j.tjnut.2022.09.001

73. Williams AM, Couch CA, Emmerich SD, Ogburn DF. Ultra-processed food consumption in youth and adults: United States, August 2021–August 2023. NCHS Data Brief. Aug 2025;(536). doi:10.15620/cdc/174612

74. Lane MM, Gamage E, Du S, et al. Ultra-processed food exposure and adverse health outcomes: Umbrella review of epidemiological meta-analyses. BMJ. Feb 28 2024;384:e077310. doi:10.1136/bmj-2023-077310

75. Dicken SJ, Jassil FC, Brown A, et al. Ultraprocessed or minimally processed diets following healthy dietary guidelines on weight and cardiometabolic health: A randomized, crossover trial. Nat Med. Oct 2025;31(10):3297–3308. doi:10.1038/s41591-025-03842-0

76. Hall KD, Ayuketah A, Brychta R, et al. Ultra-processed diets cause excess calorie intake and weight gain: An inpatient randomized controlled trial of ad libitum food intake. Cell Metab. Jul 2 2019;30(1):67–77.e3. doi:10.1016/j.cmet.2019.05.008

77. Preston JM, Iversen J, Hufnagel A, et al. Effect of ultra-processed food consumption on male reproductive and metabolic health. Cell Metab. Oct 7 2025;37(10):1950–1960.e2. doi:10.1016/j.cmet.2025.08.004

78. Souza M, Moura FS, Lima LCV, Amaral MJM. Association between higher consumption of ultra-processed foods and risk of diabetes and its complications: A systematic review &

updated meta-analysis. Metabolism. Apr 2025;165:156134. doi:10.1016/j.metabol.2025.156134

79. Liang S, Zhou Y, Zhang Q, Yu S, Wu S. Ultra-processed foods and risk of all-cause mortality: An updated systematic review and dose-response meta-analysis of prospective cohort studies. Syst Rev. Mar 3 2025;14(1):53. doi:10.1186/s13643-025-02800-8
80. Wang L, Steele EM, Du M, et al. Association between ultra-processed food consumption and mortality among US adults: Prospective cohort study of the National Health and Nutrition Examination Survey, 2003–2018. J Acad Nutr Diet. Jul 2025;125(7):875–887.e7. doi:10.1016/j.jand.2024.11.014
81. Astrup A, Monteiro CA. Does the concept of “ultra-processed foods” help inform dietary guidelines, beyond conventional classification systems? Debate consensus. Am J Clin Nutr. Dec 19 2022;116(6):1489–1491. doi:10.1093/ajcn/nqac230
82. U.S. Food and Drug Administration. Small Entity Compliance Guide: Trans Fatty Acids in Nutrition Labeling, Nutrient Content Claims, and Health Claims. U.S. Department of Health and Human Services. Updated Aug 2003. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/small-entity-compliance-guide-trans-fatty-acids-nutrition-labeling-nutrient-content-claims-and
83. U.S. Food and Drug Administration. Health Claim Notification for Saturated Fat, Cholesterol, and Trans Fat, and Reduced Risk of Heart Disease. Food and Drug Administration. Updated Mar 28 2024. https://www.fda.gov/food/nutrition-food-labeling-and-critical-foods/health-claim-notification-saturated-fat-cholesterol-and-trans-fat-and-reduced-risk-heart-disease
84. U.S. Food and Drug Administration. Brominated Vegetable Oil (BVO). U.S. Food and Drug Administration. Updated Jul 2 2024. https://www.fda.gov/food/food-additives-petitions/brominated-vegetable-oil-bvo
85. Calcaterra V, Cena H, Loperfido F, et al. Evaluating phthalates and bisphenol in foods: Risks for precocious puberty and early-onset obesity. Nutrients. Aug 16 2024;16(16). doi:10.3390/nu16162732
86. Giuliani A, Zuccarini M, Cichelli A, Khan H, Reale M. Critical review on the presence of phthalates in food and evidence of their biological impact. Int J Environ Res Public Health. Aug 5 2020;17(16). doi:10.3390/ijerph17165655
87. Kappenstein O, Vieth B, Luch A, Pfaff K. Toxicologically relevant phthalates in food. Exp Suppl. 2012;101:87–106. doi:10.1007/978-3-7643-8340-4_4
88. Liao C, Kannan K. Concentrations and profiles of bisphenol A and other bisphenol analogues in foodstuffs from the United States and their implications for human exposure. J Agric Food Chem. May 15 2013;61(19):4655–4662. doi:10.1021/jf400445n
89. Petersen JH, Jensen LK. Phthalates and food-contact materials: Enforcing the 2008 European Union plastics legislation. Food Addit Contam Part A Chem Anal Control Expo Risk Assess. Nov 2010;27(11):1608–1616. doi:10.1080/19440049.2010.501825
90. Schecter A, Malik N, Haffner D, et al. Bisphenol A (BPA) in U.S. food. Environ Sci Technol. Dec 15 2010;44(24):9425–9430. doi:10.1021/es102785d

91. Sewwandi M, Wijesekara H, Rajapaksha AU, Soysa S, Vithanage M. Microplastics and plastics-associated contaminants in food and beverages; Global trends, concentrations, and human exposure. Environ Pollut. Jan 15 2023;317:120747. doi:10.1016/j.envpol.2022.120747

92. Velickova Nikova E, Temkov M, Rocha JM. Occurrence of meso/micro/nano plastics and plastic additives in food from food packaging. Adv Food Nutr Res. 2023;103:41–99. doi:10.1016/bs.afnr.2022.08.001

93. Marfella R, Prattichizzo F, Sardu C, et al. Microplastics and nanoplastics in atheromas and cardiovascular events. N Engl J Med. Mar 7 2024;390(10):900–910. doi:10.1056/NEJMoa2309822

94. Liu S, Wang C, Yang Y, et al. Microplastics in three types of human arteries detected by pyrolysis-gas chromatography/mass spectrometry (Py-GC/MS). J Hazard Mater. May 5 2024;469:133855. doi:10.1016/j.jhazmat.2024.133855

95. Rozati R, Reddy PP, Reddanna P, Mujtaba R. Role of environmental estrogens in the deterioration of male factor fertility. Fertil Steril. Dec 2002;78(6):1187–1194. doi:10.1016/s0015-0282(02)04389-3

96. Nihart AJ, Garcia MA, El Hayek E, et al. Bioaccumulation of microplastics in decedent human brains. Nat Med. Apr 2025;31(4):1114–1119. doi:10.1038/s41591-024-03453-1

97. Bora SS, Gogoi R, Sharma MR, et al. Microplastics and human health: Unveiling the gut microbiome disruption and chronic disease risks. Front Cell Infect Microbiol. 2024;14:1492759. doi:10.3389/fcimb.2024.1492759

98. Adams J. The NOVA system can be used to address harmful foods and harmful food systems. PLoS Med. Nov 2024;21(11):e1004492. doi:10.1371/journal.pmed.1004492

99. Monteiro CA, Levy RB, Claro RM, Castro IR, Cannon G. A new classification of foods based on the extent and purpose of their processing. Cad Saude Publica. Nov 2010;26(11):2039–2049. doi:10.1590/s0102-311x2010001100005

100. Jung S, Kim JY, Park S, Lee JE, UPF Working Group. Potential misclassification of ultra-processed foods across studies and the need for a unified classification system: A scoping review. Nutr Res Pract. Jun 2025;19(3):331–344. doi:10.4162/nrp.2025.19.3.331

101. Shan Z, Rehm CD, Rogers G, et al. Trends in dietary carbohydrate, protein, and fat intake and diet quality among US adults, 1999-2016. JAMA. Sep 24 2019;322(12):1178–1187. doi:10.1001/jama.2019.13771

102. Drewnowski A, Popkin BM. The nutrition transition: New trends in the global diet. Nutr Rev. Feb 1997;55(2):31–43. doi:10.1111/j.1753-4887.1997.tb01593.x

103. Popkin BM, Nielsen SJ. The sweetening of the world's diet. Obes Res. Nov 2003;11(11):1325–1332. doi:10.1038/oby.2003.179

104. U.S. Department of Agriculture, Economic Research Service. Food Availability (Per Capita) Data System. U.S. Department of Agriculture. Updated Jun 26 2025. https://ers.usda.gov/data-products/food-availability-per-capita-data-system

105. Dunford EK, Miles DR, Ng SW, Popkin B. Types and amounts of nonnutritive sweeteners purchased by US households: A comparison of 2002 and 2018 Nielsen Homescan

purchases. J Acad Nutr Diet. Oct 2020;120(10):1662–1671.e10. doi:10.1016/j.jand.2020.04.022

106. Dunford EK, Miles DR, Popkin B. Food additives in ultra-processed packaged foods: An examination of US household grocery store purchases. J Acad Nutr Diet. Jun 2023;123(6):889–901. doi:10.1016/j.jand.2022.11.007
107. Ricciuto L, Fulgoni VL, Gaine PC, Scott MO, DiFrancesco L. Trends in added sugars intake and sources among US children, adolescents, and teens using NHANES 2001–2018. J Nutr. Feb 8 2022;152(2):568–578. doi:10.1093/jn/nxab395
108. U.S. Department of Agriculture, Agricultural Research Service. FoodData Central. https://fdc.nal.usda.gov/
109. Chi DL, Scott JM. Added sugar and dental caries in children: A scientific update and future steps. Dent Clin North Am. Jan 2019;63(1):17–33. doi:10.1016/j.cden.2018.08.003
110. Chiavaroli L, Cheung A, Ayoub-Charette S, et al. Important food sources of fructose-containing sugars and adiposity: A systematic review and meta-analysis of controlled feeding trials. Am J Clin Nutr. Apr 2023;117(4):741–765. doi:10.1016/j.ajcnut.2023.01.023
111. Huang Y, Chen Z, Chen B, et al. Dietary sugar consumption and health: Umbrella review. BMJ. Apr 5 2023;381:e071609. doi:10.1136/bmj-2022-071609
112. Lee D, Chiavaroli L, Ayoub-Charette S, et al. Important food sources of fructose-containing sugars and non-alcoholic fatty liver disease: A systematic review and meta-analysis of controlled trials. Nutrients. Jul 12 2022;14(14). doi:10.3390/nu14142846
113. Malik VS, Pan A, Willett WC, Hu FB. Sugar-sweetened beverages and weight gain in children and adults: A systematic review and meta-analysis. Am J Clin Nutr. Oct 2013;98(4):1084–1102. doi:10.3945/ajcn.113.058362
114. Malik VS, Popkin BM, Bray GA, Despres JP, Willett WC, Hu FB. Sugar-sweetened beverages and risk of metabolic syndrome and type 2 diabetes: A meta-analysis. Diabetes Care. Nov 2010;33(11):2477–2483. doi:10.2337/dc10-1079
115. Witkowski M, Nemet I, Alamri H, et al. The artificial sweetener erythritol and cardiovascular event risk. Nat Med. Mar 2023;29(3):710–718. doi:10.1038/s41591-023-02223-9
116. Lim J, Hong HG, Huang J, et al. Serum erythritol and risk of overall and cause-specific mortality in a cohort of men. Nutrients. Sep 14 2024;16(18). doi:10.3390/nu16183099
117. Witkowski M, Nemet I, Li XS, et al. Xylitol is prothrombotic and associated with cardiovascular risk. Eur Heart J. Jul 12 2024;45(27):2439–2452. doi:10.1093/eurheartj/ehae244
118. Reynolds A, Mann J, Cummings J, Winter N, Mete E, Te Morenga L. Carbohydrate quality and human health: A series of systematic reviews and meta-analyses. Lancet. 2019;393(10170):434–445. doi:10.1016/s0140-6736(18)31809-9
119. Appel LJ, Moore TJ, Obarzanek E, et al. A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group. N Engl J Med. Apr 17 1997;336(16):1117–1124. doi:10.1056/NEJM199704173361601

120. John JH, Ziebland S, Yudkin P, et al. Effects of fruit and vegetable consumption on plasma antioxidant concentrations and blood pressure: A randomised controlled trial. Lancet. Jun 8 2002;359(9322):1969–1974. doi:10.1016/s0140-6736(02)98858-6

121. McCall DO, McGartland CP, McKinley MC, et al. Dietary intake of fruits and vegetables improves microvascular function in hypertensive subjects in a dose-dependent manner. Circulation. Apr 28 2009;119(16):2153–2160. doi:10.1161/CIRCULATIONAHA.108.831297

122. Macready AL, George TW, Chong MF, et al. Flavonoid-rich fruit and vegetables improve microvascular reactivity and inflammatory status in men at risk of cardiovascular disease—FLAVURS: A randomized controlled trial. Am J Clin Nutr. Mar 2014;99(3):479–489. doi:10.3945/ajcn.113.074237

123. Daniels JA, Mulligan C, McCance D, et al. A randomised controlled trial of increasing fruit and vegetable intake and how this influences the carotenoid concentration and activities of PON-1 and LCAT in HDL from subjects with type 2 diabetes. Cardiovasc Diabetol. Jan 14 2014;13:16. doi:10.1186/1475-2840-13-16

124. Duthie SJ, Duthie GG, Russell WR, et al. Effect of increasing fruit and vegetable intake by dietary intervention on nutritional biomarkers and attitudes to dietary change: A randomised trial. Eur J Nutr. Aug 2018;57(5):1855–1872. doi:10.1007/s00394-017-1469-0

125. Wastyk HC, Fragiadakis GK, Perelman D, et al. Gut-microbiota-targeted diets modulate human immune status. Cell. Aug 5 2021;184(16):4137–4153.e14. doi:10.1016/j.cell.2021.06.019

126. Deehan EC, Yang C, Perez-Munoz ME, et al. Precision microbiome modulation with discrete dietary fiber structures directs short-chain fatty acid production. Cell Host Microbe. Mar 11 2020;27(3):389–404.e6. doi:10.1016/j.chom.2020.01.006

127. Beam A, Clinger E, Hao L. Effect of diet and dietary components on the composition of the gut microbiota. Nutrients. Aug 15 2021;13(8). doi:10.3390/nu13082795

128. Seethaler B, Nguyen NK, Basrai M, et al. Short-chain fatty acids are key mediators of the favorable effects of the Mediterranean diet on intestinal barrier integrity: Data from the randomized controlled LIBRE trial. Am J Clin Nutr. Oct 6 2022;116(4):928–942. doi:10.1093/ajcn/nqac175

129. Brichacek AL, Florkowski M, Abiona E, Frank KM. Ultra-processed foods: A narrative review of the impact on the human gut microbiome and variations in classification methods. Nutrients. Jun 1 2024;16(11). doi:10.3390/nu16111738

130. Rondinella D, Raoul PC, Valeriani E, et al. The detrimental impact of ultra-processed foods on the human gut microbiome and gut barrier. Nutrients. Feb 28 2025;17(5). doi:10.3390/nu17050859

131. Whelan K, Bancil AS, Lindsay JO, Chassaing B. Ultra-processed foods and food additives in gut health and disease. Nat Rev Gastroenterol Hepatol. Jun 2024;21(6):406–427. doi:10.1038/s41575-024-00893-5

132. Blasbalg TL, Hibbeln JR, Ramsden CE, Majchrzak SF, Rawlings RR. Changes in consumption of omega-3 and omega-6 fatty acids in the United States during the 20th century. Am J Clin Nutr. May 2011;93(5):950–962. doi:10.3945/ajcn.110.006643

133. Centers for Disease Control and Prevention, National Center for Health Statistics. National Health and Nutrition Examination Survey (NHANES) Data, 2021–2023. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention. https://wwwn.cdc.gov/nchs/nhanes/continuousnhanes/default.aspx?Cycle=2021-2023

134. Okamoto T, Matsuzaki H, Maruyama T, Niiya I, Sugano M. Trans fatty acid contents of margarines and baked confectioneries produced in the United States. J Oleo Sci. 2001;50(2):137–142. doi:10.5650/jos.50.137

135. Heckers H, Melcher FW. Trans-isomeric fatty acids present in West German margarines, shortenings, frying and cooking fats. Am J Clin Nutr. Jun 1978;31(6):1041–1049. doi:10.1093/ajcn/31.6.1041

136. American Heart Association, Central Committee for Medical Community Program. Dietary fat and its relation to heart attacks and strokes. JAMA. 1961;175(5):389–391. doi:10.1001/jama.1961.63040050001011

137. Rationale of the diet-heart statement of the American Heart Association. Report of the AHA nutrition committee. Arteriosclerosis. Mar–Apr 1982;2(2):177–191.

138. Chait A, Brunzell JD, Denke MA, et al. Rationale of the diet-heart statement of the American Heart Association. Report of the Nutrition Committee. Circulation. Dec 1993;88(6):3008–3029. doi:10.1161/01.cir.88.6.3008

139. American Heart Association. The Facts on Fats: 50 Years of American Heart Association Dietary Fats Recommendations. Jun 2015. https://www.heart.org/-/media/files/healthy-living/company-collaboration/inap/fats-white-paper-ucm_475005.pdf

140. U.S. Department of Health and Human Services, Food and Drug Administration. Food labeling: General provisions; nutrition labeling; nutrient content claims; health claims; ingredient labeling; state and local requirements; and exemptions; proposed rules. Federal Register. Nov 27 1991;56(229):60366–60878.

141. U.S. Department of Health and Human Services, Food and Drug Administration. Food labeling: Mandatory status of nutrition labeling and nutrient content revision; format for nutrition label. Final rule. Federal Register. Jan 6 1993;58:2079–12113.

142. Adlof RO, Emken EA. Distribution of hexadecenoic, octadecenoic and octadecadienoic acid isomers in human tissue lipids. Lipids. Sep 1986;21(9):543–547. doi:10.1007/BF02534049

143. Mosley EE, Wright AL, McGuire MK, McGuire MA. trans Fatty acids in milk produced by women in the United States. Am J Clin Nutr. Dec 2005;82(6):1292–1297. doi:10.1093/ajcn/82.6.1292

144. Ohlrogge JB, Emken EA, Gulley RM. Human tissue lipids: Occurrence of fatty acid isomers from dietary hydrogenated oils. J Lipid Res. Aug 1981;22(6):955–960.

145. Wada Y, Yoshida-Yamamoto S, Wada Y, Nakayama M, Mitsuda N, Kitajima H. Trans fatty acid accumulation in the human placenta. J Mass Spectrom. Mar 2017;52(3):139–143. doi:10.1002/jms.3910

146. Allison DB, Egan SK, Barraj LM, Caughman C, Infante M, Heimbach JT. Estimated intakes of trans fatty and other fatty acids in the US population. J Am Diet Assoc. Feb 1999;99(2):166–174; quiz 175–176. doi:10.1016/S0002-8223(99)00041-3

147. Guyenet SJ, Carlson SE. Increase in adipose tissue linoleic acid of US adults in the last half century. Adv Nutr. Nov 2015;6(6):660–664. doi:10.3945/an.115.009944

148. National Academies of Sciences, Engineering, and Medicine. Dietary fats: Total fat and fatty acids. Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids. The National Academies Press; 2005:422–541:chap 8.

149. Idris NA, Dian NL. Inter-esterified palm products as alternatives to hydrogenation. Asia Pac J Clin Nutr. 2005;14(4):396–401.

150. Cropper SL, Kocaoglu-Vurma NA, Tharp BW, Harper WJ. Effects of locust bean gum and mono- and diglyceride concentrations on particle size and melting rates of ice cream. J Food Sci. Jun 2013;78(6):C811–C816. doi:10.1111/1750-3841.12073

151. Glatz JF, Soffers AE, Katan MB. Fatty acid composition of serum cholesteryl esters and erythrocyte membranes as indicators of linoleic acid intake in man. Am J Clin Nutr. Feb 1989;49(2):269–276. doi:10.1093/ajcn/49.2.269

152. Bourre JM, Piciotti M, Dumont O, Pascal G, Durand G. Dietary linoleic acid and polyunsaturated fatty acids in rat brain and other organs. Minimal requirements of linoleic acid. Lipids. Aug 1990;25(8):465–472. doi:10.1007/BF02538090

153. Boyd JT, LoCoco PM, Furr AR, et al. Elevated dietary omega-6 polyunsaturated fatty acids induce reversible peripheral nerve dysfunction that exacerbates comorbid pain conditions. Nat Metab. Jun 2021;3(6):762–773. doi:10.1038/s42255-021-00410-x

154. U.S. Department of Agriculture, Economic Research Service. Oil Crops Yearbook. U.S. Department of Agriculture. Accessed Dataset, https://www.ers.usda.gov/data-products/oil-crops-yearbook

155. U.S. Environmental Protection Agency. EPA-FDA Advice about Eating Fish and Shellfish. https://www.epa.gov/choose-fish-and-shellfish-wisely/epa-fda-advice-about-eating-fish-and-shellfish

156. U.S. Food and Drug Administration. Advice about Eating Fish. https://www.fda.gov/food/consumers/advice-about-eating-fish

157. Krauss RM, Eckel RH, Howard B, et al. AHA Dietary Guidelines: Revision 2000: A statement for healthcare professionals from the Nutrition Committee of the American Heart Association. Stroke. Nov 2000;31(11):2751–2766. doi:10.1161/01.str.31.11.2751

158. Sacks FM, Lichtenstein AH, Wu JHY, et al. Dietary fats and cardiovascular disease: A presidential advisory grom the American Heart Association. Circulation. Jul 18 2017;136(3):e1–e23. doi:10.1161/CIR.0000000000000510

159. Miettinen M, Turpeinen O, Karvonen MJ, Elosuo R, Paavilainen E. Effect of cholesterol-lowering diet on mortality from coronary heart-disease and other causes. A twelve-year clinical trial in men and women. Lancet. Oct 21 1972;2(7782):835–838. doi:10.1016/s0140-6736(72)92208-8

160. Mozaffarian D, Micha R, Wallace S. Effects on coronary heart disease of increasing polyunsaturated fat in place of saturated fat: A systematic review and meta-analysis of randomized controlled trials. PLoS Med. Mar 23 2010;7(3):e1000252. doi:10.1371/journal.pmed.1000252

161. Chowdhury R, Warnakula S, Kunutsor S, et al. Association of dietary, circulating, and supplement fatty acids with coronary risk: A systematic review and meta-analysis. Ann Intern Med. Mar 18 2014;160(6):398–406. doi:10.7326/M13-1788

162. Leren P. The effect of plasma cholesterol lowering diet in male survivors of myocardial infarction. A controlled clinical trial. Acta Med Scand Suppl. 1966;466:1–92.

163. Hooper L, Al-Khudairy L, Abdelhamid AS, et al. Omega-6 fats for the primary and secondary prevention of cardiovascular disease. Cochrane Database of Systematic Reviews. 2018;(11). doi:10.1002/14651858.CD011094.pub4

164. GRADE Working Group. Overview of the GRADE approach: Certainty of evidence. GRADE Working Group. Accessed October 6, 2025, https://book.gradepro.org/guideline/overview-of-the-grade-approach#certainty-of-evidence

165. Ramsden CE, Zamora D, Leelarthaepin B, et al. Use of dietary linoleic acid for secondary prevention of coronary heart disease and death: Evaluation of recovered data from the Sydney Diet Heart Study and updated meta-analysis. BMJ. Feb 4 2013;346:e8707. doi:10.1136/bmj.e8707

166. Maki KC, Slavin JL, Rains TM, Kris-Etherton PM. Limitations of observational evidence: Implications for evidence-based dietary recommendations. Adv Nutr. Jan 1 2014;5(1):7–15. doi:10.3945/an.113.004929

167. Kristal AR, Peters U, Potter JD. Is it time to abandon the food frequency questionnaire? Cancer Epidemiol Biomarkers Prev. Dec 2005;14(12):2826–2828. doi:10.1158/1055-9965.EPI-12-ED1

168. Willett W. Nutritional Epidemiology. Oxford University Press; 2012.

169. Marklund M, Wu JHY, Imamura F, et al. Biomarkers of dietary omega-6 fatty acids and incident cardiovascular disease and mortality. Circulation. May 21 2019;139(21):2422–2436. doi:10.1161/CIRCULATIONAHA.118.038908

170. Goodman DS, Shiratori T. Fatty acid composition of human plasma lipoprotein fractions. J Lipid Res. Jul 1964;5(3):307–313.

171. Raatz SK, Bibus D, Thomas W, Kris-Etherton P. Total fat intake modifies plasma fatty acid composition in humans. J Nutr. Feb 2001;131(2):231–234. doi:10.1093/jn/131.2.231

172. Ramsden CE, Ringel A, Feldstein AE, et al. Lowering dietary linoleic acid reduces bioactive oxidized linoleic acid metabolites in humans. Prostaglandins Leukot Essent Fatty Acids. Oct–Nov 2012;87(4–5):135–141. doi:10.1016/j.plefa.2012.08.004

173. Sprecher DL. Triglycerides as a risk factor for coronary artery disease. Am J Cardiol. Dec 17 1998;82(12A):49U–56U; discussion 85U–86U. doi:10.1016/s0002-9149(98)00953-9

174. Cullen P. Evidence that triglycerides are an independent coronary heart disease risk factor. Am J Cardiol. Nov 1 2000;86(9):943–949. doi:10.1016/s0002-9149(00)01127-9

175. Laramee P, Leonard S, Buchanan-Hughes A, Warnakula S, Daeppen JB, Rehm J. Risk of all-cause mortality in alcohol-dependent individuals: A systematic literature review and meta-analysis. EBioMedicine. Oct 2015;2(10):1394–1404. doi:10.1016/j.ebiom.2015.08.040

176. Huang Y, Cai X, Mai W, Li M, Hu Y. Association between prediabetes and risk of cardiovascular disease and all cause mortality: Systematic review and meta-analysis. BMJ. Nov 23 2016;355:i5953. doi:10.1136/bmj.i5953

177. Klempfner R, Erez A, Sagit BZ, et al. Elevated triglyceride level is independently associated with increased all-cause mortality in patients with established coronary heart disease: Twenty-two-year follow-up of the Bezafibrate Infarction Prevention study and registry. Circ Cardiovasc Qual Outcomes. Mar 2016;9(2):100–108. doi:10.1161/CIRCOUTCOMES.115.002104

178. Rahmani J, Miri A, Namjoo I, et al. Elevated liver enzymes and cardiovascular mortality: A systematic review and dose-response meta-analysis of more than one million participants. Eur J Gastroenterol Hepatol. May 2019;31(5):555–562. doi:10.1097/MEG.0000000000001353

179. Esser MB, Leung G, Sherk A, et al. Estimated deaths attributable to excessive alcohol use among US adults aged 20 to 64 years, 2015 to 2019. JAMA Netw Open. Nov 1 2022;5(11):e2239485. doi:10.1001/jamanetworkopen.2022.39485

180. Gonzalez-Gonzalez JG, Violante-Cumpa JR, Zambrano-Lucio M, et al. HOMA-IR as a predictor of health outcomes in patients with metabolic risk factors: A systematic review and meta-analysis. High Blood Press Cardiovasc Prev. Nov 2022;29(6):547–564. doi:10.1007/s40292-022-00542-5

181. Schlesinger S, Neuenschwander M, Barbaresko J, et al. Prediabetes and risk of mortality, diabetes-related complications and comorbidities: Umbrella review of meta-analyses of prospective studies. Diabetologia. Feb 2022;65(2):275–285. doi:10.1007/s00125-021-05592-3

182. Gao X, Chen T, Zhou F, et al. The association between different insulin resistance surrogates and all-cause mortality and cardiovascular mortality in patients with metabolic dysfunction-associated steatotic liver disease. Cardiovasc Diabetol. May 9 2025;24(1):200. doi:10.1186/s12933-025-02758-w

183. Esterbauer H, Schaur RJ, Zollner H. Chemistry and biochemistry of 4-hydroxynonenal, malonaldehyde and related aldehydes. Free Radic Biol Med. 1991;11(1):81–128. doi:10.1016/0891-5849(91)90192-6

184. Yin H, Xu L, Porter NA. Free radical lipid peroxidation: Mechanisms and analysis. Chem Rev. Oct 12 2011;111(10):5944–5972. doi:10.1021/cr200084z

185. Romero A, Bastida S, Sanchez-Muniz FJ. Cyclic fatty acid monomer formation in domestic frying of frozen foods in sunflower oil and high oleic acid sunflower oil without oil replenishment. Food Chem Toxicol. Oct 2006;44(10):1674–1681. doi:10.1016/j.fct.2006.05.003

186. Miraliakbari H, Shahidi F. Oxidative stability of tree nut oils. J Agric Food Chem. Jun 25 2008;56(12):4751–4759. doi:10.1021/jf8000982

187. Marmesat S, Morales A, Velasco J, Carmen Dobarganes M. Influence of fatty acid composition on chemical changes in blends of sunflower oils during thermoxidation and frying. Food Chem. Dec 15 2012;135(4):2333–2339. doi:10.1016/j.foodchem.2012.06.128

188. Morales A, Marmesat S, Dobarganes MC, Marquez-Ruiz G, Velasco J. Quantitative analysis of hydroperoxy-, keto- and hydroxy-dienes in refined vegetable oils. J Chromatogr A. Mar 16 2012;1229:190–197. doi:10.1016/j.chroma.2012.01.039

189. Aladedunye F, Przybylski R. Frying stability of high oleic sunflower oils as affected by composition of tocopherol isomers and linoleic acid content. Food Chem. Dec 1 2013;141(3):2373–2378. doi:10.1016/j.foodchem.2013.05.061

190. Mubiru E, Shrestha K, Papastergiadis A, De Meulenaer B. Improved gas chromatography-flame ionization detector analytical method for the analysis of epoxy fatty acids. J Chromatogr A. Nov 29 2013;1318:217–225. doi:10.1016/j.chroma.2013.10.025

191. Velasco J, Morales-Barroso A, Ruiz-Mendez MV, Marquez-Ruiz G. Quantitative determination of major oxidation products in edible oils by direct NP-HPLC-DAD analysis. J Chromatogr A. Apr 27 2018;1547:62–70. doi:10.1016/j.chroma.2018.03.014

192. Wann AI, Percival BC, Woodason K, Gibson M, Vincent S, Grootveld M. Comparative (1)H NMR-based chemometric evaluations of the time-dependent generation of aldehydic lipid oxidation products in culinary oils exposed to laboratory-simulated shallow frying episodes: Differential patterns observed for omega-3 fatty acid-containing soybean oils. Foods. Oct 17 2021;10(10). doi:10.3390/foods10102481

193. Gibson M, Percival BC, Edgar M, Grootveld M. Low-field benchtop NMR spectroscopy for quantification of aldehydic lipid oxidation products in culinary oils during shallow frying episodes. Foods. Mar 15 2023;12(6). doi:10.3390/foods12061254

194. Abrante-Pascual S, Nieva-Echevarria B, Goicoechea-Oses E. Vegetable oils and their use for frying: A review of their compositional differences and degradation. Foods. Dec 23 2024;13(24). doi:10.3390/foods13244186

195. Cao J, Deng L, Zhu XM, et al. Novel approach to evaluate the oxidation state of vegetable oils using characteristic oxidation indicators. J Agric Food Chem. Dec 31 2014;62(52):12545–12552. doi:10.1021/jf5047656

196. Moumtaz S, Percival BC, Parmar D, Grootveld KL, Jansson P, Grootveld M. Toxic aldehyde generation in and food uptake from culinary oils during frying practices: Peroxidative resistance of a monounsaturate-rich algae oil. Sci Rep. Mar 11 2019;9(1):4125. doi:10.1038/s41598-019-39767-1

197. Grootveld M, Percival BC, Leenders J, Wilson PB. Potential adverse public health effects afforded by the ingestion of dietary lipid oxidation product toxins: Significance of fried food sources. Nutrients. Apr 1 2020;12(4). doi:10.3390/nu12040974

198. Grootveld M. Evidence-based challenges to the continued recommendation and use of peroxidatively-susceptible polyunsaturated fatty acid-rich culinary oils for high-temperature frying practises: Experimental revelations focused on toxic aldehydic lipid oxidation products. Front Nutr. 2021;8:711640. doi:10.3389/fnut.2021.711640

199. Martin-Rubio AS, Sopelana P, Ibargoitia ML, Guillen MD. (1)H NMR study of the in vitro digestion of highly oxidized soybean oil and the effect of the presence of ovalbumin. Foods. Jul 6 2021;10(7). doi:10.3390/foods10071573

200. Glavind J, Sylven C. Intestinal absorption and lymphatic transport of methyl linoleate hydroperoxide and hydroxyoctadecadienoate in the rat. Acta Chem Scand. 1970;24(10):3723–3728. doi:10.3891/acta.chem.scand.24-3723

201. Kanazawa K, Ashida H. Dietary hydroperoxides of linoleic acid decompose to aldehydes in stomach before being absorbed into the body. Biochim Biophys Acta. Aug 28 1998;1393(2–3):349–361. doi:10.1016/s0005-2760(98)00089-7

202. Kanazawa K, Ashida H. Catabolic fate of dietary trilinoleoylglycerol hydroperoxides in rat gastrointestines. Biochim Biophys Acta. Aug 28 1998;1393(2–3):336–348. doi:10.1016/s0005-2760(98)00088-5

203. Ferreiro-Vera C, Priego-Capote F, Mata-Granados JM, Luque de Castro MD. Short-term comparative study of the influence of fried edible oils intake on the metabolism of essential fatty acids in obese individuals. Food Chem. Jan 15 2013;136(2):576–584. doi:10.1016/j.foodchem.2012.08.081

204. Zhang Z, Emami S, Hennebelle M, et al. Linoleic acid-derived 13-hydroxyoctadecadienoic acid is absorbed and incorporated into rat tissues. Biochim Biophys Acta Mol Cell Biol Lipids. Mar 2021;1866(3):158870. doi:10.1016/j.bbalip.2020.158870

205. Esterbauer H, Jurgens G, Quehenberger O, Koller E. Autoxidation of human low density lipoprotein: Loss of polyunsaturated fatty acids and vitamin E and generation of aldehydes. J Lipid Res. May 1987;28(5):495–509.

206. Sayre LM, Zelasko DA, Harris PL, Perry G, Salomon RG, Smith MA. 4-hydroxynonenal-derived advanced lipid peroxidation end products are increased in Alzheimer's disease. J Neurochem. May 1997;68(5):2092–2097. doi:10.1046/j.1471-4159.1997.68052092.x

207. Kritharides L, Upston J, Jessup W, Dean RT. Accumulation and metabolism of low density lipoprotein-derived cholesteryl linoleate hydroperoxide and hydroxide by macrophages. J Lipid Res. Dec 1998;39(12):2394–2405.

208. Itabe H, Mori M, Fujimoto Y, Higashi Y, Takano T. Minimally modified LDL is an oxidized LDL enriched with oxidized phosphatidylcholines. J Biochem. Sep 2003;134(3):459–465. doi:10.1093/jb/mvg164

209. Markesbery WR, Kryscio RJ, Lovell MA, Morrow JD. Lipid peroxidation is an early event in the brain in amnestic mild cognitive impairment. Ann Neurol. Nov 2005;58(5):730–735. doi:10.1002/ana.20629

210. Fukuda M, Kanou F, Shimada N, et al. Elevated levels of 4-hydroxynonenal-histidine Michael adduct in the hippocampi of patients with Alzheimer's disease. Biomed Res. Aug 2009;30(4):227–233. doi:10.2220/biomedres.30.227

211. Weng X, Chen J, Fei Q, et al. The association of aldehydes exposure with diabetes mellitus in US population: NHANES 2013–2014. Chemosphere. Mar 2022;291(Pt 2):133019. doi:10.1016/j.chemosphere.2021.133019

212. Zhu Y, Liu M, Fu W, Bo Y. Association between serum aldehydes and hypertension in adults: A cross-sectional analysis of the National Health and Nutrition Examination Survey. Front Cardiovasc Med. 2022;9:813244. doi:10.3389/fcvm.2022.813244

213. Gu L, Wang Z, Liu L, et al. Association between mixed aldehydes and bone mineral density based on four statistical models. Environ Sci Pollut Res Int. Mar 2023;30(11):31631–31646. doi:10.1007/s11356-022-24373-y

214. Handelman GJ, Frankel EN, Fenz R, German JB. Chemical changes during the early phase of in vitro oxidative damage to human LDL. Biochem Mol Biol Int. Nov 1993;31(4):777–788.

215. Leitinger N. Cholesteryl ester oxidation products in atherosclerosis. Mol Aspects Med. Aug–Oct 2003;24(4–5):239–250. doi:10.1016/s0098-2997(03)00019-0

216. Gianazza E, Brioschi M, Fernandez AM, Banfi C. Lipoxidation in cardiovascular diseases. Redox Biol. May 2019;23:101119. doi:10.1016/j.redox.2019.101119

217. D'Souza V, Rani A, Patil V, et al. Increased oxidative stress from early pregnancy in women who develop preeclampsia. Clin Exp Hypertens. 2016;38(2):225–232. doi:10.3109/10641963.2015.1081226

218. Little RE, Gladen BC. Levels of lipid peroxides in uncomplicated pregnancy: A review of the literature. Reprod Toxicol. Sep-Oct 1999;13(5):347-52. doi:10.1016/s0890-6238(99)00033-7

219. Negre-Salvayre A, Swiader A, Salvayre R, Guerby P. Oxidative stress, lipid peroxidation and premature placental senescence in preeclampsia. Arch Biochem Biophys. Nov 15 2022;730:109416. doi:10.1016/j.abb.2022.109416

220. Spiteller G. Lipid peroxidation in aging and age-dependent diseases. Exp Gerontol. Sep 2001;36(9):1425–1457. doi:10.1016/s0531-5565(01)00131-0

221. Swardfager W, Yu D, Scola G, et al. Peripheral lipid oxidative stress markers are related to vascular risk factors and subcortical small vessel disease. Neurobiol Aging. Nov 2017;59:91–97. doi:10.1016/j.neurobiolaging.2017.06.029

222. Yavuzer H, Yavuzer S, Cengiz M, et al. Biomarkers of lipid peroxidation related to hypertension in aging. Hypertens Res. May 2016;39(5):342–348. doi:10.1038/hr.2015.156

223. Yakoob MY, Shi P, Hu FB, et al. Circulating biomarkers of dairy fat and risk of incident stroke in U.S. men and women in 2 large prospective cohorts. Am J Clin Nutr. Dec 2014;100(6):1437–1447. doi:10.3945/ajcn.114.083097

224. O'Sullivan TA, Schmidt KA, Kratz M. Whole-fat or reduced-fat dairy product intake, adiposity, and cardiometabolic health in children: A systematic review. Adv Nutr. Jul 1 2020;11(4):928–950. doi:10.1093/advances/nmaa011

225. Bhavadharini B, Dehghan M, Mente A, et al. Association of dairy consumption with metabolic syndrome, hypertension and diabetes in 147 812 individuals from 21 countries. BMJ Open Diabetes Res Care. Apr 2020;8(1). doi:10.1136/bmjdrc-2019-000826

226. Trieu K, Bhat S, Dai Z, et al. Biomarkers of dairy fat intake, incident cardiovascular disease, and all-cause mortality: A cohort study, systematic review, and meta-analysis. PLoS Med. Sep 2021;18(9):e1003763. doi:10.1371/journal.pmed.1003763

227. Chazelas E, Druesne-Pecollo N, Esseddik Y, et al. Exposure to food additive mixtures in 106,000 French adults from the NutriNet-Sante cohort. Sci Rep. Oct 4 2021;11(1):19680. doi:10.1038/s41598-021-98496-6

228. Salame C, Javaux G, Sellem L, et al. Food additive emulsifiers and the risk of type 2 diabetes: Analysis of data from the NutriNet-Sante prospective cohort study. Lancet Diabetes Endocrinol. May 2024;12(5):339–349. doi:10.1016/S2213-8587(24)00086-X

229. Sellem L, Srour B, Javaux G, et al. Food additive emulsifiers and risk of cardiovascular disease in the NutriNet-Sante cohort: Prospective cohort study. BMJ. Sep 6 2023;382:e076058. doi:10.1136/bmj-2023-076058

230. Wu G. Amino acids: Metabolism, functions, and nutrition. Amino Acids. May 2009;37(1):1–17. doi:10.1007/s00726-009-0269-0

231. Lopez MJ, Mohiuddin SS. Biochemistry, Essential Amino Acids. StatPearls. 2025.

232. Li P, Yin YL, Li D, Kim SW, Wu G. Amino acids and immune function. Br J Nutr. Aug 2007;98(2):237–252. doi:10.1017/S000711450769936X

233. Wolfe RR. Regulation of muscle protein by amino acids. J Nutr. Oct 2002;132(10):3219S–3224S. doi:10.1093/jn/131.10.3219S

234. Bauer J, Biolo G, Cederholm T, et al. Evidence-based recommendations for optimal dietary protein intake in older people: A position paper from the PROT-AGE Study Group. J Am Med Dir Assoc. Aug 2013;14(8):542–559. doi:10.1016/j.jamda.2013.05.021

235. Pasiakos SM, Cao JJ, Margolis LM, et al. Effects of high-protein diets on fat-free mass and muscle protein synthesis following weight loss: A randomized controlled trial. FASEB J. Sep 2013;27(9):3837–3847. doi:10.1096/fj.13-230227

236. Weigle DS, Breen PA, Matthys CC, et al. A high-protein diet induces sustained reductions in appetite, ad libitum caloric intake, and body weight despite compensatory changes in diurnal plasma leptin and ghrelin concentrations. Am J Clin Nutr. Jul 2005;82(1):41–48. doi:10.1093/ajcn.82.1.41

237. Wolfe RR, Cifelli AM, Kostas G, Kim IY. Optimizing protein intake in adults: Interpretation and application of the Recommended Dietary Allowance compared with the Acceptable Macronutrient Distribution Range. Adv Nutr. Mar 2017;8(2):266–275. doi:10.3945/an.116.013821

238. Berryman CE, Lieberman HR, Fulgoni VL, 3rd, Pasiakos SM. Protein intake trends and conformity with the Dietary Reference Intakes in the United States: Analysis of the National Health and Nutrition Examination Survey, 2001–2014. Am J Clin Nutr. Aug 1 2018;108(2):405–413. doi:10.1093/ajcn/nqy088

239. Institute of Medicine. Protein and amino acids. In: Otten JJ, Hellwig JP, Meyers LD, eds. Dietary Reference Intakes: The Essential Guide to Nutrient Requirements. The National Academies Press; 2006.

240. Morton RW, Murphy KT, McKellar SR, et al. A systematic review, meta-analysis and meta-regression of the effect of protein supplementation on resistance training-induced gains in muscle mass and strength in healthy adults. Br J Sports Med. Mar 2018;52(6):376–384. doi:10.1136/bjsports-2017-097608

241. Anderson JJ, Darwis NDM, Mackay DF, et al. Red and processed meat consumption and breast cancer: UK Biobank cohort study and meta-analysis. Eur J Cancer. Feb 2018;90:73–82. doi:10.1016/j.ejca.2017.11.022

242. Farvid MS, Sidahmed E, Spence ND, Mante Angua K, Rosner BA, Barnett JB. Consumption of red meat and processed meat and cancer incidence: A systematic review and meta-analysis of prospective studies. Eur J Epidemiol. Sep 2021;36(9):937–951. doi:10.1007/s10654-021-00741-9

243. Ungvari Z, Fekete M, Varga P, et al. Association between red and processed meat consumption and colorectal cancer risk: A comprehensive meta-analysis of prospective studies. Geroscience. Jun 2025;47(3):5123–5140. doi:10.1007/s11357-025-01646-1

244. Moubarac JC, Batal M, Louzada ML, Martinez Steele E, Monteiro CA. Consumption of ultra-processed foods predicts diet quality in Canada. Appetite. Jan 1 2017;108:512–520. doi:10.1016/j.appet.2016.11.006

245. Martinez Steele E, Popkin BM, Swinburn B, Monteiro CA. The share of ultra-processed foods and the overall nutritional quality of diets in the US: Evidence from a nationally representative cross-sectional study. Popul Health Metr. Feb 14 2017;15(1):6. doi:10.1186/s12963-017-0119-3

246. Martini D, Godos J, Bonaccio M, Vitaglione P, Grosso G. Ultra-processed foods and nutritional dietary profile: A meta-analysis of nationally representative samples. Nutrients. Sep 27 2021;13(10). doi:10.3390/nu13103390

247. Jackson SL, King SM, Zhao L, Cogswell ME. Prevalence of excess sodium intake in the United States – NHANES, 2009–2012. MMWR Morb Mortal Wkly Rep. Jan 8 2016;64(52):1393–1397. doi:10.15585/mmwr.mm6452a1

248. National Academies of Sciences, Engineering, and Medicine; Health and Medicine Division; Food and Nutrition Board; Committee to Review the Dietary Reference Intakes for Sodium and Potassium. Dietary Reference Intakes for Sodium and Potassium. The National Academies Press; 2019.

249. Thomas DT, Erdman KA, Burke LM. American College of Sports Medicine Joint Position Statement. Nutrition and athletic performance. Med Sci Sports Exerc. Mar 2016;48(3):543–568. doi:10.1249/MSS.0000000000000852

250. Beal T, Manohar S, Miachon L, Fanzo J. Nutrient-dense foods and diverse diets are important for ensuring adequate nutrition across the life course. Proc Natl Acad Sci U S A. Dec 10 2024;121(50):e2319007121. doi:10.1073/pnas.2319007121

251. Wang L, Martinez Steele E, Du M, et al. Trends in consumption of ultraprocessed foods among US youths aged 2-19 Years, 1999-2018. JAMA. Aug 10 2021;326(6):519–530. doi:10.1001/jama.2021.10238

252. Nicholl A, Deering KE, Evelegh K, et al. Whole-fat dairy products do not adversely affect adiposity or cardiometabolic risk factors in children in the Milky Way Study: A double-blind randomized controlled pilot study. Am J Clin Nutr. Dec 1 2021;114(6):2025–2042. doi:10.1093/ajcn/nqab288

253. American Academy of Pediatrics Committee on Nutrition. Complementary feeding. In: Greer FR, Abrams SA, eds. Pediatric Nutrition. 9 ed. American Academy of Pediatrics; 2025:177–206.

254. Vanderhout SM, Aglipay M, Torabi N, et al. Whole milk compared with reduced-fat milk and childhood overweight: A systematic review and meta-analysis. Am J Clin Nutr. Feb 1 2020;111(2):266–279. doi:10.1093/ajcn/nqz276

255. Norris SA, Frongillo EA, Black MM, et al. Nutrition in adolescent growth and development. Lancet. Jan 8 2022;399(10320):172–184. doi:10.1016/S0140-6736(21)01590-7

256. Weyand AC, Chaitoff A, Freed GL, Sholzberg M, Choi SW, McGann PT. Prevalence of iron deficiency and iron-deficiency anemia in US females aged 12-21 years, 2003-2020. JAMA. Jun 27 2023;329(24):2191–2193. doi:10.1001/jama.2023.8020

257. Office of Dietary Supplements, National Institutes of Health. Calcium - Health Professional Fact Sheet. U.S. Department of Health and Human Services. Updated Jul 11 2025. https://ods.od.nih.gov/factsheets/Calcium-HealthProfessional/

258. Hereford T, Kellish A, Samora JB, Reid Nichols L. Understanding the importance of peak bone mass. J Pediatr Soc North Am. May 2024;7:100031. doi:10.1016/j.jposna.2024.100031

259. Mills KL, Siegmund KD, Tamnes CK, et al. Inter-individual variability in structural brain development from late childhood to young adulthood. Neuroimage. Nov 15 2021;242:118450. doi:10.1016/j.neuroimage.2021.118450

260. Tawfik YMK, Billingsley H, Bhatt AS, et al. Absolute and functional iron deficiency in the US, 2017-2020. JAMA Netw Open. Sep 3 2024;7(9):e2433126. doi:10.1001/jamanetworkopen.2024.33126

261. Fantus RJ, Halpern JA, Chang C, et al. The association between popular diets and serum testosterone among men in the United States. J Urol. Feb 2020;203(2):398–404. doi:10.1097/JU.0000000000000482

262. Soltani S, Hejazi M, Meshkini F, et al. The effect of low-fat diets versus high-fat diet on sex hormones: A systematic review and meta-analysis of randomized controlled trials. J Food Sci. May 2025;90(5):e70266. doi:10.1111/1750-3841.70266

263. Dorgan JF, Judd JT, Longcope C, et al. Effects of dietary fat and fiber on plasma and urine androgens and estrogens in men: A controlled feeding study. Am J Clin Nutr. Dec 1996;64(6):850–855. doi:10.1093/ajcn/64.6.850

264. Whittaker J, Wu K. Low-fat diets and testosterone in men: Systematic review and meta-analysis of intervention studies. J Steroid Biochem Mol Biol. Jun 2021;210:105878. doi:10.1016/j.jsbmb.2021.105878

265. Wang C, Catlin DH, Starcevic B, et al. Low-fat high-fiber diet decreased serum and urine androgens in men. J Clin Endocrinol Metab. Jun 2005;90(6):3550–3559. doi:10.1210/jc.2004-1530

266. Santos HO, Cadegiani FA, Forbes SC. Nonpharmacological interventions for the management of testosterone and sperm parameters: A scoping review. Clin Ther. Aug 2022;44(8):1129–1149. doi:10.1016/j.clinthera.2022.06.006

267. Abbott K, Burrows TL, Acharya S, Thota RN, Garg ML. Dietary supplementation with docosahexaenoic acid rich fish oil increases circulating levels of testosterone in overweight and obese men. Prostaglandins Leukot Essent Fatty Acids. Dec 2020;163:102204. doi:10.1016/j.plefa.2020.102204

268. Pearce KL, Tremellen K. The effect of macronutrients on reproductive hormones in overweight and obese men: A pilot study. Nutrients. Dec 14 2019;11(12). doi:10.3390/nu11123059

269. Yeap BB, Marriott RJ, Antonio L, et al. Sociodemographic, lifestyle and medical influences on serum testosterone and sex hormone-binding globulin in men from UK Biobank. Clin Endocrinol (Oxf). Feb 2021;94(2):290–302. doi:10.1111/cen.14342

270. Caldwell KL, Pan Y, Mortensen ME, Makhmudov A, Merrill L, Moye J. Iodine status in pregnant women in the National Children's Study and in U.S. women (15–44 years), National Health and Nutrition Examination Survey 2005–2010. Thyroid. Aug 2013;23(8):927–937. doi:10.1089/thy.2013.0012

271. National Academies of Sciences, Engineering, and Medicine. Review of Evidence on Alcohol and Health. The National Academies Press; 2025:252.

272. Marshall NE, Abrams B, Barbour LA, et al. The importance of nutrition in pregnancy and lactation: Lifelong consequences. Am J Obstet Gynecol. May 2022;226(5):607–632. doi:10.1016/j.ajog.2021.12.035

273. Mitchell T, Kumar P, Reddy T, et al. Dietary oxalate and kidney stone formation. Am J Physiol Renal Physiol. Mar 1 2019;316(3):F409–F413. doi:10.1152/ajprenal.00373.2018

274. Bakaloudi DR, Halloran A, Rippin HL, et al. Intake and adequacy of the vegan diet. A systematic review of the evidence. Clin Nutr. May 2021;40(5):3503–3521. doi:10.1016/j.clnu.2020.11.035

275. Mariotti F, Gardner CD. Dietary protein and amino acids in vegetarian diets—a review. Nutrients. Nov 4 2019;11(11). doi:10.3390/nu11112661

276. Lederer AK, Hannibal L, Hettich M, et al. Vitamin B12 status upon short-term intervention with a vegan diet—a randomized controlled trial in healthy participants. Nutrients. Nov 18 2019;11(11). doi:10.3390/nu11112815

277. Green R, Allen LH, Bjorke-Monsen AL, et al. Vitamin B(12) deficiency. Nat Rev Dis Primers. Jun 29 2017;3:17040. doi:10.1038/nrdp.2017.40

278. Gilsing AM, Crowe FL, Lloyd-Wright Z, et al. Serum concentrations of vitamin B12 and folate in British male omnivores, vegetarians and vegans: Results from a cross-sectional analysis of the EPIC-Oxford cohort study. Eur J Clin Nutr. Sep 2010;64(9):933–939. doi:10.1038/ejcn.2010.142

279. Haider LM, Schwingshackl L, Hoffmann G, Ekmekcioglu C. The effect of vegetarian diets on iron status in adults: A systematic review and meta-analysis. Crit Rev Food Sci Nutr. May 24 2018;58(8):1359–1374. doi:10.1080/10408398.2016.1259210

280. Vallboehmer F, Schoofs H, Rink L, Jakobs J. Zinc supplementation among zinc-deficient vegetarians and vegans restores antiviral interferon-alpha response by upregulating

interferon regulatory factor 3. Clin Nutr. Aug 2025;51:161–173. doi:10.1016/j.clnu.2025.06.010

281. Appleby P, Roddam A, Allen N, Key T. Comparative fracture risk in vegetarians and nonvegetarians in EPIC-Oxford. Eur J Clin Nutr. Dec 2007;61(12):1400–1406. doi:10.1038/sj.ejcn.1602659
282. Bickelmann FV, Leitzmann MF, Keller M, Baurecht H, Jochem C. Calcium intake in vegan and vegetarian diets: A systematic review and meta-analysis. Crit Rev Food Sci Nutr. 2023;63(31):10659–10677. doi:10.1080/10408398.2022.2084027
283. Thorpe DL, Beeson WL, Knutsen R, Fraser GE, Knutsen SF. Dietary patterns and hip fracture in the Adventist Health Study 2: Combined vitamin D and calcium supplementation mitigate increased hip fracture risk among vegans. Am J Clin Nutr. Aug 2 2021;114(2):488–495. doi:10.1093/ajcn/nqab095
284. Eveleigh ER, Coneyworth L, Welham SJM. Systematic review and meta-analysis of iodine nutrition in modern vegan and vegetarian diets. Br J Nutr. Nov 14 2023;130(9):1580–1594. doi:10.1017/S000711452300051X
285. Wallace TC, Blusztajn JK, Caudill MA, et al. Choline: The underconsumed and underappreciated essential nutrient. Nutr Today. Nov–Dec 2018;53(6):240–253. doi:10.1097/NT.0000000000000302
286. Zeisel SH, Klatt KC, Caudill MA. Choline. Adv Nutr. Jan 1 2018;9(1):58–60. doi:10.1093/advances/nmx004
287. Wallace TC, Fulgoni VL. Usual choline intakes are associated with egg and protein food consumption in the United States. Nutrients. Aug 5 2017;9(8). doi:10.3390/nu9080839
288. Lane KE, Wilson M, Hellon TG, Davies IG. Bioavailability and conversion of plant based sources of omega-3 fatty acids – a scoping review to update supplementation options for vegetarians and vegans. Crit Rev Food Sci Nutr. 2022;62(18):4982–4997. doi:10.1080/10408398.2021.1880364
289. Swanson D, Block R, Mousa SA. Omega-3 fatty acids EPA and DHA: Health benefits throughout life. Adv Nutr. Jan 2012;3(1):1–7. doi:10.3945/an.111.000893