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Perspectives

Maximizing the Value of Preclinical and Translational Animal Research Models via Next-Generation Standardized Reference Diets: a White Paper from the Laboratory Animal Nutrition Taskforce for an Education and Research Network☆

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A B S T R A C T

A new generation of standard reference diets (SRDs) is essential to enhance the integrity of research associated with the use of laboratory animal models in the study of human disease. Support for the value of this fundamental facet of experimental methodology is provided via a historical overview, an assessment of current status, and the advancements and opportunities that will be realized through further development and routine use. An outline of the extensive investment in animal nutrition research by National Institutes of Health during the past 30 y is presented with specific reference to rodent animal models and standardization in dietary methodology. Timely recommendations for renewed action that revitalize and expand the use of SRDs in rodents and other models, such as zebrafish, are provided with the aim of achieving more rigor, transparency, replicability, interpretability, and integrity in preclinical and translational animal model-

Abbreviations: AIN, American Institute of Nutrition; LANTERN, Lab Animal Nutrition Taskforce for an Education and Research Network; LANP, Lab Animal Nutrition Program; SRD, standard reference diet.

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based research. Ultimately, the benefits of these efforts will be fulfilled through expeditious development of prophylactic and therapeutic approaches for human diseases.

Keywords: rodent, zebrafsih, feed, diet, standard reference diet, ingredient, reproducibility, standardization, rigor, replicability

Objectives and Recommendations

The Laboratory Animal Nutrition Taskforce for an Education and Research Network was formed to provide constructive and implementable recommendations for updating and enhancing standard reference diets (SRDs) for multiple laboratory animal models (Text Box 1). Such enhancements are intended to increase the rigor, statistical power, transparency, replicability, interpretability, and integrity of laboratory animal research.

Widespread expertise to formulate nutrient-specific diets is lacking. This lack of expertise has further limited our ability to prioritize nutrition as a variable in experimental designs and to provide sufficient training for next-generation nutrition scientists. Adopting these recommendations can attenuate this limitation and, thereby, facilitate an increase in the rigor and replicability of nutrition research.

This perspective represents a collective opinion of a major challenge facing health research and describes an approach that will resolutely address the importance and need of the scientific community to improve laboratory animal nutrition and diets. In this paper, we will provide a brief historical summary of the combined importance of lab animal models, the importance of understanding nutrition in lab animal models, and the importance of formulating appropriate diets. We will then discuss the current status of SRDs and emphasize the advances and opportunities that they represent. We describe how these diets can rectify and accelerate preclinical and translational research, leading to positive clinical outcomes associated with nutrition and chronic human disease. We discuss the historical investment of NIH in related research, and finally describe a pathway forward.

Text Box 1
Recommendations of the Lab Animal Nutrition Taskforce for an Education and Research Network[1]

- Assemble impactful leadership founded in associations that emphasize the role of diet and nutrition, such as the *American Society for Nutrition* and related entities, to lead an effort that will promote and enhance the quality of scientific investigations that focus on nutrition in animal models of human disease.
- Establish a resource center or consortium program (suggested example; Lab Animal Nutrition Program [LANP]) with unique identity and goals to provide guidance, recognition, and development of open formulation standard reference diets for recognized animal models used in research communities.
- Collaborate with federal partners including NIH, USDA, Food and Drug Administration (FDA), and the National Academies. These partners recognize the value of this proposed investment and, in partnership with the LANP, ultimately become the centralized curator of new discoveries and sanctioning organization for dietary and nutritional research standards.
- Engage related centers or societies, commercial vendors of ingredients and diets, journals, appropriate regulatory and government agencies, foundations, and industry partners in health- and food-related fields to consolidate shareholders and ensure long-term partnerships.

[1] The Lab Animal Nutrition Taskforce for an Education and Research Network (LANTERN) is a coalition of scientific researchers and innovative opinion leaders with a unifying vision for transformative nutrition research. The LANTERN is described in Text Box 4.

The Challenge Is Clear

All animal models in biomedical research, whether rodents or other species, including fish, represent important tools for understanding factors that impact human health and disease [1]. Defining dietary requirements of rodent models and establishing SRDs have been critical in supporting biomedical research using animal models. Most research studies investigating the dietary requirements of rodents were published in the last half of the 20th century [2]. This essential undertaking enriched our scientific approach in basic and translational research. Although revolutionary at the time, the aspiration for rigor in nutritional research has waned over the last few decades. This is unfortunate, as modern research technologies have high potential to advance our understanding of the role of diet and nutrition in human health and disease. In this report, we provide a brief historical perspective of the development of dietary guidelines and SRDs for animal models and describe the limitations of our current knowledge. Accordingly, we propose a strategy that can successfully initiate a renaissance in understanding the integral role of experimental rigor and replicability (Text Box 2) in the link between diet, nutrition, and health. We believe the important tenets of precision nutrition (predicting individual responses to food and dietary patterns; NIH Nutrition for Precision Health) [3] can be developed in animal models and will contribute significantly to future advancements in human health. Finally, we recognize the ethical and moral challenges in nutrition research and are aware of the fiscal conflict we may encounter in an environment where global markets for lab animal diets approach $5 billion annually [4].

Text Box 2
Definition of "replication"

We use the National Academies' definition of "replication," which is: "replicability is obtaining consistent results across studies aimed at answering the same scientific question, each of which has obtained its own data."

A History of Success Can Support a Future of Commitment

Animal models have been an essential foundational and ongoing resource in scientific and medical research for centuries. Animal models provide a level of experimental control, rigor, and replicability that are difficult to attain in human clinical trials or in vitro studies. Within recent decades, the recognition of the importance of animal welfare as part of high-quality research has also increased and has led to an emphasis on proper husbandry to ensure optimal animal health. For these animal models to be effective, an understanding of variables that potentially compromise or otherwise influence research outcomes is necessary. Therefore, we must place an intentional focus on improving the performance of controlled experimental designs and conditions. This approach requires a level of optimization and standardization of basic care in research studies, including the informed selection of natural ingredient, experimental, and SRDs.

Animal nutrition is recognized as a critical variable that can affect experimental outcomes, replicability, and translatability [5]. The importance of dietary composition (providing adequate/sufficient nutrients) as a variable was recognized after the development of the Wistar rat as a research model in 1906. After decades of discovery, testing, and discussion, improvements in the composition of diets and reduction of nutrient variation were promoted through the development of purified diets that primarily met the daily nutrient requirements for rodents and supported basic metrics of growth and reproduction. To this end, the American Institute of Nutrition (AIN; now the *American Society for Nutrition*] encouraged rigorous and replicable research by sponsoring the development of the AIN-76 diet as the first SRD for rodent models, having an open formulation and comprised only of purified ingredients. This diet, initially published in 1977 [6], promoted consistent and replicable outcomes for rodents used in biomedical research. In 1980, this diet was slightly modified to include more vitamin K and an antioxidant to prevent oxidation of dietary oil and renamed AIN-76A. A workshop held in 1989 revealed that improvement of several nutritional and technical aspects of the AIN-76A diet should be made. This was followed by a period that solicited comments from the nutrition community and then testing of an improved formulation, AIN-93, which was released in 1993 (summarized in [2]). The AIN-93 diet was presented in 2 forms: AIN-93G to support growth, pregnancy, and lactation, and AIN-93M to support maintenance of adults. This open dietary formulation consists of purified ingredients in specified amounts and is modifiable to address specific research questions.

For their respective periods of use, AIN-76, AIN-76A, and AIN-93 resulted in significant improvements in standardization in animal breeding, husbandry, and nutrition. Although one can argue that no single diet is perfect, these diet formulations represented a vast improvement over the numerous and unstandardized (often uncontrolled for both ingredients and nutritional content) diets that were historically used in rodent models. The commitment, resolve, and determination of the individuals who participated in this endeavor, as well as the organizations that promoted the completion of these SRDs (AIN and the USDA/Agricultural Research Service (ARS) Grand Forks Human Nutrition Research Center), benefited the international research community. Most importantly, the rationale for developing and using these SRDs, which is discussed in related publications, remains universally relevant and essential to achieving a superior quality of applied science today.

When supported by appropriate dietary controls, the increased application of powerful data assessment technologies, including artificial intelligence (AI) and meta-analysis, will promote timely and improved human patient outcomes. Meta-analysis has become an important tool to leverage information derived from numerous studies to identify trends with increasing power and improved evidence. However, for analyses that seek to find causal relationships between health outcomes and diet derived from studies using experimental animal models, the use of SRDs as controls and as the base for diet modifications is fundamental. Currently, the lack of uniformity in the use of experimental diets introduces uncertainty and variability, which limits the power

TABLE 1
NIH projects and funding related to "diet," "rodent," and "standardized diet"[1] over the last 30 y, including the first and last 5-y period for which complete datasets were available after the publication of the report on AIN-93.

	Total (30 y) 1994–2023	First 5-y period 1994–1998	Last 5-y period 2019–2023
No. of projects associated with diet	115,417	11,470	25,991
Value of the funded projects ($)	40,4787,474,600	2,021,887,309	12,288,242,473
No. of projects associated with diet and rodents	46,632	2678	12,546
Value of project associated with diet and rodents ($)	14,307,608,606	386,634,743	4,753,822,345
No. of projects associated with diets, rodents, and standardized diets	140	3	53
Percent of diet projects associated with rodents[2] (%)	40.4	23.35	48.27
Percent of diet and rodent projects with standardized diets[3] (%)	0.30	0.11	0.42

Data were acquired from the NIH RePORTER as of February 2025.
Abbreviation: AIN, American Institute of Nutrition.
[1] Text searches (using advanced Boolean operands) for terms reported in the title, project terms, or abstracts. Terms for "diet" included diet and nutrition. Search terms for "rodent" included mice or mouse or murine or rat or rodent or Wistar or "Sprague Dawley" or *Rattus* or "*Rattus rattus*" or "*Rattus norvegicus*" or "C57BL/6" or "C57 Black 6." Search terms for "standardized diets" were: "AIN93" or "AIN-93" or "AIN 93" or "AIN93G" or "AIN-93G" or "AIN 93G" or "AIN93g" or "AIN-93g" or "AIN 93g" or "AIN93M" or "AIN-93M" or "AIN 93M" or "AIN93m" or "AIN-93m" or "AIN 93m" or "standard reference diet" or "standard diet" or "reference diet."
[2] Calculated as value of projects associated with ("diet" and "rodent")/("diet") × 100.
[3] Calculated as value of projects associated with ["rodent" and ("diet" and "standardized diet")]/("rodent" and "diet") × 100.

and usefulness of these analyses. In the future, the increased use of next-generation diets in publications using animal models will provide credibility in clinical outcomes and further increase the power of AI and meta-analysis.

The future of improved animal research leading to improved clinical outcomes will be supported by the community's common goal to decrease chronic disease. In addition to our history of federal support (Table 1), the NIH Office of Research Infrastructure Programs recently supported the development of SRDs in zebrafish and other aquatic animal models by sponsoring a workshop at NIH in 2018 [7]. The value of SRDs in several animal models was acknowledged, and suggestions for diet formulation and development are ongoing. Other NIH institutes and centers continue to promote related research activities and will benefit from supporting our overall approach. Soon, their investment could be coupled with the incorporation of government-supervised, industry-funded programs (Checkoff Programs) to collect and administer funds that promote research and education for specific animal research communities associated with the study of human health and disease.

Reflections and Future Guidance, and Recommendations

For almost 50 y, the AIN-76A and AIN-93 SRDs have provided a universal standard, significantly enhancing the utility and value of rodent models for in vivo scientific and biomedical research. However, nutritional science has progressed, and these diet formulations would benefit from reassessment. Recent advisements for nutrient modification include types and amounts of soluble and insoluble fiber, ratios of sucrose to starch, types of energy sources, and sources of n–6 (ω-6) and n–3 (ω-3) fatty acids [8]. We should also recognize that SRDs are dynamic by nature, and nutritional knowledge of dietary requirements will continue to evolve and may require ongoing revision. To put this approach in perspective, the national Dietary Guidelines for Americans are reviewed and updated every 5 y, largely reevaluating the efficacy of the American diet in promoting health. No such review or update for any laboratory animal model diet currently exists.

Nutrition of the rodent model was last reviewed in 1995 (*Nutrient Requirements of Laboratory Animals*, 4th Edition) [9] but has not been revisited for 3 decades, and a plan to do so has not been formalized. Moreover, in recent years, nutrition research has expanded to include other experimental animal models, yet dietary guidelines for many of these animal models have been minimally evaluated. The information presented in this 1995 treatise generally remains valid today, but our knowledge of nutrition has improved significantly. Consequently, it is imperative that SRD formulations be reassessed in rodents and established in other animal models that are being increasingly studied, such as zebrafish [10], leading to contemporary dietary guidelines for all animal models.

Reasons to Develop New Dietary Guidelines for Lab Animals

We can identify ≥3 broad-based advancements that support the need to develop new dietary guidelines for animal models. Since the publication of the formulations of the AIN-93 diets for rodents: *1*) we have made major technological advances in research, including our development and understanding of -omics and computational sciences. Now we can ask and answer more questions related to nutrition and health than at any other time in history. In addition, *2)* the culture, harvest, and processing of agricultural products traditionally used as dietary ingredients have been enhanced by technological advances in agriculture. As a consequence, *3*) new or improved dietary ingredients have been identified and further processed, and offer the ability to enhance content, quality, and availability of specific nutrients while moderating overall costs and accessibility. These new and/or improved ingredient and nutrient sources are now commercially available and of consistent quality. We believe that the use of chemically defined, quality ingredients and nutrients will effectively serve to reduce or eliminate bioactive food components, antinutritional compounds (compounds that interfere with nutrient absorption or utilization), or even toxicants, leading to a defined and replicable health and nutrition status in these models. Suffice it to say, advances in research technologies, ingredient processing, consistency, and availability of affordable products provide critical infrastructure for the production of the next-generation of SRDs.

An array of diets that have been or are currently being used for animal models includes natural ingredient diets (sometimes called chow, cereal, or colony maintenance diets). These diets, generally formulated with agricultural products, will vary in ingredient quality and quantity (based on spatial/geographic locations and seasonal/annual variations in production) and are not appropriate to replace SRDs [11,12]. Therefore, defining the characteristics of an SRD with utmost clarity is desired for each species. These characteristics and benefits are identified in Text Box 3.

Understanding these characteristics and benefits, we strongly support a contemporary evaluation of the SRD for rodents, as well as the development of corresponding diets for other animal models routinely used in human disease research, including zebrafish. This advocacy of the use of SRDs should not be interpreted as the only defensible approach in the study of the nutrition of animal models. Other experimental reference diets, natural ingredient diets (cereal or chow diets), live diets, commodity diets, least-cost diets, or chemically defined diets, among

Text Box 3
Characteristics and benefits of a standard reference diet

- *Diet is open formulation*: the ingredients, their quantities, and sources are known and commercially available.
- *Diet is consistent*: in both formulation and composition of all ingredients.
- *Ingredients are defined*: they must be chemically pure, or purified meaning that they contain defined high levels of purity and nutrient composition.
- *Ingredients of a constant nutrient composition* are maintained.
- Diet is used as a *universal nutritional control* for experiments for each model organism of choice.
- *Diet reduces experimental bias* by avoiding undesired inclusion of nutritional and antinutritional factors.
- *Diet allows temporal and spatial comparisons* among results derived from research investigations.

Text Box 4
Lab Animal Nutrition Taskforce for an Education and Research Network[1] Taskforce

Stephen A. Watts—Professor, Director of the NIH Nutrition and Obesity Research Center (NORC) Lab Animal Nutrition Core at The University of Alabama at Birmingham (UAB); NIH Office of Research Infrastructure Programs Chair of Committee on Defined Reference Diets for Zebrafish and Other Aquatic Biomedical Research Models.
David B. Allison—Endowed Professor of Pediatrics, Chief of Nutrition and Director of Children's Nutrition Research Center, USDA-ARS.
Donald C. Beitz—Charles Curtis Distinguished Professor of Agriculture; Past President American Dairy Science Association; Member, Coordinating Committee of National Animal Nutrition Program.
Sarah L. Booth—Director, USDA/ARS Human Nutrition Research Center on Aging at Tufts University, President 2024–2025, *American Society for Nutrition* (ASN).
Paul M. Coates—Adjunct Professor, Indiana University School of Public Health: Chair, ASN Foundation Board of Trustees; Past President, American Society for Nutrition; Former Director of NIH Office of Dietary Supplements, NIH; former Deputy Director of National Institite of Diabetes and Digestive and Kidney Diseases (NIDDK) Division of Nutrition Research Coordination, NIH.
Louis R. D'Abramo—Member of Committee on Nutrient Requirements of Fish and Shrimp, National Academies. Past-President and Fellow of the World Aquaculture Society.
Teresa A. Davis—Editor-in-Chief, Critical Reviews in Food Science and Nutrition;
Editor in Chief Emerita, *Journal of Nutrition*; Past-President ASN; Past-President American Society of Animal Science; Director of Texas A&M AgriLife Institute for Advancing Health Through Agriculture; Member National Academy of Medicine.
Ryan N. Dilger—Professor of Animal Sciences and Institutional Animal Care and Use Committee (IACUC) Chair, University of Illinois at Urbana-Champaign; Coordinating Committee (member) and Feed Composition Committee (Chair), National Animal Nutrition Program
John W. Erdman Jr.—Member National Academy of Medicine; Mary S. Rose Senior Investigator Award, Chair of NASEM Standing Committee for the Review of the Dietary Reference Intakes Framework and Past-President of ASN.
George C. Fahey, Jr.—Professor Emeritus of Animal Sciences and Nutritional Sciences and Kraft Foods Endowed Professor Emeritus of Human Nutrition, University of Illinois Urbana-Champaign; Member of NRC Subcommittee on Nutrient Requirements of Laboratory Animals; coauthor of *Journal of Nutrition* article on AIN-93 purified diets of laboratory rodents; Fellow of ASN and American Society of Animal Science.
Marta L. Fiorotto—Director, Mouse Metabolic Research Unit, USDA/ARS at the Children's Nutrition Research Center, Department of Pediatrics, Baylor College of Medicine; Deputy Editor *Journal of Nutrition*.
Jesse F. Gregory—Professor Emeritus of Food Science and Human Nutrition, AIN-93 Committee, Associate Editor *Journal of Nutrition*.
James O. Hill—Director of UAB Nutrition and Obesity Center at UAB; past-President of ASN and the Obesity Society; Member of National Academy of Medicine.
David M. Klurfeld—Past National Program Leader for Human Nutrition in ARS; Fellow of the ASN; David Kritchevsky Career Achievement Award from ASN.
Steven D. Leach—Professor of Molecular and Systems Biology, Surgery and Medicine at Dartmouth's Geisel School of Medicine; Preston T. and Virginia R. Kelsey Distinguished Chair in Cancer; Director of the Dartmouth Cancer Center; Fellow of the American Association for the Advancement of Science (AAAS); Member of the National Academy of Medicine.
Phillip S. Miller—Kermit Wagner Distinguished Professor, University of Nebraska at Lincoln; Chair, Coordinating Committee of National Animal Nutrition Program; AFIA Award in Non-Ruminant Nutrition Research, Associate Editor, *Journal of Animal Science*.
Forrest H. Nielsen—Organizer and Chair of the workshop that was the basis for the codevelopment, testing, and implementation of the AIN-93G and AIN-93M reference rodent diets; Past Director of the USDA-ARS Grand Forks Human Nutrition Research Center; Distinguished Fellow of the ASN.
Kevin L. Schalinske—Morrill Professor, Iowa State Food Science and Human Nutrition, Past-President, ASN.
Daniel Smith, Jr.—Director, Animal Models, NIH NORC Core and Small Animal Phenotyping Subcore, UAB. Leader, Comparative Organismal Energetics Control, UAB Nathan Shock Center.
Zoltan M. Varga—Director, Zebrafish International Resource Center, University of Oregon.

[1] The Lab Animal Nutrition Taskforce for an Education and Research Network is a coalition of scientific researchers and innovative opinion leaders with a unifying vision for transformative nutrition research. Convened at the Experimental Biology Conference in San Diego on 5 April, 2016, and at the ASN annual meeting in Orlando on 31 May, 2025, they are committed to supporting research integrity in basic and translational sciences by inculcating rigor, replicability, reproducibility, and transparency in the development of next-generation dietary standards for lab animal models of human disease.

others, have appropriate applicability in relation to the research question of interest. For example, most research institutions use a natural ingredient colony maintenance diet for their rodent populations. These diets are effective in maintaining good growth and reproductive profiles of rodents held as breeding stock and are comparatively inexpensive. However, these diets are largely composed of unrefined ingredients and are not characterized by consistent quality and content [4,12]. These diets can also contain undesired bioactive food components or antinutritional factors. Most of these are closed formulations. Consequently, they are not appropriate for experiments designed to evaluate nutrients or non-nutrient-related pharmaceuticals, nutraceuticals, or toxicants. In fact, the use of colony maintenance diets could be suspect if used as controls in any animal experiment relating to human health where nutrition is presumed to be a factor contributing to variation in the study outcomes. Instead, to maintain replicability and rigor, as well as reproducibility across institutions, SRDs should be used as an integral component of any experiment in which the outcomes can be influenced by diet and/or other unknown bioactive food components eliciting a metabolic or physiologic response.

The Current Status Defines Future Needs

Standards in all aspects of animal husbandry, including those standards for diets, decrease variability in research outcomes. Use of standards in research projects using animal models will definitely improve rigor and replicability and lead to comparable results among and within laboratories. Historically, the scientific community recognized the obvious importance of diet

and nutrition, and we continue to invest significantly in research projects that involve diet and nutrition (Table 1). With this acknowledged investment, the research community can take advantage of using the latest modernized technologies to ask new and vital questions related to human health and disease. Hopefully, investigators will continue to recognize the value of dietary standardization and the need for control of this important variable in their experimental designs. Regrettably, it was noted in a recent conversation with Dr. Teresa Davis (editor-in-chief emerita, *Journal of Nutrition*) that "the majority of manuscripts submitted to the journal for publication have inadequate or inappropriate nutritional experimental design and diets." Therefore, it is prudent that we facilitate an awareness of the importance of diet and nutrition in preclinical and translational research that uses animal models. Simply put, a lack of understanding of nutrition and the continued use of unsuitable research diets in many animal models will compromise our ability to translate knowledge gained from the study of animal models concerning the onset, progression, and management of disease to humans, regardless of the time and financial investment.

Let us summarize the challenges and opportunities in nutrition research. For >100 y, the use of rodents as preclinical and translational animal models has been of great value in the progress of biomedical research. The development and integration of the AIN-76A and AIN-93G/M SRDs to support this animal model was a transformative event. Unfortunately, despite their extraordinary utility, those diets are not perfect, and we recognize that changes in the current formulation may be desirable. Furthermore, the number of scientists who are aware of the utility and value of an SRD is apparently lacking. Even more surprising is the lack of dietary standards for other animal models. At this time, except for rodents, no other animal model has a commercially available, open formulation SRD. In many studies, it would appear that nutrition as a variable is unrecognized. The authors of this report are resolute in agreement that unifying guidelines to develop dietary standards for a number of animal models are needed. The working group duly acknowledges the need to revisit and redefine the guidelines associated with the development and use of SRDs. Not only should guidelines be redefined, but they should also provide for documentation in research proposals to be funded by federal grants and ultimately in journals that publish this research.

What is needed to move this initiative forward? The initiative requires the continued investment of time and engagement of thoughtful discussions, the initial ideas of which should be peer reviewed and published. It requires a willingness of the scientific community to acknowledge and improve the science of nutrition in basic and translational animal research. In addition, an investment of funds and the willingness of funding sources to recognize and acknowledge the importance of nutritional standardization are essential.

We proposed the recommendations listed above to reaffirm diets and nutrition as critical variables that affect experimental outcomes and replicability in all animal models. These recommendations provide a foundation for our need to accept the ethical and fiscal responsibilities associated with quality animal research and promote its value as we seek to understand, prevent, and treat human disease. A proposed entity, such as the LANP, can be empowered with this responsibility and, in addition, uniquely assume the establishment and promotion of training modules for graduate students, early career investigators in nutrition, and established scientists who seek to incorporate nutritional variables in their research. This training is essential for those individuals who review manuscripts and grant proposals, and for those who will train future students.

The Economics of Investment in Nutrition Research

Basic information on investments in diet and nutrition research is tractable (Table 1). We used the NIH Report database and searched with the RePORTER (Research Portfolio Online Reporting Tools) tool using advanced Boolean operands (https://report.nih.gov/). As part of our search, we evaluated datasets related to funded projects and funding for: *1*) the 5-y fiscal period after publication of the report on AIN-93 (1994–1998); *2*) the latest 5-y fiscal period available (2019–2023); and *3*) the encompassed years 1994 to 2023, a 30-y period.

Over the last 30 y, 115,417 projects identified by inclusion of the terms *diet* or *nutrition* were funded at an average of $350,706 per project. Of these projects, ~40% also contained reference to the use of rodents (Table 1 for search terms). Although many diet/nutrition projects were associated with the use of rodent animal models, <1% contained reference to dietary standardization in either the title, project terms, or abstract. We must acknowledge that these low levels of reporting may also reflect an author's emphasis on concepts other than dietary standardization.

From 2019 through 2023, the number of diet/nutrition projects more than doubled the number of those funded from 1994 through 1998, indicating that investment in diet/nutrition research has increased over the last few decades. An additional comparison of these 2 periods also reveals a disproportionately large increase in projects containing reference to rodents from 2019 through 2023, further suggesting an increasingly important role of animal models in diet/nutrition research. When funded projects are adjusted for inflation, the funding agencies still approved 2.6 times more spending in the latter period relative to the former.

Substantial investment in diet and nutrition research has occurred over time, and the use of animal models has reached an all-time high. Despite this investment in both preclinical and clinical nutrition research, many human diseases recognized to be influenced by diet and nutrition continue to increase in human populations, including obesity, type 2 diabetes, cardiovascular disease, and metabolic syndrome, to name a few. Despite our extent of national investment, outcomes related to human disease are often variable and disparate among studies. We believe the lack of nutritional rigor involving appropriate dietary controls and experimental design leads to a lack of replicability and confusion, limiting our ability to understand and ultimately affect measures to reduce the risk of human diseases. Although progress is noteworthy, we strongly advocate a continued investment in diet and nutrition research and a renewed investment in nutritional education and practitioner training.

Seize the Challenge and Identify a Path to Move Forward

Government and industry funding remains an important source of support for the study of diet and nutrition in humans and their surrogate animal models. Progress in our understanding of diet and nutrition as it relates to our understanding of prevention, onset, progression, and therapeutic modalities of human disease will continue, but are we optimizing our efforts and financial investments to provide a timely solution to these health challenges? Reductions in investment or changes in governmental fiscal policies may negatively impact our ability to continue research efforts that yield timely and significant progress. Thus, we must accordingly increase the rigor of our animal experiments by reducing known nutritional variables for studies where animal models are essential. Intentional experimental design, appropriate diets, and accurate reporting will be relevant for enhancing the robustness of all animal models. We believe the use of next-generation SRDs and other appropriate experimental or reference diets will be the best option for future experimental approaches. The nutritional environment for all animal models must be held to the highest standards possible.

To support these goals and to maintain appropriate leadership and standards of excellence in health research, we propose a national program, such as a LANP, to establish guidelines for progress and to:

1) Identify high-priority issues in lab animal nutrition.
2) Develop a sanctioning process by which diets, ingredients, and nutrients can be characterized and recorded.
3) Facilitate high-priority research to develop SRDs and related study diets.
4) Provide guidance in diet development for all animal models used in human health and disease research in collaboration with commercial vendors, science communities, professional societies, and federal partners.
5) Identify, collect, assemble, collate, and share science-based information related to diet and nutrition.
6) Provide appropriate training modules to educate research scientists embarking on nutrition research.
7) Serve as a resource to federal funding agencies and scientific journals to ensure the best laboratory practices and reporting.

If the program is initiated through the previously stated points of action, many benefits to the science and layperson communities will be realized. An effective program will:

1) Promote the enhancement of lab animal performance and welfare.
2) Enhance experimental rigor, replicability, reproducibility, interpretability, and transparency of experimental outcomes.
3) Increase the rate of scientific progress in understanding nutrition and human disease.
4) Stimulate accurate and timely translation to human health.
5) Reduce the long-term cost of research.
6) Reduce the human cost of disease and improve the quality of life.

Within the above approach, key phrases include time and cost. Scientific progress that increases our overall knowledge is important; however, producing outcomes that lead to a reduction in the time and effort required to reduce human disease will also reduce the overall costs currently associated with variable and disparate research, which itself is often the result of poor nutritional design. Furthermore, we cannot ignore the human cost of disease, both in terms of lost productivity and quality of life. We believe time and cost can be minimized with the implementation of effective nutritional research strategies that eliminate ill-considered experimental designs and diets. There are prevailing efforts to reduce animal-based research in favor of human-based research with the use of new approach methodologies. Whereas it would not be prudent to eliminate all animal research at this time, our recommended approach would increase the performance efficiency of future animal research. This would be accomplished by integrating experimental designs with appropriate diets, thus improving the value of the outcomes for mitigating the onset and improving the treatments for human diseases. The adoption of the aforementioned approaches will also minimize the number of animals used in research. With a focus on this approach, everyone benefits.

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Author contributions

SAW: had primary responsibility for the final content of the manuscript; and all authors: read and approved the manuscript, with many providing textual comments and suggestions.

Conflict of interest

The authors report no conflicts of interest.

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Declaration of generative AI in scientific writing

No AI was used in the preparation of the text, nor was it used to generate or interpret content in the manuscript.

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