

Concept Clearance

Branch: Population Health Branch

Council Period: 201810

Concept Title: "Environmental Influences on Aging: Effects of Extreme Weather and Disaster Events on Aging Processes and Aging Populations"

We are proposing two complementary FOAs on environmental influences on aging processes and populations that explore both the fundamental scientific mechanisms of aging and the epidemiological and social scientific factors affecting specific aging populations. We envision this as an integrated program that focuses on topics that have been identified as research gaps and that remain relatively understudied to date. This initiative represents NIEHS' increased interaction with the National Institute on Aging and other NIH ICs with common interests in population health disparities and the effects of environmental factors on aging processes. The linked FOAs we are proposing relate to the effects of disasters and extreme weather on aging populations and aging processes.

Background information: A trans-federal workshop entitled, Extreme Events, Environmental Health and the Elderly, held on June 13-14, 2017, identified specific gaps in the current research on aging and the environment. This includes gaps in understanding how extreme weather affects those with co-morbidities of specific types, the processes of aging in context of extreme or cumulative environmental exposures (in animal models), epigenetic changes due to lifelong environmental and health disparities and their effect on morbidity and mortality, the differences between effects at different ages (e.g., 65 vs. 85, 50 vs. 70 years of age), and how to prevent environmentally induced stressors among aged populations (e.g., the feasibility of promoting resilience and sociocultural support of aged individuals from a variety of ethnic and racial backgrounds).

The workshop led to establishment of two related trans-NIH FOA planning teams to begin development of linked Funding Announcements entitled, "**Environmental Influences on Aging: Effects of Extreme Weather and Disaster Events on Aging Processes and Aging Populations**".

- NIEHS is leading the development of a Population Studies FOA that focuses on aging populations
- NIA is leading the development of a Fundamental Studies FOA focused on basic mechanisms of aging

Objective: Although the focus of the workshop was extreme weather events and disasters, environmental influences on aging populations and aging processes is multifactorial and is seen as an under-researched window of susceptibility that NIEHS and NIA (and other ICs) are proposing to explore in these FOAs that would examine how a variety of environmental factors influence the aging process and disease outcomes in specific aging populations. The FOAs we are proposing today would encourage multidisciplinary research that considers the influences of environmental exposures on aging populations related to extreme weather and disaster events, the built environment and socioecological factors; as well as research that elucidates the fundamental mechanisms underlying the aging process on the molecular, cellular, organ and whole-body levels.

The scientific justification for the two FOAs are based on four converging factors:

- 1) the rapidly increasing proportion of the US population over the age of 50 and increased life expectancy;
- 2) the recognition of the health disparities among aging populations related to the interplay among environmental, sociocultural, molecular and economic factors;
- 3) the need to fill research gaps on combined exposures and on exposures across the lifespan;
- 4) the increasing severity and occurrence of superstorms, hurricanes, tornados, floods, earthquakes, wildfires and other natural and manmade disasters and their effects on the most vulnerable segments of the population.

Overarching research approaches that will be encouraged for the two FOAs are

- 1) Fundamental studies on the mechanisms of aging across the lifespan in the context of environmental factors.
- 2) Epidemiological research on combined and accumulative exposures across the lifespan.
- 3) Social scientific and behavioral research on the effects of extreme events and increasingly extreme weather on subpopulations.
- 4) Dissemination and implementation research on risk communication in the context of disasters.

Although two separate FOAs are being proposed, we will encourage the population-based and fundamental mechanistic research projects to consider endpoints or pathways that can be measured in both model systems and human populations to allow for closer integration and translation of findings. This integration will further be ensured through annual meetings that bring together investigators funded through both FOAs.

General Research Areas of Interest for the two FOAs include:

- a) **Fundamental Studies on combined and aggregated exposures across the lifespan.** This would include lifespan and health span studies in laboratory animals given early-life versus midlife exposures to factors released by one or more types of extreme environmental events. The goals would be to understand how extreme environmental factors add to or exacerbate pathological conditions of laboratory animals and the effects of multiple and/or persistent chemical exposures in aging laboratory animal populations.
- b) **Population studies on combined and aggregated exposures across the lifespan.** This would include epidemiological studies, analysis of mixtures, studies on environmental factors in the context of co-morbidities. How do environmental factors released during disasters or increased because of extreme weather add to or exacerbate existing medical conditions? Importantly, for both the basic and

population FOAs, the study of differences in the impacts on males and females is encouraged.

- c) **Fundamental research on the disparate responses to changed environmental risks in older organisms compared to mid-life adults, with an emphasis on differential prior chronic stress as a mimic for conditions of health disparities.** In considering health disparities in human populations, there is evidence that long-term stresses of poverty and disadvantaged social and economic conditions may depress resilience and increase frailty. This could be modeled using laboratory organisms that have been subjected to mild stresses such as erratic food deprivation, high fat diets, low levels of oxidative challenges, and other conditions that do not cause acute stress responses, as well as sporadic and nonlethal exposures to viral or bacterial infections.
- d) **Social scientific and behavioral research on the sociocultural influences on environmental health risks among specific elderly subpopulations.** This includes research that focuses on specific subpopulations and that would consider how sociocultural beliefs and/or socioeconomic conditions influence the response to disaster events or extreme weather conditions? How is risk perceived by individuals and communities from different ethnic and racial subpopulations? Studies are encouraged that consider social support, concepts of risk, resilience, poverty, and other social factors that combine with environmental factors to affect aging populations and produce health disparities.
- e) **Dissemination and Implementation (D&I).** This would include studies on the development and delivery of risk messages, education and preparedness resources for specific elderly populations; research on the efficacy of existing resources/risk messaging/education (e.g., reverse 9-1-1); communications research that explores community-based efforts to educate and communicate risk factors affecting aging populations, family members and caregivers. We would encourage D&I expertise in all the population studies but also to consider including it for the basic studies in order to ensure that findings are communicated to the public.

Suggested Research Topics for the Population Studies FOA include but are not limited to:

The FOAs are expected to address issues and answer research questions related to

- a. The impacts of natural disasters on the onset and progression of chronic health conditions
- b. Aging in place and the stress of displacement during disasters and extreme weather events
- c. Health services delivery and access to medical equipment and supporting infrastructure
- d. Sensory decline or deficits and their influence on perception, cognition, and behavior
- e. Dementias including Alzheimer's and the effects of lead and other toxic exposures
- f. Analysis of mixtures (the burden of lifetime exposures coupled with extreme exposures)
- g. Health promotion and resilience (reducing vulnerability and increasing preparedness of populations)
- h. Environmental health literacy related to disaster or extreme weather-driven exposures for aging individuals, caregivers, health professionals
- i. The influences of the built and social environment on aging
- j. Circadian rhythm changes over the course of aging, in response to extreme weather and disasters, and their effect on health and wellbeing
- k. Biopsychosocial mechanisms of exposure and aging

Suggested Research Topics for the Fundamental Studies FOA include but are not limited to:

- a. Analysis of mixtures. This includes the burden of lifetime and ongoing exposures coupled with extreme exposures.
- b. Slow disasters and increasingly extreme weather. Laboratory animals, as with humans, are impacted by relatively modest changes in their environments, such as periods of greater heat, cold or significantly altered humidity.
- c. Resilience. Studies are encouraged to examine parameters associated with resilience, including speed, amplitude and duration of response, return to baseline and refractory periods after an exposure. Consideration should also be given to longitudinal studies with lab animals to track longer-term functional health and impacts on the aging health trajectory.
 - i. In laboratory animals that have identifiable social hierarchies, research to elucidate or distinguish between individual and community resilience, (e.g., resilience of networks).
 - ii. In humans: impacts on telomere lengths and telomerase, viral loads, epigenetic clocks and immune cell subtype distributions.
- d. Environmental interactions with immune function and immune senescence, including tissue-resident immune cells, inflammatory resolution
- e. Changes in circadian rhythm and molecular signatures that track with circadian rhythms (including DNA repair, cellular senescence, and proteostasis).
- f. Impacts on wound healing and repair supported by stem cells and other mechanisms altered by aging.
- g. Impacts on burden of senescent cells
- h. Interaction with senolytics

We are proposing a PAR for, similar to the ongoing interest shown in the community driven Research to Action program, environmental influences on aging is attracting increased attention as an understudied area and, based on the number of inquiries from investigators, is of interest to a variety of researchers as well as to several NIH Institutes and Centers. In addition to NIEHS and the National Institute of Aging, the National Institute on Minority Health and Health Disparities, Office of Behavioral and Social Scientific Research, and National Institute on Nursing Research have all participated in planning this FOA concept based on their IC interests and research needs.

A PAR is needed as this type of research would benefit from multidisciplinary teams and would not therefore be appropriately reviewed by any one standing study section. In addition, we expect to publish both the Population Studies and Fundamental Studies FOAs in parallel and would need Special Review Panels geared to the specific goals of each of these related FOAs. Given the expertise at NIEHS in both environmental health research review and aging research review, we believe the appropriate special review panel will be assembled that can adequately and appropriately review these grants.

We are proposing an R01 mechanism for these initial FOAs and a timeline as follows:

Sep 2018	Present population health concept to NIEHS Council and NIA Council
Dec – Jan 2019	Publish FOAs
Mar – Apr 2019	Receipt of applications
Summer 2019	Reviews
Sep 2019	Present program plan to NIEHS Council
Oct 2019 (FY2020)	Awards
2020-2025	Annual Grantee meetings that bring together Fundamental Study and Population Study PIs for cross fertilization and collaboration on risk communications to affected populations.