

# Request for Information: Improving our understanding of the role of diet and other factors in the Developmental Origins of Health and Disease (DOHaD)

**Notice Number:**

NOT-OD-22-157

## Key Dates

**Release Date:** July 7, 2022

**Response Date:** August 15, 2022

## Related Announcements

None

## Issued by

Office of Nutrition Research ([ONR](#))

## Purpose

NIH is planning a research project on the role of diet, food environment and related exposures on the developmental origins of health and diseases (DOHaD). This research is a priority, in part, because the United States is experiencing an unprecedented rise in diet-related diseases, particularly obesity and diabetes. In the last 30 years, obesity rates have doubled in adults, tripled in children, and quadrupled in adolescents. There is abundant evidence that the main risk factors for these diseases are set during early development. In addition, preferences for healthy and unhealthy food are similarly being formed or imprinted during fetal development and early life stages. The evidence for this has led to the DOHaD hypothesis, which posits that parental diet, life events/traumas/stress, medications, health and nutritional status, microbiome ecology, and related environmental exposures during development lead to traditional epigenetic alterations. These factors can combine with macro- or micronutrient malnutrition during critical windows of development and are thought to be responsible for future diet-related disease risk. While the evidence for the DOHaD hypothesis is undeniable, there is a need for the deep profiling of a family's exposome and biology in order to test complex, dynamic and multi-measure hypotheses. Research in this area could illuminate how family nutrition status and feeding practices periconceptionally, during pregnancy, and in early life affect growth and development and eating behaviors and patterns, along with future diet-related disease susceptibility. Objectives that begin to address these questions are found in the [2020-2030 NIH Strategic Plan for Nutrition Research](#) (pp 15-17) and the strategic plans of other NIH Institutes, Centers, and Offices.

The above-described research could provide a platform to address other trans-NIH strategic research objectives and federal data needs. For example:

- [Dietary requirements and diet-disease relationships during pregnancy and postpartum](#). Federal agencies and offices and others have highlighted the need for more research and data to develop the Dietary Reference Intake (DRI) studies to support the Dietary Guidelines for Americans during pregnancy. Notably, DRI values have expanded beyond traditional values in the last few years to address chronic disease risk reduction (CDDR values). Developing CDDRs would require information about diet and disease risk, during pregnancy and potentially beyond the period that children were being studied post-partum.
- [Human milk composition](#). It is not an exaggeration to acknowledge that very little is known about human milk composition. There is a great deal of interest from a public health perspective about various nutrients and other exposure-related components present in human milk, and how the composition impacts U.S. children. Although human milk is considered ideal for infants and is the food upon which infant formulas are based, strikingly little is known about how it affects healthy development in the first few years of life. Human milk contains many bioactive factors, in addition to nutrients, and varies dramatically between women, depending on maternal age, previous childbirth, genetics, and diet. Composition also changes over time (over the course of a day, weeks, and months, and even during a single breast-feeding session). Other gaps include whether and how other factors (ethnicity and race) or exposures (e.g., life events or traumas, medications, etc.) impact milk composition. These research gaps may have relevance for optimizing infant formulas, as well as for understanding the role of various milk nutrients in health and disease. This initiative could potentially address the biological and dietary basis for the extraordinary interindividual variation in human milk composition and help develop measures to quantify human milk composition of nursing mothers in the U.S. across the course of lactation and investigate which early life measures in the triad (family-child-human milk) are predictive of DOHaD.
- [The influence of diet and nutritional status on developmental outcomes](#). Federal agencies and offices, others, and the Agriculture Act of 2014 have highlighted the need for more research and data to support the Dietary Guidelines for Americans for infants and toddlers from birth to 24 months. It is expected that this study would support some of those needs. The first 2 years of life are a critical period, yet it remains unclear how diet and feeding patterns support optimal physical growth, neurological development, immunity, and health. Unanswered research questions include defining the influence of infant feeding practices, maternal diet, and other behavioral and lifestyle-related exposures on health outcomes, susceptibility to food allergies and intolerances, and impacts on an individual's microbiome. Other research could investigate psychosocial and cultural influences on breastfeeding—as well as how the timing, order, type, and quantity in which foods are provided to children affects food preferences, allergies, and intolerances.
- [Development of the infant microbiome](#). This research could serve as a platform to address questions around the environmental origins of the microbiome, diet-host-microbiome interrelationships, and the impact of antibiotic use.

In conclusion, the relationship between early life nutrition and DOHaD is multi-generational and multi-modal, involving diet, biology, the social and cultural environment, and the physical environment with rapid changes occurring over a short period of time. There are many research gaps that span across many scientific disciplines. To this end, the NIH is seeking input from the broad scientific community on what research activities are possible and should be prioritized related to early life nutrition and DOHaD that are most likely to propel this field forward for the greater benefit of biomedical research.

## Information Requested

This RFI seeks input from individuals throughout the scientific research community along with relevant key community, private/public partnerships and other interested parties (food bank alliances, restaurant industry, health systems, payors, professional associations, patient groups which should be engaged) regarding any of the following topics:

1. Research gaps related to the DOHaD hypotheses, woman's health, and child development that could be addressed by a longitudinal cohort study beginning pre- or periconceptionally for infant and maternal health during and after pregnancy.
2. Pre- to periconceptual interventions that would be important to capture (e.g., perinatal education programs or training, lactation teaching/consultation programs, the role of other family/community-based supports to caregivers (moms) etc.).
3. Approaches to overcome logistical or scientific barriers to research in this area. This could include, but is not limited to, strategies for and issues with integrating electronic health records (EHR) from multiple sites where the EHR software provider may be different, linking maternal and infant EHR, and making the emerging data findable, accessible, interoperable, and reusable (FAIR).
4. Eating behaviors and patterns, lifestyle factors, social determinants, structural inequalities the impact of health disparities, and discrimination around nutrition and DOHaD for understudied, under-represented and vulnerable populations of Americans disproportionately affected by developmental or diet-related diseases that could be rigorously investigated in a cohort study design that addresses these issues.
5. Recommended measures and/or outcomes of interest to address research gaps for such a study (e.g., genetics, epigenetics, continuous monitoring of nutrients, microbiome composition, measures of social determinants of health, use of digital tools and technologies such as wearables and sensors to assess behaviors, etc.).
6. Recommended measures in human milk composition, infant feeding and complementary feeding practices.
7. Challenges, acceptability, and feasibility of obtaining biospecimens/tissue samples, imaging, and other relevant metabolic, biobehavioral, and environmental measures in real-time and at sensitive time periods from mothers, infants, young children, and families (and strategies to address/overcome these challenges).
8. Research gaps specific to ethnically diversified racial and ethnic minority and other NIH-designated populations that experience health disparities and how this knowledge, or absence of knowledge impacts health during and after pregnancy, along with the healthy development and future disease risk of the infant.
9. Information about emerging cohorts and or teams of family medicine physicians that provide obstetric and pediatric care, OB/GYN and pediatric physician teams or other investigator teams or networks in the U.S. that could seamlessly conduct such longitudinal research in parents and offspring.
10. Information about research coordinating centers that could conduct such research including through the use of Other Transactional Authority.
11. Any other topic the respondent feels would be relevant for the NIH to consider in developing this concept.

## How to submit

Responses to this RFI should be submitted electronically to [nutritionresearch@nih.gov](mailto:nutritionresearch@nih.gov). [There are no official forms to use, nor page limitations](#). Responses in the body of an email or using an email attached PDF or MS Word document is acceptable. Responses must be received by 11:59 p.m. on Aug 15, 2022. Responses to this RFI are voluntary. Do not include any proprietary, classified, confidential, trade secret, or sensitive information in your response. NIH also has a limited amount of time slots for Zoom-based listening sessions with individuals or groups about this activity and request. If you or your investigator team would like to do so, please request a *listening session* at [nutritionresearch@nih.gov](mailto:nutritionresearch@nih.gov).

The responses will be reviewed by NIH staff, and no individual feedback will be provided to any responder. The Government will use the information submitted in response to this RFI at its discretion. The Government reserves the right to use any submitted information on public NIH websites, in reports, in summaries of the state of the science, in any possible resultant solicitation(s), grant(s), or cooperative agreement(s), or in the development of future funding opportunity announcements.

This RFI is for information and planning purposes only and shall not be construed as a solicitation, grant, or cooperative agreement, or as an obligation on the part of the Federal Government, the NIH, or individual NIH Institutes and Centers to provide support for any ideas identified in response to it. The Government will not pay for the preparation of any information submitted for this RFI or for the Government's use of such information. No basis for claims against the U.S. Government shall arise as a result of a response to this request for information or from the Government's use of such information.

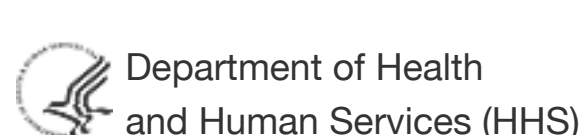
NIH looks forward to your input, and this RFI document may be shared widely among the research colleagues.

## Inquiries

Please direct all inquiries to:

Krista A. Zanetti, Ph.D., M.P.H., R.D.N.  
Office of Nutrition Research  
Telephone: 301-451-1667  
Email: [nutritionresearch@nih.gov](mailto:nutritionresearch@nih.gov)

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