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Title	Principal Investigators	Abstract
Susceptibility to Accelerated Aging: Transitions in Weight and Socioeconomic Status across the Lifecycle	John Batsis, University of North Carolina at Chapel Hill, Penny Gordon-Larsen, University of North Carolina at Chapel Hill, Annie Howard, University of North Carolina at Chapel Hill	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.
Structural Racism and Biological Risk Factors for AD/ADRD among a National Cohort of Young Adults	Chantel Martin, University of North Carolina at Chapel Hill; Taylor Hargrove, University of North Carolina at Chapel Hill	The purpose of this ancillary application is to merge contextual data on structural racism to Add Health respondents; location of residence at Waves IV and V. We propose state-level, county-level, and Census-tract data linkages to describe Black-White inequities in (1) economic opportunity, (2) political context, and (3) the criminal justice system context. This contextual database will allow for innovative research that investigates how structural racism at various geographic levels influences health, behavior, social, and economic outcomes during young adulthood and the transition from young adulthood to the beginning of midlife. We will use these contextual measures to investigate the relationship between structural racism and risk for Alzheimer's Disease and Alzheimer's Related Dementias (AD/ADRD). Specifically, we aim to test whether various components of structural racism shape racial disparities in biological risk factors for AD/ADRD, including hypertension, type 2 diabetes, inflammation, and key biomarkers of AD/ADRD risk (e.g., tau, neurofilament light, DNA methylation markers implicated in AD/ADRD), when respondents are 33-43 years old. We also intend to use simulation models to compare the effects of hypothetical population-based policy changes and targeted interventions on racial inequalities in outcomes of AD/ADRD risk.
The Mental Health Consequences of Life Course-Varying Exposure to Structural Sexual Minority Stigma: Advancing Causal Inference Using Longitudinal Models Moderated by Sexual Orientation	Arjan Van der Star, San Diego State University	An expanding body of theory-driven research has consistently shown how factors related to sexual minority stigma, including structural, interpersonal, and intrapersonal factors, may drive sexual orientation-based mental health disparities. However, public health research has so far been unable to produce strong causal, longitudinal evidence on how structural forms of sexual minority stigma may jeopardize mental health outcomes among sexual minorities, including suicidal ideation, suicide attempts, or depressive symptoms, where 1) temporality, 2) a dose-response gradient, and 3) specificity of results have been lacking. Using Add Health data, this proposed study will 1) quantify the level of structural sexual minority stigma for each US state between 2001 and 2018 and calculate individuals' exposure over time, 2) examine the associations between structural sexual minority stigma and suicidal ideation, suicide attempts, and depressive symptoms in longitudinal models, and 3) examine if the associations between structural sexual minority stigma and mental health outcomes in longitudinal models vary by sexual orientation. The analysis will include advanced three-level multi-membership longitudinal models to examine three key aspects yet missing to facilitate causal inferencing regarding the mental health sequelae of structural sexual minority stigma exposure.

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The Add Health Human Microbiome: Genetic, Environmental and Body Mass Influences	Matthew McQueen, University of Colorado - Boulder; Ken Krauter, University of Colorado - Boulder; Kathleen Mullan Harris, University of North Carolina at Chapel Hill	Microbes in the mouth and gut can exert surprising influences on human physiological, developmental and psychological outcomes. DNA sequence-based phylogenetic classification and computational approaches to uncover correlations between microbes and human phenotypes have been used to characterize some of these influences. Obtaining statistically significant findings with such approaches depends upon effective sampling of the microbial populations present in each niche, as well as studying a sufficiently large cohort of human subjects to account for substantial variability in the microbial composition between individuals. In this proposal we will study the oral and gut microbiomes obtained from The National Longitudinal Study of Adolescent to Adult Health (Add Health). This is a nationally representative study of over 20,000 subjects who were initially sampled as adolescents in the United States between 1994 and 1995 and then followed through adolescence and into adulthood with four in-home interviews (Waves I-IV). A fifth wave (Wave V) of Add Health was recently funded and will collect new information on ~14,000 original Add Health respondents between 2015-2017. The gut and oral microbiomes of diverse socio-economic, ethnic and racial communities from across the US will be characterized, and their association with body-mass index (BMI), waist-to-height ratio (WHtR), human genetic variation as well as environmental and behavioral factors will be investigated. Through Add Health Wave IV and affiliated projects, a saliva sample was collected and approximately 1 million single nucleotide polymorphisms (SNPs) have been generated on well over 10,000 of the original Add Health respondents. In collaboration with the Add Health Wave V project, we will obtain another saliva sample as well as a stool sample (gut) as part of this proposed project. DNA prepared from the three samples will be subjected to DNA sequence-based metagenomic analysis of the complexity and abundance of bacterial species present from each Add Health respondent. Using these microbial measures, we will test for associations between environmental factors such as age, race, sex, diet, physical activity, tobacco and alcohol use and alterations in microbial communities in each person. Next, we will assess whether there are genetic influences on the composition of each microbial community. Finally we will test for associations between measures of body mass and obesity and disruptions or alterations in microbial populations. This will be the largest and most comprehensive single study to investigate the interface between human genes, environmental and behavioral factors and microbes to date.
Add Health Children Study Database	Robert A. Hummer, University of North Carolina at Chapel Hill; Kathleen Mullan Harris, University of North Carolina at Chapel Hill; Jon Hussey, University of North Carolina at Chapel Hill; Jennifer Buher-Kane, University of California - Irvine	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. The new Add Health Children Study Database will be the first dataset of its kind in the U.S. with social, behavioral, environmental, and biological data on mothers during the pre-conception period, beginning in early adolescence, with birth certificate data on their children. It will also be the first dataset of its kind that will contain geographic data describing the mother's social environment at the time of birth, in addition to geographic data describing her social environment at multiple points in time, starting in early adolescence and spanning the transition to adulthood. Research made possible by this new database will have significant public health impact through identifying preconception causes of adverse birth outcomes and understanding the transmission of intergenerational disparities in health.

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Contextual Determinants of Sexual Minority Health in the United States	Kara Joyner, University of Texas at San Antonio, Wendy Manning, Bowling Green State University; Krista Westrick-Payne, Bowling Green State University; Lee Brady, Bowling Green State University	The purpose of this study is to produce and disseminate a contextual database that includes measures of structural support (or stigma) relevant to sexual minorities (a population typically defined on the basis of self-identification as gay, lesbian, or bisexual) for Waves 3, 4, and 5 of the National Longitudinal Study of Adolescent to Adult Health (Add Health). The database will enable researchers to identify factors driving disparities between sexual minorities and majorities in health and well-being with its addition of measures of social and legal support corresponding to the tract, county, and state levels before or around the time of Wave 3, 4, and 5. Most of these measures have been used in prior studies on sexual minority health and well-being based on other population-based surveys. The database will additionally include measures used in studies of racial/ethnic disparities to capture structural racism and it will update several existing contextual measures in Add Health (e.g., tract-level poverty).
How does neighborhood environment influence the association between adverse childhood experiences and obesity at transition to adulthood? A novel spatial approach harnessing a national sample	Krista Schroeder, Temple University College of Public Health – Department of Nursing	Neighborhood environment factors such as greenspace, crime, and healthcare access may influence both ACEs and obesity risk, yet research on ACEs-obesity associations rarely examines neighborhood environment. To begin to disentangle ACEs-neighborhood-obesity associations, we validated novel spatial analytic methods for creating a Neighborhood ACEs Index (NAI). A NAI is a spatial index that answers the question “what is the neighborhood environment of individuals with high ACEs exposure?” NAI creation methods entail linking individual-level ACEs data with spatial data capturing numerous neighborhood characteristics, such as crime and healthcare access, using Bayesian index regression. A NAI can be employed to identify best neighborhood-level targets for health interventions for individuals affected by ACEs, as well as to illuminate how neighborhood characteristics associated with high ACEs influence health outcomes (such as obesity). Building from that work, this study will employ an NAI to explore ACEs-obesity-neighborhood associations across the transition from adolescence to adulthood. We will harness nationally-representative longitudinal Add Health data, rich spatial data capturing 30 neighborhood characteristics, and robust Bayesian spatial analytic methods. Findings can establish a premise for future work focused on development and testing of upstream, place-based interventions and policies to reduce obesity for millions of Americans affected by ACEs.
Linking Incidents of Fatal and Non-Fatal Firearm Violence to the Add Health Study	Alexander Testa, University of Texas Health Science Center at Houston; Dylan Jackson, Johns Hopkins University; Daniel Semenza, Rutgers University	Exposure to firearm violence has emerged as a critical public health issue in the United States. Increasingly, research suggests that direct or vicarious exposure to firearm violence affects individuals’ mental and physical well-being. Across the United States, individuals are exposed to firearm violence in multiple ways, including fatal and non-fatal community-based shootings (i.e., citizen-on-citizen firearm violence) and fatal and non-fatal police-on-citizen shootings (i.e., police-on-citizen firearm violence). However, limited research has linked objective geospatial measures of firearm shootings to rich individual-level longitudinal data, precluding a fuller understanding of how these events impact Americans’ mental and physical well-being. We propose the linkage of data on (1) community-based fatal and non-fatal firearm shootings at the census tract level from The American Violence Project and (2) longitude and latitude measures of police on citizen fatal and non-fatal injurious firearm shooting data from the Gun Violence Achieve to Wave V of the National Longitudinal Study of Adolescent to Adult Health (Add Health). By merging these datasets, we will gain a unique opportunity to comprehensively investigate the health implications of multiple forms of exposure to firearm violence on a diverse cohort of individuals.

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Gentrification, Retail Environments, and Chronic Disease Risk	Sarah Halverson-Fried, University of North Carolina at Chapel Hill Todd Jensen, University of North Carolina at Chapel Hill	Evidence is emerging about associations between gentrification and health, but this research is limited by lack of longitudinal data. Studies to date mainly use cross-sectional or repeated cross-sectional designs, creating selection bias because 1) new residents are included in analyses and 2) original residents who stay in gentrifying neighborhoods may have more resources than those who move. Longitudinal research following original residents is needed to understand impacts on health and health equity. To address this important gap, we propose leveraging the nationally representative, longitudinal design of Add Health to examine differences in individuals' neighborhood environments, behaviors, and health outcomes among participants who experienced gentrification vs. those who did not. This study will link measures of gentrification that have been proposed for use in national public health studies for Waves 1, 3, 4, and 5 and food and tobacco retail environment measures derived from expert-informed protocols for Waves 3 and 4. We will then analyze associations between gentrification and changes in retail environments, health behaviors, social determinants of health, and chronic disease risk biomarkers. Future research can use linked data to examine associations between gentrification and additional social, behavioral, and health outcomes, as well as between retail access and these outcomes.
Archiving Contextual Determinants of Sexual and Gender Diverse Population Health	Wendy Manning, Bowling Green State University, Kara Joyner, University of Texas San Antonio	We propose to append 23 indicators of structural cis-heterosexism to the SOGI-SES data to allow for rigorous evaluations of the effects of structural stigma. Currently we are appending contextual measures to the earlier waves of the Add Health (Joyner R01MD016417) and the addition of the SOGI-SES data will offer an unprecedented opportunity to assess SGD health. These data will provide a unique resource to a multidisciplinary community of researchers. The long-term goal is to contribute to scientific study of SGD health by making data available in a timely manner and enhance the value of the investments made in the Add Health. We are poised to accomplish our immediate objective of producing and disseminating a structural stigma database in collaboration with the Add Health at the University of North Carolina (UNC) following their strict and regulated process. These contextual data will also be distributed to the broader research community via the Contextual Determinants of Health at IPUMS and Data Sharing for Demographic Research archive at ICPSR. We propose to 1) produce a contextual database 2) Disseminate the database; and 3) Support users of the data by sharing information about these innovative data.

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The Add Health Epigenome Resource: Life course stressors and epigenomic modifications in adulthood	Allison Aiello, Columbia University; Kathleen Mullan Harris, University of North Carolina at Chapel Hill	Disparities by race/ethnicity and socioeconomic status exist across a range of cardiometabolic and mental health outcomes in adulthood, and have been traced to exposure to psychosocial stressors across the life course. The discovery of the epigenome provides a remarkable opportunity to identify the pathways by which psychosocial exposures get into the body to produce inequalities in health and disease. However, a major limitation of extant research on life course exposures and epigenetic modifications has been a dearth of prospective social and contextual data collection. Indeed, the majority of existing social epigenomic studies focus on an exposure at a single life stage or rely on retrospective report of only a few indicators of early life socioeconomic status. To more fully understand the ways in which psychosocial stressors influence the epigenome, it is paramount to connect rich longitudinal data on psychosocial stressors with epigenetic data and markers of health and disease. Our proposed research will examine “allostatic load”-related gene DNA methylation (DNAm) and expression relevant to life course psychosocial stressors, among participants in the National Longitudinal Study of Adolescent to Adult Health (Add Health). Specifically, our proposal seeks to uncover the impact of life course psychosocial stressors on functional epigenomic alterations, and to identify the epigenomic bridges that link psychosocial stressors with the emergence of poor mental health and cardiometabolic conditions in the US population. We hypothesize that exposure to psychosocial stressors across the life course, will be associated with allostatic load-related gene DNAm, and that these patterns will vary significantly by race/ethnicity and sex. Moreover, we hypothesize that life course stress-related methylation differences will be associated with cardiometabolic and mental health outcomes, and partially mediated by gene expression. We will test these hypotheses through the following specific aims: (1) Conduct DNAm testing and assess variation by age, race/ethnicity, sex, and SES among 4,200 Add Health participants; (2) Assess whether life course psychosocial stressors (e.g. socioeconomic adversity, trauma) are associated with DNAm in allostatic load genes among Add Health participants, including a subset of siblings and twins; and (3) Examine whether allostatic load gene DNAm is associated with cardiometabolic health and depression measures in adulthood. We will also assess whether these associations are mediated by gene expression. Overall, our proposal will provide an unprecedented epigenetic resource available to the global scientific community, and will identify novel pathways by which life course psychosocial stressors influence functional- and health relevant DNAm in the largest US nationally representative, racially/ethnically-diverse longitudinal study of social exposures on health.