

Study Name	Principal Investigators	Abstract
The Life Course Microbiome Study - LCMB	Kenneth Krauter, Kathleen Mullan Harris, Jason Boardman, Allison Aiello	We will study the oral microbiomes obtained from ~6000 respondents of the The National Longitudinal Study of Adolescent Health (Add Health) Wave IV. This request is in response to an NIH grant review requesting that pilot/preliminary data be conducted on Add Health saliva samples (Wave IV).
Using record linkage to generate the Add Health Children Study Database	Robert A. Hummer, Kathleen Mullan Harris, Jon Hussey	To advance scientific understanding of the developmental origins and intergenerational transmission of health and well-being, we need new data sources containing rich biological, genetic, social, psychological, behavioral, environmental, and economic information on both parents and children. The goal of this R21 is to establish the feasibility of creating such a data source that links the birth records of children born to mothers and fathers in the Add Health Study. We propose to pilot the linkage of births to female Add Health respondents living in three U.S. states. Add Health is the ideal study with which to build an intergenerational database with its longitudinal design, national representation, and substantial racial, ethnic, and socioeconomic diversity and will position Add Health as one of the preeminent data resources for studying the developmental origins of health and disease.
Add Health Parent Study: A Biosocial Resource for the Study of Multigenerational Racial/Ethnic Disparities in Alzheimer's Disease and Related Dementias (AD/ADRD)	Kathleen Mullan Harris, Vincent Joseph Hotz, Erica A. Boerwinkle, Naomi Duke, Krista Perreira	Significant knowledge gaps exist regarding intergenerational dimensions of cognitive aging and risk for Alzheimer's Disease and Alzheimer's Disease Related Dementias (AD/ADRD), and how these processes differ across race and ethnic groups. The proposed Add Health Parent Study (AHPS) Phase 2 is designed to address these gaps. AHPS is an ongoing study of social, behavioral, and biological factors influencing healthy aging and the development of AD/ADRD in a national sample of adults currently aged 58-90. Sample members are parents of the National Longitudinal Study of Adolescent to Adult Health (Add Health) cohort, initially interviewed in Add Health in early midlife (1994-95) before differential survival could contribute bias to sample representation. Phase 1 of AHPS (2015-17) collected longitudinal data on a random subsample of parents and their spouse/partners (S/P, N= 3001), the majority (73%) of whom were Non-Hispanic (NH) White. Phase 2 of AHPS will collect social, behavioral, and health data on all available NH Black and Hispanic parents (BHS supplement, N= 2,505), and cognitive assessments and DNA data on all AHPS Phase 1 and BHS sample parents and their current S/P (total N= 5,506). By adding NH Black and Hispanic parents, AHPS will be sufficiently statistically powered to address, for the first time, measurement of health, social, and behavioral differences in AD/ADRD risk and protective factors across race/ethnic groups and socioeconomic strata. Combined data from AHPS Phases 1 and 2 will be linked with rich longitudinal data on original Add Health respondents to create and disseminate the first nationally representative multigenerational biosocial resource with cognitive, genomic, behavioral, and social data for the study of racial/ethnic disparities in cognitive aging and AD/ADRD risk. Cognition and genomic data will be harmonized across the two generations of parents and children for innovative analysis of intergenerational predictors of AD/ADRD; the role of genetic processes in AD/ADRD etiology; and intergenerational and lateral caregiving.
Add Health Accelerated Aging	John Batsis, Penny Gordon-Larsen, Annie Green Howard, Misa Graff	The antecedents of Alzheimer's Disease (AD) and AD related dementias (ADRD) begin early in life and are shaped by chronic low-grade inflammation and cellular senescence. Unremitting metabolic and physiologic stress during the lifecycle induced by obesity may accelerate biologic aging and the risk of developing AD/ADRD late in life. Geroscience biomarkers proposed by the Targeting Aging with Metformin (TAME) workgroup offer modifiable mechanistic targets that can help our understanding of the heterogeneity observed in preventing, managing, and reducing AD/ADRD before disease onset. We aim to address these biologic antecedents across this transition period from adolescence to mid-adulthood using Add Health by 1) generating the remaining five serum TAME biomarkers in wave V and determine whether earlier onset, higher, and sustained, weight gain from adolescence to mid-adulthood is associated with a higher risk of accelerated biologic aging in mid-adulthood; 2) determine if known genetic markers of AD/ADRD accelerate biologic aging and differ depending on timing, duration, and severity of weight gain; and 3) estimate the effects of parental and mid-adulthood socioeconomic status on accelerated biological aging and whether these effects operate independently and/or through timing, duration, and severity of weight gain. We capitalize on a portion of life before disease onset which will provide insight into factors to reduce and delay accelerated aging and offset the genetic risk of AD/ADRD. Findings will inform geroscience-based targets to increase lifespan and promote healthy aging.

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Identifying Place-based Factors that Shape AD\ADRD Risks	Michael Esposito, Jessica Finlay	<p>The proposed study will use a sequential mixed-method approach to identify the neighborhood risk and protective factors influencing cognitive decline across the adult life course. First, qualitative seated and mobile interviews in four socio-geographically diverse metropolitan areas (led by expert teams in San Francisco, Denver, Atlanta, and New York) will investigate how individuals of different ages navigate their local environments to engage in lifestyle behaviors that reduce dementia risk (e.g., social engagement, physical activity). Second, we will use these insights as the basis for quantitative model construction (e.g., age-specific feature selection; grounded coding of “access” and “exposure” variables) in an integrative data analysis of four national longitudinal cohort studies spanning adolescence to late-age (AddHealth; American Changing Lives; Reasons for Geographic And Racial Differences in Stroke; Health and Retirement Study). This study will assess whether exposure to specific neighborhood amenities and hazards across the life course systematically predict cognitive function and decline. Results will inform community interventions to support healthy aging and reduce dementia risk, address structural barriers and broader socio-geographic health disparities, and advance exposome and life course knowledge and theories.</p>
Racially and Ethnically Diverse-Air Pollution EXposure (RED-APEX) consortium	Mercedes Bravo, Kathleen Mullan Harris, Fang Fang, Eric Johnson, Dana Hancock	<p>The central objective of the proposed research is to identify mechanistic pathways through which air pollution affects CMD in different racial/ethnic groups and across the lifecourse. We have created the Racially and Ethnically Diverse-Air Pollution EXposure (RED-APEX) consortium to bring together multiple cohort studies, harmonize and expand upon their existing data, and address three aims:</p> <p>Aim 1: Leveraging RED-APEX, harmonize CMD outcome data, attach multi-year estimates of air pollution exposure, and describe characteristics across the lifecourse. We will (1a) harmonize data across RED-APEX cohorts (total N=to be determined); and (1b) attach multiple years of high-resolution air pollution data (PM2.5, O3, and NO2). We will describe characteristics by exposure heterogeneity and geography, racial/ethnic, age, and socioeconomic diversity, as a foundation for examining exposure to and health effects of air pollution across the lifecourse.</p> <p>Aim 2. Estimate associations between air pollution exposures and multiple CMD outcomes in RED-APEX. We will estimate associations between air pollution exposures and multiple CMD measures (e.g., blood pressure, cholesterol, glucose). Specifically, we will: (i) evaluate differences in air pollution-CMD associations by race/ethnicity and age group; and (ii) estimate associations between air pollutant mixtures and CMD.</p> <p>Aim 3. For pollutants associated with CMD, develop DNAm biomarkers of air pollution exposure and evaluate whether DNAm is a biological mechanism by which air pollution exposure affects CMD. Specifically, in Aim 3(a), we examine individual CpG sites in an epigenome-wide association study (EWAS), develop multi-CpG predictors, and evaluate whether biomarkers of exposure are consistent across racial/ethnic and age groups. In Aim 3(b), for pollutants associated with DNAm in 3(a), we test whether air pollution exposure causally affects CMD through DNAm using Bayesian-informed mediation modeling.</p>
Add Health and CJARS linkages	Lauren Gaydos, Carmen Gutierrez	<p>This is an ancillary study proposal that outlines the work we will propose to the Arnold Foundation for a planning grant to support the work necessary to establish linked data between Add Health and the Criminal Justice Administrative Records System (CJARS). CJARS is an unparalleled national data linkage effort that harmonizes and links criminal legal records obtained from state and local agencies across the United States. CJARS contains information on 40 million individuals with event-level data on arrest, conviction, incarceration, parole, and probation covering ~80% of the US population, with continuing efforts to expand coverage. We propose to link Add Health respondents to the criminal legal records available in CJARS using name, date of birth, state and county of residence, and sex, race, and ethnicity. We will determine what proportion of Add Health respondents have a linkable criminal legal record, and compare these administrative data to self-reported criminal legal contact as reported in the AH surveys. Finally, we will determine how we can disseminate these data in a manner that agrees with both Add Health and CJARS data sharing and data use agreements. The successful completion of this project will provide researchers with an unprecedented data resource for the investigation of the precursors and consequences of criminal legal system involvement.</p>
Unravelling the role of mitochondria health in the psychosocial stress-accelerated aging cascade	Caroline Trumpff	<p>Individuals vary widely in their health and aging trajectories, yet the underlying mechanisms driving these differences remain poorly understood. Growing evidence suggests that alterations in cellular energetics, particularly mitochondrial biology, contribute to accelerated aging. Modifiable factors, such as chronic psychosocial stress, may lead to accelerated aging by disrupting mitochondrial biology. However, large-scale population-based studies directly testing this hypothesis are lacking. Recent work by our group and others has identified a novel approach to investigate the Stress Mitochondria Aging cascade. Bio-banked plasma samples can be assayed for growth differentiation factor 15 (GDF15), a well-established biomarker of biological aging and mitochondrial energy transformation capacity, which is elevated in depression and acutely induced by psychological stress. We propose to leverage archived plasma from a representative subsample of 5,000 respondents in Wave V of Add Health to quantify plasma GDF15 concentrations. Findings will inform the role of mitochondrial dysregulation in stress-related accelerated aging and help identify potential intervention targets.</p>



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Assessing Residual Population Stratification in PGI Research Using Geographic Residualization	Callie Burt, Robbe Wedow	<p>The inclusion of polygenic indices (PGIs)—composite genetic scores based on genome-wide association studies (GWAS)—in social science research has accelerated in recent years, offering new insights into the interplay between genes and environments in shaping human behavior and health. However, concerns about the confounding effects of population stratification (PS) persist, particularly when PGIs are applied in population-based samples. Evidence indicates that even after standard corrections (e.g., principal components analysis), PGIs often exhibit geographic clustering, suggesting the persistence of residual PS-confounding, especially for socially patterned traits like educational attainment or body mass index (BMI).</p> <p>The goal of this ancillary study is to examine the extent and implications of residual PS-confounding in PGI analyses in the U.S. context, using data from the National Longitudinal Study of Adolescent to Adult Health (Add Health). We propose a novel and scalable solution: leveraging high-resolution geographic information to detect and correct residual PS-confounding in PGIs. Specifically, we will assess whether PGIs residualized on Wave I geocoordinates—termed R-geo PGIs—show reduced predictive power compared to standard PGIs, indicating correction of PS-related bias.</p>
Medicaid and Labor Market Shocks: Impacts on Health Outcomes and Economic Well-Being	Yannick Reichlin	<p>This ancillary study combines methods from genetics and economics to study how the interaction between individuals' genetic endowments and their environment affects labor market and health outcomes throughout the life span. The goal is to study the impact of automation, the technological production proves in which industrial robots replace workers' task. We are interested in how automation shocks shape individuals' labor market, education, and health outcomes, and whether their impact is ameliorated or reinforced by an individual's genetic predispositions, measured by polygenic indices. We will estimate linear regressions of an extensive set of primary and secondary outcomes on measurements for genetic predispositions, changes in automation, and their interaction.</p>
Impact of Immigrants' Access to Food Assistance on Children's Long-term Economic and Social Outcomes	Rita Hamad, Daniel Collin	<p>The Supplemental Nutrition Assistance Program (i.e., Food Stamps) is the largest food assistance program and among the largest poverty alleviation programs in the nation. However, due to changing federal and state eligibility criteria, access to Food Stamps has fluctuated for different groups. For example, federal welfare reform in 1996 (as part of the Personal Responsibility and Work Opportunity Reconciliation Act, PRWORA), led to the exclusion of most immigrant families from eligibility for Food Stamps. In response to PRWORA, nine states restored Food Stamp benefits to immigrant families using their own funds: California, Connecticut, Maine, Massachusetts, Minnesota, Nebraska, Rhode Island, Washington and Wisconsin. Federal criteria loosened again with the passage of the Farm Security and Rural Investment Act (Farm Bill) in 2002, and pre-PRWORA documented immigrants were once again eligible in April 2003. No studies to our knowledge have examined the long-term impacts on later-life outcomes for children of immigrants exposed to these policy variations in Food Stamps. Our study will fill this critical knowledge gap, providing new evidence on how changes in state and federal eligibility criteria for the Food Stamp Program influenced health and social outcomes during two decades of follow-up.</p>
Smoking Bans on School Campuses	Mathiue Lambotte	<p>This study develops a theoretical model and empirical test to examine the intergenerational transmission of smoking behavior in a society with overlapping generations. Individuals are socialized during childhood through parental influence (vertical transmission) and non-parental factors (horizontal transmission). We explore key mechanisms for vertical transmission (cultural substitution and complementarity) and horizontal transmission (cultural conformity and distinction). To test and inform the model, we adapt Chetty and Hendren's (2018) mover-design framework, exploiting variations in student transitions between colleges to assess the causal impact of exposure to tobacco-free campuses on smoking behavior. Empirical results are used to calibrate and estimate the model, providing insights into health policy effects on adolescent and young adult behaviors.</p>
The Add Health Epigenomic Resource: A Longitudinal Cohort for Advancing Research on Cognitive Function and Alzheimer's Disease Risk	Allison Aiello	<p>Neurodegenerative diseases, including Alzheimer's disease and related dementias (AD/ADRD), pose a substantial and growing public health burden. Identifying molecular processes that precede clinical symptoms is essential for improving early detection and intervention. DNA methylation (DNAm) is a promising biomarker of these early processes, reflecting biological aging, inflammation, immune dysregulation, and cognitive function across the life course. Although DNAm-based aging measures, inflammatory and immune-aging profiles, and emerging DNAm predictors of cognition show potential for detecting AD/ADRD risk well before onset, these biomarkers have rarely been examined longitudinally in large, diverse midlife populations. This project will generate DNAm data for Wave VI of the National Longitudinal Study of Adolescent to Adult Health (Add Health), a nationally representative U.S. cohort followed from adolescence into midlife. By harmonizing new Wave VI DNAm assays (ages ~45) with existing Wave V data (ages ~38), we will create a unique longitudinal epigenetic resource. We will derive DNAm-based measures of biological aging, inflammation, immune aging, and cognitive function, including a novel DNAm-based predictor of midlife cognition. We will also test cross-sectional and longitudinal associations between these biomarkers and cognitive performance from the Add CAPS battery.</p>