

1. Obtaining the Greatest Return from Federal Investment in Nutrition Research

Nutrition is an important, highly promising, and cross-cutting interdisciplinary research area. Partnerships between academic, federal government, industry, and nutrition professional organizations are essential to meet stakeholder needs and provide the best return on federal investment. The greatest return for federal investment in nutrition research takes place when research is put into practice. Approximately 100 million US adults have obesity, with diet-related diseases, including cardiovascular disease, cancer, and diabetes, accounting for half of the deaths in the US each year. Government spending, including Medicare and Medicaid, to treat cardiovascular disease, cancer, and diabetes accounted for 54% of the \$383.6 billion in health care spending, a 30% increase from 2009 to 2018. Slowing or preventing chronic diseases with nutrition and diet-related efforts will provide improved cost-effective outcomes for Americans, as nutrition research is translated into better human health. Nutrition is a modifiable risk factor for numerous chronic diseases, representing a highly viable approach to reduce adverse health outcomes.

a. Crucial Evidence Gaps in Nutrition Research

Due to historical underfunding of nutrition research for decades, nutrition science lags behind other biomedical sciences. Fundamental gaps in our understanding of nutrition science (which are outlined below) and how it relates to altered physiologic states and prevention of chronic disease impede our ability to move forward with nutrition research, policy, prevention, and interventions. Significant increases in nutrition research support are necessary to continue to clarify linkages between diet and health and to enhance nutrition-related disease prevention. Interdisciplinary nutrition research needs to be a funding priority. Increased funding of nutrition research will provide increased fundamental knowledge of diet and nutrition, contributing to evidence-based solutions to the health and economic challenges resulting from diet-related diseases, as well as implementation of nutrition science-based practice and policy.

Relationships Between Nutrients, Foods, Dietary Patterns, Health Promotion and Disease Prevention

Nutrition research is needed to evaluate and strengthen the fundamental evidence underlying the relationships between nutrients, foods, dietary patterns and health and disease prevention. Research to assess the effectiveness and efficiency of nutrition assistance and education programs needs to be undertaken to improve health and nutrition security. In addition, research is needed to better understand what factors impact food and eating behavior, habits, and decision making of people. Nutrition science is vast, encompassing molecular mechanisms all the way to population health. This includes the role of diet on the gut microbiome, exosomes that act as cell-to-cell communicators, epigenetic modifications, and metabolic profiles of chronic disease. These areas all require extensive research and consistent funding across a broad spectrum of interdisciplinary fields.

¹ Government Accountability Office. 2021. Chronic Health Conditions: Federal Strategy Needed to Coordinate Diet-Related Efforts. GAO Publication No. 21-593. Washington, D.C.: U.S. Government Printing Office. Retrieved from IIe, MD 20850 https://www.gao.gov/assets/gao-21-593.pdf.

T: 240.428.3650 | F: 240.404.6797 info@nutrition.org | www.nutrition.org | www.nutrition.org

Research on Intake and Health Outcomes, Particularly for High-Risk Subpopulations

Our ability to measure what people consume accurately is essential to all nutrition research and is an area of active study. (See below under c. Tools, Methods, and Other Resources Needed for more about dietary assessment needs.) Research on assessing diet exposure, nutritional status, and impact on health should be considered from a lifespan perspective. The data for younger and older populations and for females are especially inadequate and are crucial evidence gaps in nutrition research.

Foundational and Translational Nutrition Research, Including on Dietary Bioactive Components and Botanicals

More foundational and translational research is needed for all nutrients, including bioactive food components. We still lack fundamental knowledge of nutrition, such as understanding the basic nutrient requirements necessary for various populations to achieve optimal health and understanding how nutrients and bioactives interact and improve human health. Research is needed to identify new and refine existing biomarkers for metabolic and other diet-related disease outcomes. This includes increased understanding of how to add precision to nutrient and bioactive recommendations based on individuals' requirements, responses, and genetic/racial/ethnic backgrounds.

Nutrient Requirement Research

The Dietary Reference Intake (DRI) values, including the Recommended Dietary Allowance (RDA), for several essential vitamins, minerals, and fatty acids, as well as fiber, are either outdated or lacking altogether. The absence of established RDAs is primarily due to insufficient evidence to define optimal intake levels for various populations, a consequence of no federal funding for nutrient requirement research and no federal agency lead for these efforts. We also need more research to estimate Chronic Disease Risk Reduction (CDRR) values where relationships between nutrients and diet-related chronic diseases, such as cardiovascular disease and type 2 diabetes, are established. This will require better and larger prospective cohort studies and randomized controlled trials (RCT).

Food Production and Processing for Increased Nutritional Quality

Agriculture is inextricably linked to food and nutrition and must therefore be an integral part of nutrition research. Research is needed to increase the nutrient density of food crop commodities to positively impact human health and incentives should be provided to increase production of fruits, vegetables, and other specialty food crops. Knowledge gaps persist regarding food production, ranging from innovative farming techniques to advanced processing, efficient packaging, and reliable transportation, which can collectively contribute to the optimization of nutritional content. Furthermore, evidence gaps in nutrition security, its origins, environmental impacts, and how to mitigate its effect on health center on understanding how to create resilient food systems that guarantee access to nutritious foods for all segments of the population, regardless of socioeconomic and other circumstances.

b. Steps PCAST Should Recommend to Fill Evidence Gaps

A federal commitment to support nutrition research, including establishment of nutrient requirements, is vital, as nutrition research dramatically improves the quality of life for Americans while reducing healthcare costs. A coordinated national nutrition science strategy that aims to improve nutrition research coordination, collaboration, and data sharing across all federal agencies will improve nutrition policies and programs. Expanding our investment in federal nutrition research will foster research efficiency, maximize impact, and increase return on investment, while promoting equity, nutrition security, and health.

Improve Coordination of Federal Nutrition Research

PCAST should recommend steps to improve coordination and integration of federal research on food and nutrition. Given nutrition's inherently interdisciplinary nature, an ongoing, strong coordinating mechanism across all government agencies is essential, as recommended by the 2021 US Government Accountability Office (GAO) report¹, Chronic Health Conditions: Federal Strategy Needed to Coordinate Diet-Related Efforts, in order to achieve the many promising opportunities in nutrition. The GAO report noted that nutrition currently crosses 21 federal agencies and 200 disjointed efforts. The work of the trans-federal government Interagency Committee on Human Nutrition Research (ICHNR) is critical to achieve this goal but must be further amplified to allow for increased harmonization of and more effective nutrition research initiatives across agencies and cabinet level departments. Currently the ICHNR is composed of knowledgeable experts in positions of responsibility. However, it is structured as a volunteer group with no infrastructure. The ICHNR should be given the staff, authority, and budget needed to align all federal agencies to focus on nutrition research support and coordination across the federal government. Specifically, increased resources and investment are needed for the NIH Office of Nutrition Research and to establish a similar office with a coordinating role for USDA nutrition research.

Catalyze Nutrition Research Public-Private Partnerships

The US government should determine incentives to catalyze public-private partnerships for nutrition research, including private sector and philanthropic research funding, that stimulates high-integrity, transparent, and unbiased research to address the nation's priorities related to hunger, nutrition, and health. In addition, a nutrition science-specific advisory council that would engage stakeholders outside of the federal government, including state, local, and tribal governments, as well as experts from academia and the private sector, would be extremely beneficial to obtain the greatest return from federal investment in nutrition research.

Request a Study Outlining Nutrition Research Needs

Following 50+ years of nutrition research, the field of nutrition remains in a weakened position to advise Americans about the food they should eat to improve health and longevity. A study to establish priority research needs and opportunities in nutrition would guide current and future federal approaches across all federal agencies, similar to the ASN Nutrition Research Priorities that were established in the 2013 publication, "<u>Nutrition research to affect food and a healthy life span</u>²," which has been cited by more than 75 publications.

² Ohlhorst S, Russell R, Bier D, Klurfeld DM, Li Z, Mein JR, Milner J, Ross AC, Stover P, Konopka E. 2013. Nutrition research to affect food and a healthy life span. *Am J Clin Nutr*. 98(2):620-5. doi: 10.3945/jn.113.180638

Increase the Nutrition Research Workforce

PCAST should also recommend steps to propel efforts to recruit cutting-edge nutrition scientists to the federal agencies and to other institutions and to train the next generation of nutrition scientists and practitioners to usher in new initiatives that will enhance nutrition with profound effects for the health of all Americans.

c. Tools, Methods, and Other Resources Needed

Innovative research tools are needed for the federal agencies responsible for nutrition research and for nutrition researchers at institutions everywhere. A 2020 ASN white paper, "Valuing the Diversity of Research Methods to Advance Nutrition Science³," highlights the wide breadth of methods used in nutrition science and how each confer value. The paper also touches on the key considerations and limitations of various methods, as well as needs in nutrition research method evolution.

Improved Dietary Intake Assessment Methods

Current dietary assessment methods need to be improved and validated using biomarker studies in humans. Our limited ability to objectively measure dietary intake and the ability to correct measurement biases in diet and disease association studies using related intake biomarkers hinders progress. For example, studies using doubly labeled water for short-term energy assessment show energy underestimation by about 30-40% among individuals with overweight and obesity, though much less among persons who are not overweight or obese. Systematic biases of this magnitude, if uncorrected, can play havoc with energy intake and disease association analyses. Few nutrients or diet components or dietary patterns have objective methods available for determining intake. Metabolomic signatures, big data, and artificial intelligence may help to identify novel biomarkers of exposure and of disease processes that can propel nutrition research into the future.

Updated Food and Dietary Supplement Composition Databases

Particularly with the current emphasis on moving toward personalized (individual) and precision (subgroup) nutrition, it is essential to know what people are eating and the range of variability for nutrients in common foods. Foundational tools to help nutrition researchers do this include the US Department of Agriculture (USDA)'s food composition databases, such as FoodData Central. However, many food composition database entries do not reflect the realities of the current food supply nor the realities of our increasingly diverse nation, which may negatively impact research, programs, and policies based on this information. Many of the foods within these databases have not been updated for years. Plant and animal breeder practices, as well as industry reformulations, have changed both the macro- and micronutrient contents of many commonly consumed foods. In addition, about half the fruits and vegetables eaten in the US are imported from various other countries, with different soil nutrients, fertilization patterns, and climate conditions, resulting in variable nutrient content for these foods. Similar changes have occurred

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³ Mattes RM, Rowe SB, Ohlhorst SD, Brown AW, Hoffman DJ, Liska DJ, Feskens EJM, Dhillon J, Tucker KL, Epstein LH, Neufeld LM, Kelley M, Fukagawa NK, Sunde RA, Zeisel SH, Basile AJ, Borth LE, Jackson E. 2022. Valuing the Diversity of Research Methods to Advance Nutrition Science. *Adv Nutr.* 13(4):1324-1393. https://doi.org/10.1093/advances/nmac043.

in animal-sourced foods with breeding and feed alterations leading to markedly different nutrient content patterns. Food databases also need to be updated for cultural appropriateness to reflect the common foods and beverages of racially and ethnically diverse populations and immigrant communities in the US to improve the accuracy of nutrient and food intake and dietary exposure estimates among these subgroups.

Reinvigorated Nutrition Surveillance and Data Monitoring

Increased federal investment in health and nutrition surveillance and data monitoring are also crucial. Nutrition monitoring findings are essential for multiple government agencies, as well as the public and private sector, to track what Americans are eating, inform nutrition and dietary guidance policy, evaluate the effectiveness and efficiency of nutrition assistance programs, and study nutrition-related disease outcomes. Nutrition and health data, largely collected through the National Health and Nutrition Examination Survey (NHANES) and What We Eat in America, are essential for tracking the nutrition, health, and well-being of the American population, and are especially important for observing nutritional and health trends in our nation's children and persons 65 and older. The 2023 ASN paper, "Critical Data at the Crossroads: National Health and Nutrition Examination Survey Faces Growing Challenges⁴," provides a comprehensive review of challenges and opportunities for the future of NHANES.

Cutting-Edge Technology and Systems Approaches

Nutrition research should take advantage of the latest technologies and systems approaches to tackle pressing research questions for topics ranging from obesity to food and nutrition security. Metabolomic signatures, big data, and artificial intelligence may help to identify novel biomarkers of exposure and of disease processes. Combining systems approaches with analytical approaches will enable our ability to understand the interactions and pathways (e.g., biological, behavioral, social, and environmental) involved in the complex interactions of diet and health, diet and weight, weight and chronic disease occurrence, and behavior and diet, among others. Systems methods can elucidate the dynamic behavior of systems and help generate hypotheses to explain why systems act in certain ways. For example, systems approaches were advocated to be applied to development of the *Dietary Guidelines for Americans (DGAs)*⁵.

Changes to Glean More Information from Federal Nutrition Research

Suggested changes to the federal government grant process may help improve the field of nutrition research. For example, clinical intervention proposals should include planned retrospective analyses to explain potential differences in response, which can inform precision nutrition. This should be required in the initial proposal, rather than as an add-on after the end of the study, to ensure scientific rigor and integrity. This will in turn improve the design of future research studies. Required reporting of baseline study characteristics should be outlined for specific nutrition research study designs. For example, studies examining energy balance (whether positive, negative, or neutral) need to consider activity level and diet intake since both can impact the findings. Other examples that can influence intake-outcome relationships include

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⁴ Taylor CL, Madans JH, Chapman NN, Woteki CE, Briefel RR, Dwyer JT, Merkel JM, Rothwell CJ, Klurfeld DM, Seres DS, Coates PM. 2023. Critical data at the crossroads: the National Health and Nutrition Examination Survey faces growing challenges. *Am J Clin Nutr* 117, 5, 847-858, https://doi.org/10.1016/j.ajcnut.2023.03.007.

⁵ National Academies of Sciences, Engineering, and Medicine. 2017. *Redesigning the Process for Establishing the Dietary Guidelines for Americans*. Washington, DC: The National Academies Press. https://doi.org/10.17226/24883

age, sex, gender, disease status, and baseline nutritional status.⁶ Like age or gender, nutrition status should be considered a biological variable as there are many interacting factors affecting and affected by nutritional status.

d. Barriers to Research

Lack of Coordination of Federal Nutrition Research

(See *Improve Coordination of Federal Nutrition Research* above.) At present there is no single source or repository across departments that contains up-to-date information on the nutrition research being funded with federal dollars, making it difficult to avoid duplication or to fill crucial gaps.

Workforce Challenges

Increasing the workforce and the diversity of workforce trained in nutrition research is of utmost importance to progress the field of nutrition research. Both the number and diversity of talent within nutrition research must increase to support the field. Currently, a very small pool of undergraduate students apply for graduate level nutrition training. Graduate school for 4+ years, typically followed by a postdoctoral fellowship must be made appealing to potential students, especially financially, to retain the students needed to build the nutrition research workforce. In ASN's response to an NIH Request for Information regarding re-envisioning postdoctoral research training and career progression in the biomedical research field, ASN highlighted the importance of postdoctoral positions for nutrition research and recommended increasing postdoctoral salaries, especially for starting postdoctoral researchers, and implementing a regional cost-of-living adjustment. The need to address student loan repayment is also emphasized to encourage nutrition students to pursue graduate school and postdoctoral positions.

Infrastructure Challenges

Nutrition research to fill crucial evidence gaps requires infrastructure that is not currently present in many academic nutrition programs. Infrastructure for food and nutrition research and laboratory classroom teaching is lacking at many institutions due to decades of inadequate funding needed to update facilities. Examples include teaching laboratories for nutrition and dietary assessment, whole room calorimeters, and biometric laboratories for assessing anthropometry. A Gordian report found that more than 69% of research facilities at land-grant university colleges of agriculture, a home for some nutrition programs, are at the end of their usefulness⁶. Researchers are often expected to perform 21st century science in facilities constructed in the 1950s and '60s⁷. This is also true at Historically Black Colleges and Universities (HBCUs) and Hispanic-Serving Institutions, contributing to declines in the diversity of the field of nutrition.

Need for Comprehensive Mentoring

⁶ Perspective: Nutritional Status as a Biological Variable (NABV): Integrating Nutrition Science into Basic and Clinical Research and Care. Adv Nutr. 2021; 12(5): 1599–1609. doi: 10.1093/advances/nmab046

⁷ Reeves P, Mason S, Sanders L. 2021. A National Study of Capital Infrastructure at Colleges and Schools of Agriculture. Retrieved from: https://www.aplu.org/wp-content/uploads/a-national-study-of-capital-infrastructure-at-colleges-and-schools-of-agriculture-an-update-1.pdf

It is important to acknowledge that comprehensive mentoring during training, as well as continued mentoring beyond the graduate and postdoctoral years, plays a pivotal role in advancing research efforts. Mentoring that encompasses a holistic approach to understanding basic, interventional, and community-based research, as well as health outcomes, is imperative. A multifaceted mentoring approach enables researchers to develop a well-rounded understanding of the intricate nuances of the field. It enhances an individual's ability to conduct rigorous and impactful research and equips them with the necessary skills to translate research findings into meaningful interventions and policies that address real-world challenges. Mentoring is particularly important for those underrepresented in the field and necessary for enhancing the pipeline of diverse, well-trained nutrition professionals and researchers.

Need for Cross-Disciplinary Training

The significance of integrated training in nutrition cannot be overstated. While specialized training in nutrition is critical, it should be complemented by in-depth training in biology, physiology, immunology, endocrinology, psychology, biostatistics, etc., as determined by the research questions of interest. Nutrition research is inherently multidisciplinary, and researchers must possess a comprehensive grasp of various aspects ranging from molecular mechanisms to population-level health outcomes. By offering integrated training that spans the diverse dimensions of nutrition, researchers are better equipped to tackle complex issues and drive innovative solutions that cater to the diverse needs of individuals, communities, and societies at large and provide the greatest return from federal investment.

e. Models to Fill Evidence Gaps in Nutrition Research

Medicine is a field that integrates knowledge of multiple systems and may be closest to the diversity that nutrition incorporates but has not always proven to be a good model for nutrition research since food/nutrition and drugs are more different than alike. Implementing standards for rigor in nutrition research for diet composition, well controlled diets, power calculations, inclusion and diversity of subjects, researchers, etc., would benefit the research reputation of nutrition. Many fields have specific criteria for data management, repositories, inclusion and exclusion criteria, genomic data criteria, data reporting, and so on. Research rigor is essential to provide high quality and reliable contributions to the knowledge base, which forms the bedrock for the development of nutrition policy and guidance. Nutrition research has often suffered from the lack of rigor demanded in other fields, the lack of bona fide validated, reliable, and accurate tools and study designs, and should be improved to build more confidence in scientific knowledge that informs public health dietary guidance. As such, ASN has implemented best practice recommendations to ensure better trust in ASN and in nutrition science.

2. Introducing Research-based Interventions into Federal Programs

It is important that federal food and nutrition policies, regulations, and programs be aligned with the DGAs and other nutrition standards such as the DRIs to ensure science-based nutrition guidance that will lead to improved health. However, while the DGAs are reviewed on a mandated cyclical basis, there is no dedicated funding for establishing the DGAs. It is imperative to secure funding to support the implementation and coordination of forthcoming DGAs among federal agencies and to ensure the research gaps and opportunities from previous Dietary

Guidelines Advisory Committee Scientific Reports are addressed. Importantly, dedicated research funds for a comprehensive, multi-armed, multi-site RCT (like the original Dietary Approaches to Stop Hypertension [DASH] study) to assess the impact of the *DGAs* on health outcomes should be considered.

While some food as/is medicine provisions are already being introduced into federal programs, a systematic approach for establishing evidence-based and scalable interventions is required. Evidence-based guidelines should be informed by the totality of the evidence, including consideration of strengths, weaknesses, and knowledge gaps, through the systematic identification and critical appraisal of the evidence. Integration of nutrition experts, healthcare providers, educators, and policymakers will ensure robust engagement of the target public. Targeted community programs should be implemented, when applicable, preferably that offer incentives to bolster healthier lifestyles. Robust evaluation mechanisms must be established to assess effectiveness of programs with flexibility to then refine programs. Through harmonious multi-disciplinary collaboration among stakeholders, a comprehensive and impactful strategy can aid in diet-related chronic disease prevention.

3. Equitable Access to Federal Nutrition Research Investment Benefits

Diet-related chronic diseases are a leading cause of death in the US and research has shown that low-income and other under-served populations, including communities of color and tribal communities, are disproportionately affected by diet-related chronic diseases. One of the nutrition-related challenges faced by low-income and other under-served populations that has far-reaching consequences, including increased incidence of diet-related chronic diseases, is food and nutrition insecurity.

Improve Nutrition Education for Medical and Health Care Professionals

Inherent in any effort is the need to be mindful of nutrition equity and equitable translation of nutrition science to practice. As such, it is important to have a nationally coordinated, sustained approach for nutrition education for medical and health professional students including dentists, nurses, advanced care providers, physical and occupational therapists, and other care providers. The field of medicine requires the integration of knowledge from multiple systems, but medical school graduates receive little or no training in nutrition. Dietary recommendations and counseling must be an integral part of diet-related disease management.

Diversify Nutrition Research Workforce and Institutions

In addition, there must be federal efforts to recruit and nurture wide representation to the field of nutrition research so that the next generation of nutrition researchers more closely resembles the US population, and the research topics and solutions are more equitable and diverse. Ensuring diversity, equity, and inclusion at all levels of the nutrition research continuum, from trainees, researchers, workforce, subjects in specific research projects, and the population served by research translation, should be a priority. ASN supports efforts to establish or expand policies and programs that increase representation in nutrition research, such as the NIH Institutional Research and Academic Career Development Awards (IRACDA) program and USDA's NextGen. Awareness and education about available nutrition research funding, tools, resources, and more should be equitably accessible for all research institutions and researchers. Grant

programs should have a goal to promote research that provides important evidence on how to increase accessibility to healthy diets for all populations. Distribution of awards to minority-serving institutions is imperative, as well as awards for programs engaging in collaborative partnerships and community-based participatory research.

4. Conclusion

The American Society for Nutrition appreciates PCAST's efforts to identify scientific opportunities and priorities to advance nutrition science and we thank you for the opportunity to provide input to inform PCAST's recommendations to the President. ASN welcomes the opportunity to serve as a resource to PCAST as you move forward with the evaluation of nutrition science. The ASN membership has a wealth of expertise in nutrition science across the entire research spectrum from basic science to health policy, from discovery to application. As referenced throughout this response, ASN publishes many documents to inform and advance the field of nutrition research and we would be pleased to help spread the word of PCAST's recommendations. In closing, we reiterate the recommendations put forward above under b. Steps PCAST Should Recommend to Fill Evidence Gaps for your consideration and action. Please contact Sarah Ohlhorst, MS, RD, ASN's Chief Science Policy Officer [240-428-3647; sohlhorst@nutrition.org], should you have any questions or if ASN may provide additional information.