

Expert Meeting on the Harmonization and Coordinated Analysis of Behavioral and Psychological Phenotypes

**The National Academies of Sciences, Engineering, and Medicine
Division of Behavioral and Social Sciences and Education
Board on Behavioral, Cognitive, and Sensory Sciences**

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Meeting Summary

Introduction

The National Institute on Aging (NIA) Division of Behavioral and Social Research (BSR) supports longitudinal studies of many small- to mid-size cohorts that gather a significant range of detailed phenotypic data and that collectively span the life course. To investigate the direct factors and mediators affecting health and well-being in later life, the studies amass rich and wide-ranging data on behavioral and psychological processes related to personality, stress, emotion, social relationships, self-regulation, decision-making, and health behaviors. Many of these studies include detailed cognitive assessments. The studies also use a variety of data collection protocols and include an increasing number of useful biomarker and neuroimaging assessments.

Principal investigators and staff of four pertinent longitudinal studies joined members of the Board on Behavioral, Cognitive, and Sensory Sciences (BBCSS) of the National Academies of Sciences, Engineering, and Medicine and NIA staff to discuss the challenges, opportunities, and potential benefits of increasing coordination and collaboration among these and similar studies. Participants also discussed ways to encourage more multicohort publications to help address replication issues and extend findings to different demographic subgroups and settings. Researchers can use the multicohort studies to identify new mediators and processes that influence health or disease progression while exposing limitations of previous findings. The meeting agenda and list of attendees are included as Appendices 1 and 2, respectively.

In terms of next steps, the investigators embraced the idea of coordinating their research studies. They agreed that the meeting helped to establish new working relationships, elucidate the value of small-cohort studies, and generate ideas to integrate data and harmonize constructs from their longitudinal studies. The investigators also identified challenges in developing a new generation of multicohort studies.

Specifically, participants agreed that small-cohort studies tend to be lower cost, agile, easier to implement and modify, and more risk tolerant. The studies also offer more innovation and granular measures revealing detailed data about factors that can influence health and well-being across the lifespan. Many small-cohort studies assess similar constructs such as personality types, stress, cognitive changes, and physiologic changes over time. Harmonized data from these studies could reveal the trajectory of events and uncover potential causal mechanisms on the pathway to development of Alzheimer's disease (AD) and other aging-relevant diseases and conditions. Such findings could inform the design of prevention, health promotion, and other early interventions. At the same time, participants warned against overly harmonizing data because investigators can learn from comparing findings on similar constructs derived from different measures and protocols.

Measurement and methodological issues dominated the discussion of research challenges that could hamper small-cohort coordination and collaboration. Like other longitudinal studies, small-cohort studies must address the fact that, as science progresses, new technologies

emerge, biological samples degrade, and pertinent standards or diagnostic criteria change. Funding for new ventures, peer review, and lack of time also pose potential obstacles.

As one solution, participants strongly endorsed forming a collaborative network for small-cohort studies. Comprised of no more than five or six existing studies, a network could be organized to address and test several critical questions or hypotheses. In addition, participants enthusiastically suggested a range of workgroups, workshops, and symposia to augment or precede network formation. These activities could include a forum for investigators to produce topic-specific findings of joint concern using data from their individual studies. Comparing results derived from studies using different methodological approaches could highlight topics for future collaborations. Participants suggested supporting new platforms to share information on methodological issues, genotyping, and measures focused on mediators of behavior change. Finally, participants urged NIA to share the meeting's recommendations by widely disseminating the report and hosting mini-symposia at annual meetings of various societies. NIA reminded participants that researchers with existing projects can seek supplemental funding to support initial collaborations, and NIA has issued annual calls for researchers to supplement ongoing studies with AD measures.

Setting the Stage: Perspectives from NIA and Investigators

Introductory Remarks from NIA

Lis Nielsen, Division of Behavioral and Social Research, National Institute on Aging

To better understand the variables and processes that influence health and well-being in later life, NIA supports a range of longitudinal studies; some, like the Health and Retirement Study and its sister studies around the world, have as many as 20,000 participants. Over the years, NIA has sought to harmonize the measures and outcomes of these studies to create an open-access database for widespread use. As a result, a new generation of multidisciplinary researchers specializing in secondary data analyses now use these large data sets to launch their research careers.

NIA also supports smaller longitudinal studies of individual behavioral and social processes whose data may be less readily available to researchers outside the investigative team. No set threshold defines the sample size of these studies. Rather, while the primary purpose of population-based studies is to generate a data set for use by the broader research community, the smaller studies are designed to test specific hypotheses. They also tend to be psychologically oriented and capture different parts of the life course.

Compared to larger population-based studies, smaller studies can offer mobile monitoring, in-depth measures, and the ability to measure both cognitive and biological aging with more comprehensive assessments. Many studies contain rich data on individuals' everyday life experiences. Many include biomarkers or challenge tasks; some include neuroimaging. Often, these studies measure similar constructs and, thus, collectively hold promise for informing understanding of factors that contribute to successful or unsuccessful aging trajectories. Historically, NIA has not engaged in strategic efforts to bring together these studies to explore

the potential for collaboration and collective research advances. This meeting is a first step to explore the potential value of harmonizing constructs or conducting harmonized analyses by providing a forum to encourage collaboration among principal investigators or small-cohort studies.

Description of Cohorts, Designs, Measurements, and Findings

Moderator: Susan Fiske, Princeton University, National Academy of Sciences (NAS), Chair, BBCSS

The Dunedin Multidisciplinary Health and Development Study¹

Terrie Moffitt, Duke University and Member, BBCSS

Over 45 years, the Dunedin Multidisciplinary Health and Development Study has amassed detailed data on a New Zealand birth cohort. Started in 1972, the study was founded as a multidisciplinary, longitudinal research enterprise that could evolve over the years to explore different domains. The study has retained about 94 percent of its original 1,037 participants, largely because of concerted staff efforts to remove participation barriers. The study continues to focus on different research themes, including mental health and cognition, cardiovascular health, respiratory health, sexual and reproductive health, oral health, and psychosocial functioning. The data link to a broad range of New Zealand administrative, clinical, and biomarker data derived from brain imaging, blood work, and genetic analyses. Because of its breadth, the study offers a wide range of collaborative and secondary research opportunities.

One of the study's notable strengths is its focus on questions of child health development; it attempts to understand not only the nature and prevalence of early developmental problems but also some of their correlates and long-term implications. The archival data set contains an extensive list of measures ranging from childhood socioeconomic status (SES) characteristics and myriad health-compromising behaviors, to personality, psychopathology, and fitness, and to multiple biomarkers such as adiposity, telomere length, and hormonal and inflammatory measures.

Because the Dunedin Study is known for its remarkable retention rates, meeting participants were eager to understand the basis for its success. One key factor is staff's time and effort to tailor and schedule assessments to meet the personal needs of the study participants. In addition, the investigators held follow-up assessments over 2 years and, because of the way that different assessments were scheduled, attrition was not cumulative. Even if participants could not participate in one assessment, all participants were invited back. Finally, the cohort and the community continue to have a personal investment in the study and its findings.

Given its outstanding retention and data collection strategies, the Dunedin Study has generated many interesting findings:

¹ R. Poulton, T.E. Moffitt, P.A. Silva PA, "The Dunedin Multidisciplinary Health and Development Study: overview of the first 40 years, with an eye to the future," *Soc. Psychiatry Psychiatr. Epidemiol.* 50(5), 679–693 (2015), <https://doi.org/10.1007/s00127-015-1048-8>.

- **Lead exposure contributes to downward mobility:** Many people aged 40-60 (Baby Boomers) were uniquely exposed to large levels of lead given its widespread use in everything from paint to gasoline. With New Zealand lead exposures more equally distributed across SES classes, investigators found that study participants exposed to the highest levels of lead experienced the greatest loss of social mobility compared to their parents. High-exposure study participants also lost 3 IQ points, which contributed to their downward social mobility.
- **Variations in trajectories of psychiatric disorders:** Examining 17 disorders over four decades, investigators found that individuals moved in and out of different psychiatric disorder categories, often in a hydraulic-like random process and in unique patterns. These findings underscore how multiple diagnoses and variability in patterns can prove to be a general liability for the psychopathology that flows through the life course and can bubble up at different times. The findings also suggest that investigators can fail to gain a rich understanding of what occurs in individuals with psychiatric disorders if the research only addresses one disorder at a time.
- **Pace of aging:** Reviewing evidence across 18 different biomarkers, investigators found that physical fitness began to decline noticeably by age 38. Blood pressure increased, as did blood sugar levels and other progressive markers over time. When trying to model this decline, researchers discovered that some individuals aged “biologically” up to 2 years in a single year compared to others who did not age at all during the same period.

The Adult Health and Behavior Project²

Stephen B. Manuck, University of Pittsburgh

The Adult Health and Behavior (AHAB) Project was originally created as an institutional resource for the study of midlife individual differences, particularly with respect to potential genetic influences. As the study evolved, it provided synergistic data from multiple domains that have continued to fertilize publications on topics ranging from personality, preclinical vascular disease, and health behaviors to cognition, self-regulation, and neural processing of emotion and reward.

AHAB recruited its original 1,295-person cohort from southwestern Pennsylvania. The project started in 2001 as a community-based registry and collected initial data through 2005 from healthy individuals, ages 30-54, with modest exclusions. The cohort is representative of the surrounding geographic region in marital status and workforce participation and maps regional variation in educational attainment and income levels.

For the core protocol, individuals underwent four 5-hour sessions, which broadly assessed lifetime SES, early-life family environment, medical and psychiatric history and symptomatology, chronic disease risk factors and health behaviors, social relationships, personality, and cognitive abilities, as well as instrumented measures of cardiovascular,

² S.B. Manuck, “Descriptive materials for the Adult Health and Behavior (AHAB) Project: BBCSS workshop on harmonization and coordinated analysis of behavioral and psychological phenotypes” (unpublished paper, June 6, 2019).

metabolic, autonomic, and immune functioning and genetic variation in pathways germane to registry phenotypes. In addition, investigators designed seven sub-studies with 110-450 individuals each, which included vascular and brain imaging, ambulatory physiological studies, and centrally acting neuropharmacologic challenge.

AHAB's diverse measurement framework allowed multiple ancillary and subsidiary grants to be funded, hypotheses to be tested, and many articles to be published. Examples of the latter include studies of personality; sleep and circadian disruptions in cardiometabolic risk; the role of long chain fatty acids in mood and cognition; effects of childhood SES disadvantage on impulsive decision-making in adulthood; and behavioral and brain correlates of systemic inflammation and oxidative stress. Then, in 2017, with support from NIA, the investigators launched wave two of AHAB, which is designed to examine the physiological and psychological changes that the original study participants may have sustained over the years since their initial enrollment time. The investigators also launched a successor study to the original AHAB project, AHAB2, supported by the National Heart, Lung, and Blood Institute, that focused on evaluating neural correlates of emotion, emotion regulation, and reward processing in association with cardiovascular risk factors and preclinical vascular disease. AHAB2 is also currently in wave two, with a primary goal of examining the role of metabolic and inflammatory mechanisms in mediating age-related changes in brain morphology and cognitive functioning, as associated with SES disparities.

Given the overlap of many measurements in AHAB and AHAB2, the investigators obtained supplemental NIA funding to consolidate the two protocols to create a single, larger longitudinal aging cohort. This consolidation is termed AHAB+, and investigators have added measurements, such as neuroimaging, so that all of the same phenotypes are collected on all participants. The AHAB studies also host extensive facilities for storing blood and other biological specimens that will allow investigators to collect additional samples and seek collaborations to extend their work into novel areas, such as cellular aging, epigenetic profiling, and polygenic scoring.

The Effects of Stress on Cognitive Aging, Physiology, and Emotion (ESCAPE) Project³

Martin J. Sliwinski, Pennsylvania State University

The ESCAPE Project examines the effects of psychological stress in daily life and its mediators on cognition and aging. ESCAPE emphasizes measuring experiences and cognitive function in natural settings and in real time. The project also aims to develop and validate assessment protocols and software collection strategies using mobile technology.

ESCAPE consists of a relatively small, systematic, probability sample of 320 individuals chosen from registered voter lists of Co-Op City residents in the Bronx, New York. Participants are ages 25-65, which helps investigators to evaluate age gradients in stress and cognition before social safety-net programs and the effects of selective mortality and preclinical dementia can

³ B. Scott, "The effects of stress on cognitive aging, physiology, and emotion, (ESCAPE) project," *BMC Psychiatry* 15, 146 (2015), <https://doi.org/10.1186/s12888-015-0497-7>.

influence findings. Although the sample is diverse demographically, the investigators can hold constant the effect of neighborhood exposure and related SES factors.

The project uses a prospective longitudinal measurement design with participants completing a baseline assessment and three follow-up waves of data collection. During each assessment, participants completed a 14-day burst of brief daily surveys including when they first awoke and before going to bed. In addition to personality tests, clinical interviews, medical evaluations, and neurological assessments, participants also completed Ecological Momentary Assessments (EMAs) throughout the day to improve the temporal precision of measurements.

Primary analyses examined three domains: (1) stress, including early childhood adversity, role stressors, chronic stress, major life events, and minor daily hassles; (2) the role that repetitive thoughts played in mediating the effects of stress; and (3) detailed features of cognition. In addition, the project will continue to add biomarkers, such as those for inflammation, metabolic function, and DNA methylation.

Some of the most important findings are methodological and relate to the design and validation of the EMA cognitive tests on mobile devices. The investigators designed a dozen tests to be brief, intuitive, and difficult to cheat on. Among others, a working memory test and a speed of processing test proved to be particularly useful, quick to administer, and highly valid. Two days of EMA testing, which corresponds to only 5 minutes of testing, produced more reliable estimates than researchers could obtain in a laboratory setting. In addition, the researchers found that the EMA tests correlate highly with results on gold standard tests.

To encourage future collaborations and data harmonization, ESCAPE investigators are developing an open-science Wiki platform with NIA support to help other investigators administer the mobile cognitive tests and share data. For each cognitive test, the platform will provide an overview, references, lists of studies using the measure, screen shots, videos, technical specifications, and analysis scripts.

St. Louis Personality and Aging Study^{4,5,6}

Thomas Oltmanns, Washington University in St. Louis

The goal of the St. Louis Personality and Aging Study is to better understand the stability and impact of personality pathology in middle age and later life with detailed and comprehensive analysis of phenotypic personality characteristics. Starting in 2007, with funding from the National Institute on Mental Health, investigators aimed to study the trajectory of personality

⁴ T.F. Oltmanns, M.M. Rodrigues, Y. Weinstein, M.E.J. Gleason, "Prevalence of personality disorders at midlife in a community sample: disorders and symptoms reflected in interview, self, and informant reports," *J. Psychopathol. Behav. Assess.* 36(2):177–188 (2013), <https://doi.org/10.1007/s10862-013-9389-7>.

⁵ C.C. Conway, M. Boudreaux, T.F. Oltmanns, "Dynamic associations between borderline personality disorder and stressful life events over five years in older adults," *Personality Disorders: Theory, Research, and Treatment* 9(6):521–529 (2018). <http://dx.doi.org/10.1037/per0000281>.

⁶ J. McClendon, J. Jackson, R. Bogdan, T.F. Oltmanns, et al., "Trajectories of racial and gender disparities during later midlife: connections to personality," *Cultur. Divers. Ethnic Minor. Psychol.* 25(3), 359–370 (2019), <http://dx.doi.org/10.1037/cdp0000238>.

disorders that begin in early life. The original community-based sample included 1,630 individuals, ages 55 to 64, who reflected the demographics of St. Louis and surrounding suburbs. The researchers used semi-structured diagnostic interviews and informant data to examine personality disorders, personality traits, and maladaptive behaviors.

In 2014, the investigators launched Phase 2 of the study with NIA support, adding biomarkers and collecting measures of stress hormones, inflammation cytokines, and cortisol levels. The study also amassed additional blood and saliva samples to conduct genotyping and other tests. Started in 2019, Phase 3 collects data on the children and grandchildren of the original cohort to investigate the transgenerational transmission of stress and health disparities.

Current data sets include variables pertaining to sleep problems, depression, loneliness, relationship satisfaction, partner aggression, and social network support. The study recently added IQ measures; measures of religiosity, ethnic identity, and neighborhood features; and data from the AD8, a brief informant questionnaire about changes in memory and other cognitive functions. In addition, the investigators added an everyday discrimination scale to better understand how exposure and reactions to discriminatory events influence cognitive functioning and health disparities.

Among its findings, the St. Louis Study has shown that, at some time in their lives, most subjects experienced major depression. About 10 percent had met the criteria for at least one personality disorder at baseline. In addition, features of Borderline Personality Disorder (BPD) that are associated with increased health problems are also associated with such factors as lower levels of social integration, not being married, more frequent divorce, and loneliness. Methodologically, the investigators also found that it is useful to assess what happens at the maladaptive extremes to find stronger associations between personality and health. Although it can be expensive to do so, it is also very useful to obtain reports from informants because they are more likely to report BPD at lower and more detailed levels. It is also important to assess the different facets associated with the main personality types.

Discussion

Moderator: Terrie Moffitt

Over the years, human cohort studies have changed greatly. Once dominated by small-cohort studies designed to test very specific hypotheses, the field is increasingly moving toward extremely large cohort studies designed to provide large, open access data sets. This shift has changed the research culture, specifically in the types and composition of research teams. In addition, rather than creating their own data sets, younger researchers are turning to mega-cohort studies to jumpstart their careers. Therefore, the more modest-sized cohort studies, such as those represented by the meeting participants, fill an important niche that has yet to be fully exploited for its detailed and rich combination of psychosocial, behavioral, and biomarker data. NIA supports a wide range of these studies, which, when harmonized, present a host of future research opportunities for junior as well as established investigators.

No matter the topic, participants repeatedly returned to measurement and methodological issues. These common themes emerged from most discussions regarding the feasibility of collaborating and harmonizing data in both small- and large-cohort studies. Participants explained that, regardless of cohort size, longitudinal and developmental studies assess constructs and key variables that change over time. However, many measurements, assays, technology, and standards for defining and assessing these constructs may change rapidly as science progresses. In addition, biological samples can degrade over time and the platforms for testing them change—creating challenges for smaller studies, which often assess personality constructs and biomarker data with more granularity. It also complicates harmonization of data among small-cohort studies that use different age groupings, where an instrument or construct applied when the cohort was younger may not be appropriate as the cohort ages. Finally, investigators themselves may change over time, raising issues of internal consistency.

Participants also discussed the challenges that etiological factors and changes in classification of diagnoses may pose for identifying psychiatric disorders over time. For example, etiological factors for some psychiatric disorders lack needed specificity, which is complicated by the fact that some disorders overlap in their diagnostic criteria or share causal roots. Although most research looks at a current diagnosis, it is highly possible that within a few years the same individuals may be diagnosed with a completely different disorder. To make sense of changing diagnoses over time and to determine whether observed changes are real, researchers should assure the validity and reliability of the initial diagnostic tests, measurements, or criteria used to identify a psychiatric disorder. This assurance can be accomplished by conducting extensive test/retest procedures during the study's pilot phases and/or by conducting test/retest procedures at shorter intervals and determining the magnitude of change relative to test/retest results obtained at a much longer intervals.

Participants then discussed a set of questions about the best ways to collaborate and harmonize data, which was distributed before the meeting. Their ideas and suggestions are summarized below.

Question 1: Era of Large Data Collections

In this era, data-collection is increasingly being assigned to large-N contractors (UK Biobank, All of US, NIDA's ABCD Study, HRS, Scandinavian-style government registers). This means that research by individual social and behavioral scientists is increasingly done as secondary data analysis. What are some of the advantages and pitfalls of this new system?

Participants raised several concerns that are pertinent to large-N studies. For example, larger studies and data sets tend to use variables that, while appropriate for use in such population-based data-gathering efforts, may not be as precise or detailed as those that can be obtained in small-cohort studies. The data gathered could serve as proxies for the specific constructs in question. However, this approach can limit the scope and detail of hypotheses that can be generated and the granularity that can be gained in the secondary data analyses of larger studies.

At the same time, even small-cohort studies of the size described here can often detect small differences in outcome measures; however, the difficulty lies in understanding the meaning of these small effect sizes. For example, some smaller studies have detected differences as small as 0.01 to 0.03 standard deviation unit per year in cognitive functioning in the aging population. To make sense of these small changes, investigators may need to describe them in relation to a norm or their equivalency. For example, stating that “these small changes may be equivalent to a 3-year change in cognitive age” provides context and meaning to small effect findings. Another way to make sense of small effect sizes at the individual level is to look at them at a population-based or public health level, as occurred with smoking studies. The link between smoking and cancer was relatively small at the individual level, but the public health impact became evident when the link was viewed at the population level.

Question 2: Possible Contributions of Smaller-Scale Studies

In an era of mega-N samples, what contributions can best be made by smaller-scale ongoing cohort projects?

Participants believed that it may be easier for smaller studies to manage rapid changes in the way that key descriptive variables, constructs, diagnoses, biological measures, and assays are measured over time, including changes in the Diagnostic and Statistical Manual of Mental Disorders (DSM). This agility is partly due to the smaller size of the studies and their ability to reassess clinical findings using both old and new criteria or to collect extra biological specimens to repeat assays using new standards.

In addition, meeting participants believed that smaller studies can be hubs for innovation and testbeds for developing new technologies and measurements. Later, when sharing them with large-cohort studies, the newly devised, more detailed and refined measures can become benchmarks against which larger studies can validate their more wholesale measures.

Participants agreed that, in most cases, neither informant nor self-reported data were more reliable than the other. Often, investigators see them as complementary and use them in a two-tiered approach or combine them to develop composite measures and gain predictive power.

Finally, smaller studies often engage multiple informants to enhance construct validity, which can be particularly useful when identifying and trying to characterize personality disorders in the aging population. The in-depth histories usually obtained for each participant in smaller studies can also provide fertile data for examining new research questions. Similarly, because of their size, smaller longitudinal studies can be nimble and take advantage of natural experiments that may occur due to historical events, allowing investigators to develop new hypotheses and research topics over the course of the study.

Question 3: The Pros and Cons of Collaborations

How have ongoing cohort studies engaged with the open-science movement so far? What are the advantages of open science for these cohorts and what are the pitfalls?

Participants noted that NIA may first wish to explore issues pertaining to team science, the sociology of data harmonization, and the creation of new knowledge structures. This effort would include identifying the infrastructure needed to encourage small-cohort investigators to collaborate and share data in a meaningful way. It would also include understanding how best to build an environment that is conducive to collaboration among multidisciplinary researchers. Participants also noted that collaborations among small-cohort studies could increase sample size enough to reveal new and significant findings, fill important data gaps, and test a variety of hypotheses.

In terms of challenges, some meeting participants noted that it is not uncommon for peer reviewers to find that small-cohort studies are underpowered or lack innovation if they choose to use well-researched measures. They also cautioned against over-harmonizing data among small-cohort studies because much can be learned by comparing findings on similar constructs derived from different instruments and protocols. In addition, participants noted that investigators could be reluctant to collaborate given the time and work involved and the preference for solo publication rights. Finally, even though methodological papers that compare differences in research approaches or address how to collaborate on long-term cohort studies should be a natural by-product of these collaborations, such papers are often difficult to publish.

Question 4: Forming Networks and Other Suggestions

Is there any merit in small cohorts banding together in some sort of network? How might this look, in terms of network aims?

Participants discussed a range of next steps, which are summarized below.

Networks: Participants voiced strong support for developing small-cohort networks to enhance collaboration and harmonization. This network should consist of no more than five or six existing studies, and investigators should agree on standards of excellence, the need for face-to-face interactions, and how to build on the strength of shared approaches and data. The network could investigate a variety of common constructs such as personality and personality disorders, stress, child abuse and neglect, basic physiologic and SES variables, and cognitive functioning. The network could also seek to fill data gaps related to social networks, measures of subjective well-being, didactic interactions, and features of social interaction. As a first step, the network could develop small studies to align measures and outline hypotheses.

Workgroups, workshops, and symposia: In addition to forming a network, participants can continue to learn from each other through workgroups, workshops, and symposia. Workgroups could circulate protocols and measurement data to learn ways to enhance their own studies. They could also serve as “innovation panels,” aiding the development of new measures of key constructs, which ultimately could be adopted by population-based studies. A similar but

broader effort could be approached as a trans-NIH activity led by the Office of Behavioral and Social Sciences Research. During another workshop, investigators could share their approach to exemplar research topics (up to three) and the findings from their individual data sets.

Participants also suggested workshops during which investigators (1) share the successes and failures of certain methodological approaches; (2) identify the shared hypotheses, questions, or measures that could form the basis a network; (3) discuss ways to facilitate collaboration among the different research cultures represented in the cross-section of small-cohort studies; and (4) identify ways to take advantage of existing research infrastructures to aid collaboration.

Joint research papers and publications: Joint papers or publications would be the natural byproduct of networks, workgroups, and workshops. Participants suggested many topics, including a meta-level description of how best to design and implement long-term cohort studies and how to enhance collaborations among investigators who are testing competing hypotheses or working with complementary conceptual models. Collaborators could also produce a paper that explains a discrepant idea that emerges from a workshop and how the discrepancies can be explained using data from different small-cohort studies. A similar paper could review the findings from multiple studies and compare the discrepancies in methodologies that led to diverse and/or similar outcomes. Finally, participants suggested a paper about the meaning and influence of time as a variable: for example, the impact of historical forces over time (e.g., the Great Depression's or the Vietnam War's impact on constructs such as personality development or depression).

Infrastructure: Participants agreed on the need to support infrastructure that will facilitate collaborations among small-cohort studies. New platforms could be developed or existing platforms (e.g., National Archive of Computerized Data on Aging) leveraged to share information on methodological issues, samples used for genotyping, and measures focused on mediators of behavior change. A comprehensive database that characterizes small-cohort studies, including summaries of their designs, cohorts, hypotheses, and key measures, would also be useful.

Communications and outreach: To build on the momentum generated by the meeting and to fuel future ideas, participants urged NIA to widely share the workshop's report beyond a website posting. Dissemination activities could include summarizing the workshop findings in an e-newsletter to like-minded researchers. To engender enthusiasm across disciplines, NIA could also encourage scientific outreach through "multi-cohort mini-symposia" at the annual meetings of different societies.

Funding: Participants suggested the set-aside of funding to help researchers establish integrated cohort studies. Proposals could be solicited through a Funding Opportunity Announcement for a network or through a research call to address methodological or other issues identified during the meeting. Alternatively, additional funding could be made available through supplements to existing projects using standard NIH funding mechanisms. NIA's annual call for researchers to supplement ongoing studies with AD measures may be appropriate for some smaller cohort studies.

Conclusions, Reflections, and Ideas for Moving Forward

Lis Nielsen and Terrie Moffitt

Participants were excited to meet, learn about each other's research, and discuss possible ways to collaborate and harmonize data. They agreed that small-cohort studies can offer many advantages including lower cost, greater flexibility and innovation, and a more in-depth look at the many factors and mediators that influence health and well-being across the lifespan.

At a meta-level, small-cohort studies face similar measurement and methodological obstacles, and, beyond new technologies, enhanced collaborations would help to address some of these issues. However, funding for new ventures, peer review, and lack of time pose potential obstacles to collaboration. Participants suggested expanding existing or supporting new networks to address some of these obstacles, as well as supporting a variety of workgroups, workshops, and symposia and new avenues for disseminating information. Joint papers and administrative supplements could help existing investigators to expand their research interests and new researchers to tackle important measurement, methodological, and theoretical concerns.

Appendix 1. Meeting Agenda

- 1:00 pm Welcome to the National Academies, Brief Introductions
Susan Fiske (NAS), Princeton University & Chair, BBCSS
- 1:10 pm Introductory Remarks from the National Institute on Aging
Lis Nielsen, Division of Behavioral and Social Research
- 1:20 pm Setting the Stage for the Seminar
Terrie Moffitt (NAM), Duke University & Member, BBCSS
- 1:30 pm Participants Describe Cohorts, Designs, Measurements, and Findings
Moderator: Susan Fiske
- Terrie Moffitt, Duke University
 - Stephen B. Manuck, University of Pittsburgh
 - Martin J. Sliwinski, Penn State University
 - Thomas Oltmanns, Washington University in St. Louis
- 3:00 pm BREAK
- 3:15 pm Questions and Discussion
Moderator: Terrie Moffitt
- Questions for invited experts, BBCSS members, and invited guests:
- In this era, data-collection is increasingly being assigned to large-N contractors (UK Biobank, All of US, NIDA's ABCD Study, HRS, Scandinavian-style government registers). This means that research by individual social and behavioral scientists is increasingly done as secondary data analysis. What are some of the advantages and pitfalls of this new system?
 - In an era of mega-N samples, what contributions can best be made by smaller-scale ongoing cohort projects?
 - How have ongoing cohort studies engaged with the open-science movement so far? What are the advantages of open science for these cohorts, and what are the pitfalls?
 - Is there any merit in small cohorts banding together in some sort of network? How might this look, in terms of network aims?
- 4:30 pm Conclusions and Reflections
Lis Nielsen
- 4:50 pm Final Thoughts: Priorities for Moving Forward
Terrie Moffitt
- 5:00 pm Adjourn

Appendix 2. List of Participants

**Member, Board on Behavioral, Cognitive, and Sensory Sciences (BBCSS),
Division of Behavioral and Social Sciences and Education*

*John Baugh, PhD, Washington University in St. Louis
*Laura L. Carstensen, PhD, Stanford University
*Judy R. Dubno, PhD, Medical University of South Carolina
*Susan T. Fiske, PhD, Princeton University
*Wilson S. Geisler, PhD, University of Texas, Austin
*Michele Gelfand, PhD, University of Maryland, College Park
*Nancy G. Kanwisher, PhD, Massachusetts Institute of Technology
*Janice Kiecolt-Glaser, PhD, The Ohio State University College of Medicine
Stephen B. Manuck, PhD, University of Pittsburgh
*William M. Maurer, PhD, University of California, Irvine
*Terrie E. Moffitt, PhD, Duke University and King's College, London
Thomas Oltmanns, PhD, Washington University in St. Louis
*Steven E. Petersen, PhD, Washington University Medical School
*Elizabeth A. Phelps, PhD, Harvard University
Martin J. Sliwinski, PhD, Pennsylvania State University

Guests

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