A. Aims

We propose to expand a multi-center randomized-controlled trial (RCT) to investigate whether experimentally-induced reductions in poverty can also protect against age-related chronic diseases, including Alzheimer's disease and Alzheimer's disease-related dementias (AD/ADRD). Poverty is believed to accelerate human aging through two major pathways: 1) it deprives people of access to healthy food, medical care, and other health-producing goods and services; 2) it causes psychological stress, which can damage neural systems involved in memory, executive function (e.g., setting and achieving goals), and homeostasis (e.g., the regulation of blood pressure or glucose). Extensive research has elucidated the pathways linking poverty and poverty-associated stress to premature aging, frailty, AD/ADRD and death. **However, whether anti-poverty interventions can alter these pathways to prevent or delay biological changes that ultimately lead to development of AD/ADRD remains unknown.**

Our proposal is designed to better define the relationship between poverty and aging in a way that is efficient and inexpensive since it leverages an already-funded ongoing trial. This trial, *MyGoals for Employment Success,* was designed by Manpower Development Research Corporation (MDRC) in consultation with neuroscientists, behavioral psychologists, the Department of Health and Human Services, and employment program practitioners. It randomized 1,798 unemployed public housing participants to a three-year intervention vs. a control group. The intervention comprised: 1) **experimentally-proven** employment incentives; 2) intensive executive function coaching; 3) incentives each time the participant engages a coach; 4) additional incentives for maintaining employment and coach engagement; and 5) an “income disregard” in which the participants’ higher earnings do not disqualify them from other welfare programs. The control group received no additional intervention. *MyGoals for Employment Success* included a validated measure of executive function, social outcome measures, and economic outcome measures. Follow-up was 80%.

Economic outcomes can be assessed over the short-term, but aging and cognitive outcomes require longer-term intervention and follow up. Therefore, **the Columbia and MDRC team added an additional year of intervention to the original study in the hope that we could convert it into a future aging study.** The proposed study, *MyGoals for Healthy Aging,* seeks to ascertain whether social policy can intervene in the aging process with 3 years of intervention and 6 years of follow up. The first phase of the proposed study was funded via an R56 mechanism (NIA R56AG062485). The main goals of that study were to fund cohort maintenance efforts and to convene a panel of leading experts to design the conceptual framework and outcome measures for the proposed study. This work was completed successfully.

MyGoals for Healthy Aging has four aims: three data collection/analysis aims through the fifth study year and a 4th aim to enable longer-term investigations via state-of-the-art data linking and biobanking methodologies.

Aim 1) To test the hypothesis that the intervention improves economic and behavioral pathways that may influence the risk of aging and future AD/ADRD. Economic wellbeing (employment, income, housing, crime, health insurance) and health behavior (diet and exercise) will be measured from administrative records and validated survey instruments and compared between intervention and control groups.

Aim 2) To test the hypothesis that the intervention improves mental-health, physical health, and cognitive pathways to aging and AD/ADRD. Mental and physical health (sleep, loneliness, psychological stress, depression, obesity, health-related quality of life, C-reactive protein, and HbA1C) and executive function will be measured from validated survey instruments and laboratory assays of blood samples and compared between intervention and controls groups.

Aim 3) To test the hypothesis that the intervention slowed aging-related biological changes contributing to risk for AD/ADRD. We will measure aging-related biological changes from whole-genome DNA methylation data derived from blood samples using Illumina EPIC arrays. We will use validated algorithms to quantify the pace of biological aging (DunedinPoAm) and biological age (GrimAge clock). Analysis will compare DunedinPoAm pace of aging and Grim Age between treatment and control groups.

Aim 4) To enable longer-term outcome assessments via cutting-edge data linkages and biobanking. We will curate data into a shareable resource with administrative outcomes added on an ongoing basis.

Our team consists of leading experts in randomized trials, social policy, aging, and cognitive science. Our proposed study fulfills NIA’s goal of a “multidisciplinary approach to understanding the mental, physical and social health of individuals, which incorporates … life span … concepts...to influence population-level health disparities” and supports minority investigators. Collectively, these aims may provide causal inference for an intervention on the social determinants of health, to ascertain whether the intervention alters biological changes driving AD/ADRD risk, and to establish a powerful, unique, and sharable resource.