

# Second Annual Meeting of the Harmonized Cognitive Assessment Protocol (HCAP) Network

***National Institute on Aging***

October 29–30, 2019

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## Acronym Definitions

AAIC	Alzheimer’s Association International Conference
AD	Alzheimer’s disease
AD/ADRD	Alzheimer’s disease and Alzheimer’s disease-related dementias
ADL	activities of daily living
ADNI	Alzheimer’s Disease Neuroimaging Initiative
APOE	Apolipoprotein E
BSR	Behavioral and Social Research Division
CADAS	Caribbean American Dementia and Aging Study
CAPI	Computer-Assisted Personal Interviews
CDR	Clinical Dementia Rating
CHARLS	China Health and Retirement Longitudinal Study
CRP	C-Reactive Protein
DAD	Diagnostic Assessment of Dementia
dbGaP	Database of Genotypes and Phenotypes
DBS	dried blood spot
ELSA	English Longitudinal Study of Ageing
GeSS	Genomics for Social Scientists
GSA	Gerontological Society of America
GWAS	genome-wide association studies
HAALSI	Health and Aging Study in Africa: A Longitudinal Study of an INDEPTH Community in South Africa
HbA1c	hemoglobin A1c
HCAP	Harmonized Cognitive Assessment Protocol
HRS	Health and Retirement Study
KLoSA	Korean Longitudinal Study of Aging
LASI	Longitudinal Aging Study in India
MAR	Missing at Random
MCI	mild cognitive impairment
Mex-Cog	MHAS Cognitive Aging Ancillary Study
MHAS	Mexican Health & Aging Study
MMSE	Mini-Mental State Exam
MRI	magnetic resonance imaging

NEAT	Non-Equivalent Anchor Test (Linking)
NIA	National Institute on Aging
NIAGADS	National Institute on Aging Genetics of Alzheimer's Disease Data Storage Site
NICOLA	Northern Ireland Cohort for the Longitudinal Study of Ageing
PET	positron emission tomography
PGS	polygenic scores
SHARE	Survey of Health, Ageing and Retirement in Europe
SPS	(Chilean) Social Protection Survey
TILDA	The Irish Longitudinal Study on Ageing
USC	University of Southern California
WHICAP	Washington Heights/Inwood Columbia Aging Project

## Table of Contents

<b>Acronym Definitions</b> .....	<b>ii</b>
<b>Executive Summary and Action Items</b> .....	<b>v</b>
<b>Meeting Summary</b> .....	<b>1</b>
<b>Introduction</b> .....	<b>1</b>
<b>NIA Perspectives on Harmonization</b> .....	<b>1</b>
<b>HCAP Network Cores: Resources and Plans</b> .....	<b>3</b>
Outreach Core .....	3
Biomarker Core .....	3
Protocol Core.....	7
<b>International HCAP Studies</b> .....	<b>7</b>
HAALSI-HCAP .....	7
ELSA-HCAP .....	10
Mexican Health & Aging Study (MHAS) and MHAS Cognitive Aging Ancillary Study.....	12
HRS-HCAP .....	13
LASI-DAD.....	13
CHARLS-HCAP .....	15
<b>Future International HCAP Studies</b> .....	<b>16</b>
Chilean SPS .....	16
SHARE .....	17
TILDA .....	18
NICOLA.....	18
CADAS.....	19
<b>Statistical Harmonization</b> .....	<b>20</b>
Friday Harbor Workshop .....	20
Missing Data .....	21
Non-Equivalent Anchor Test Linking .....	21
<b>Diagnosis and Validation</b> .....	<b>22</b>
HRS-HCAP Approach and Update.....	23
Validation of HRS-HCAP in Clinical Populations .....	23
MHAS Harmonization and Validation.....	24
NICOLA Harmonization and Validation .....	25
Classification Algorithms for Cognitive Impairment in LASI-DAD .....	25
<b>Wrap Up Discussion</b> .....	<b>26</b>
<b>Appendix A: Meeting Agenda</b> .....	<b>27</b>
<b>Appendix B: Meeting Participants</b> .....	<b>30</b>

## Executive Summary and Action Items

With funding from the National Institute on Aging (NIA), the Harmonized Cognitive Assessment Protocol (HCAP) R24 Network (henceforth referred to as HCAP Network) met on October 29–30, 2019 in Bethesda, Maryland, to discuss harmonization of data collection, analysis, and algorithms across HCAP studies that are currently under way or planned, to ensure the greatest likelihood of international comparability.

The HCAP Network's **Outreach Core** developed a draft of the HCAP website and logos, as well as a style guide, which can be circulated to HCAP study investigators. The HCAP Network must reflect on whether investigators intend the HCAP website to be an outward-facing site or primarily an internal communication tool.

Because cross-study comparisons using biomarkers have been hindered by protocol and sample collection differences, the **Biomarker Core** collects information from each study cohort about existing biomarkers, planned collections, calibrations, and validations and shares this detailed information with the HCAP Network. The ongoing Health and Retirement Study (HRS)-HCAP neuroimaging project in collaboration with Alzheimer's Disease Neuroimaging Initiative (ADNI) co-investigators will help to facilitate harmonization and comparisons of neuroimaging data across studies.

The HCAP **Protocol Core** assists with licensing and communication across HCAP studies to promote harmonized procedures. The creation of an HCAP Network web resource will facilitate these efforts. David Weir suggested that HRS-HCAP and sister studies consider developing and validating their own test, which would enable the HCAP Network to move forward without dependence on external licensing.

HRS has 4 years of NIA funding to hold a **Genomics for Social Scientists** summer training workshop at the University of Michigan, aimed at providing an overview of collection, analysis, and reporting of genetic methods for studying human complex traits. Jessica Faul will notify the HCAP Network when applications for the June 2020 workshop opens in November 2019.

In addition to the HRS, the **Health and Aging Study in Africa: A Longitudinal Study of an INDEPTH Community in South Africa** (HAALSI), **English Longitudinal Study of Ageing** (ELSA), **Mexican Health and Aging Study** (MHAS), **Longitudinal Aging Study in India** (LASI), and **China Health and Retirement Longitudinal Study** (CHARLS) have completed HCAP assessments in their respective countries. Issues, challenges, and concerns were discussed:

- The HAALSI-HCAP subsample is not representative of HAALSI Baseline Cognitive Screening and has very high missing data rates for written tests, because of the low literacy levels of respondents. Therefore, HAALSI investigators are adjusting the HCAP assessment to address the missing data issue by removing tests with low accuracy.

- MHAS investigators asked HCAP investigators how to harmonize MHAS with HCAP sister studies for cases in which only cognitive or informant assessments were completed. Investigators are considering ways to address the hundreds of participants without both measures, but in the interim, MHAS will continue to retain all cases.
- LASI-DAD (Diagnostic Assessment of Dementia) developed and validated an online clinical consensus diagnostic tool as an effective alternative to in-person clinical conferences; its investigators will make disagreement data and disciplinary or geographical differences in diagnosis data available to other HCAP investigators.
- A CHARLS-HCAP validation survey consisted of individuals selected from CHARLS respondents and hospital neuropsychiatric patients, resulting in a remarkably high response rate. The first CHARLS-HCAP national survey had a 99 percent response rate. Full HCAP assessments will be included in future CHARLS waves, beginning in 2024. However, in 2021, CHARLS-HCAP will conduct an interim HCAP assessment on one-fourth randomly selected respondents who received HCAP in 2018, resulting in a subsample with HCAP completed every 3 years, rather than waiting for the next regularly scheduled full HCAP in 2024.

The **Chilean Social Protection Survey (SPS)**; **Survey of Health, Ageing and Retirement in Europe (SHARE)**; **The Irish Longitudinal Study on Ageing (TILDA)**; **Northern Ireland Cohort for the Longitudinal Study of Ageing (NICOLA)**; and **Caribbean American Dementia and Aging Study (CADAS)** plan to begin HCAP assessments. Issues and challenges concerning implementation of new HCAP international studies were discussed:

- Because assessment scoring may be challenging, SPS-HCAP investigators requested additional input from the MHAS team, beyond their instrument, manual, and study protocol support, to ensure harmonization.
- Because restrictions regarding how to collect samples differ in each of the 28 countries anticipated to participate in SHARE-HCAP, a condition validation experiment was conducted. Investigators plan to repeat the experiment across several potential participating countries.
- SHARE-HCAP investigators are assessing the need for cross-national/cross-cultural adaption of the HCAP instrument and may seek experts to provide appropriate translations of tests, because most tests in HCAP do not have a readily available translation in the relevant languages (or are of poor quality). Weir and Salima Douhou planned to discuss aspects of SHARE-HCAP that may need harmonization with HCAP studies.
- CADAS investigators will build on earlier 10/66 Dementia Research Group (henceforth referred to as 10/66) assessments conducted on individuals in urban catchment areas. CADAS will collect new nationally representative refresher samples that will supplement existing 10/66 samples.
- CADAS investigators are concerned about how some HCAP measures will accurately assess illiterate populations. Separately, Weir suggested that CADAS investigators use

2020 U.S. census data to assess Puerto Rico and consider the use of Google mapping to identify new settlements in remote locations.

**HCAP's goals** for year 1 include (1) constructing a network of study sampling leads who can work together on harmonization, (2) compiling documentation on current HCAP study sampling design, (3) considering harmonized analysis of non-response rates from international aging studies to all HCAP studies, and (4) considering implementation of revised sampling weights.

**Advanced statistical technology** allows for refined measurements of complicated datasets (e.g., those with missing data). However, attendees emphasized it is best to choose assessments that work well in all populations. Attendees raised the possibility of using HCAP data for analysis at a Friday Harbor Workshop to determine potential issues when working directly with the data. Weir confirmed that HCAP investigators will create a working group to address issues surrounding patient refusal to answer questions and how best to handle missing data.

To ensure that HCAP contains **diagnostic harmonization and validation**, HCAP investigators evaluate the use of three diagnosis methods: (1) consensus conferences, (2) algorithmic diagnoses, and (3) probabilistic models. HRS-HCAP conducted pilot validation studies in which HCAP-trained interviewers conducted HCAP testing and informant interviews, and diagnoses were derived by clinical case conferences. The HCAP renewal application proposed developing a clinical case conference to compare HCAP algorithmic diagnoses to those derived from a consensus conference of clinicians. The following issues concerning diagnostic harmonization and validation were discussed:

- The MHAS diagnostics validation study indicated that the use of algorithmic diagnostic criteria results in inconsistent clinical diagnoses of mild cognitive impairment (MCI). However, attendees suggested contacting 10/66 investigators to determine whether the informant questionnaire aids in diagnosis. In addition, MHAS investigators asked HCAP investigators to clarify how domains will be grouped and the classification algorithms to be used.
- Attendees discussed the importance of choosing a representative clinical sample and the importance of physician training for in-home and clinic cognitive testing.
- Weir expressed concern about clinicians and senior trainees administering NICOLA's HCAP assessment. He indicated that highly trained individuals could introduce variability into the diagnoses, because most HCAP study interviewers have not been highly trained.
- Weir confirmed that NICOLA will need to recruit cognitively normal patients (i.e., controls) to conduct HCAP assessments in the clinic (e.g., hospital staff, family members).

Preliminary analysis of **LASI-DAD's classification algorithm** suggests that age and education are most predictive of cognitive status, and summed orientation scores predict cognition better than memory scores in literate and illiterate individuals. Alden Gross plans to assess the ability to perform cross-national classification with LASI algorithms. However, the purpose of this

preliminary analysis was to estimate prevalence and correlates, not to evaluate causal predictors or outcomes.

### **HRS-HCAP Action Items**

- The Outreach Core will share the HCAP logo style guide with sister studies and contact the Cohort Studies of Memory in an International Consortium to discuss methods of harmonization.
- HCAP and its sister studies will further discuss how to protect sensitive HCAP Network information.
- Jessica Faul will alert the HCAP Network when the application period for the Genomics for Social Scientists Workshop opens.
- Lindsay Ryan will share details about the multi-language, multi-culture protocol and scoring training session with the HCAP Network.
- HCAP investigators will develop a working group to address issues surrounding subject refusal to answer questions and how best to handle missing data.

### **International HCAP Sister Study Action Items**

- LASI-DAD will make disagreement data and disciplinary or geographical differences in clinical diagnosis available to investigators.
- SPS-HCAP investigators requested input from the MHAS team (Rebeca Wong and Silvia Mejia-Arango [MHAS Cognitive Aging Ancillary Study, or Mex-Cog]) to ensure appropriate HCAP respondent scoring. In addition, SPS-HCAP will contact Jennifer Manly regarding HCAP validation issues.
- William Dow will follow up with attendees to discuss how to proceed with appropriate assessments for illiterate populations in CADAS.
- SHARE-HCAP investigators will discuss aspects of SHARE-HCAP that may need harmonization with HCAP sister studies with Weir and Kenneth Langa.
- HCAP investigators should identify potential individuals to participate in a working group to address issues surrounding subject refusal to answer questions and how best to handle missing data.
- Attendees will share potential ideas for R24 Network support by January 1, 2020, with Weir and will report on progress at the next HCAP meeting.



## Meeting Summary

### Introduction

The Harmonized Cognitive Assessment Protocol (HCAP) was designed by the Health and Retirement Study (HRS) in consultation with several of its international sister studies to provide a comparable instrument for measuring cognitive function among older adults around the world. With funding from the National Institute on Aging (NIA), the HCAP R24 Network (henceforth referred to as HCAP Network) promotes continued harmonization of the HCAP studies through annual meetings and other collaborative activities. The focus of this second annual meeting of the HCAP Network, held October 29–30, 2019, in Bethesda, Maryland, was to discuss harmonization of data collection, analysis, and algorithms across HCAP studies that are currently under way or planned, to ensure the greatest likelihood of international comparability. With increasing funding appropriations for and interest in Alzheimer's disease (AD), the opportunity to assess cognitive aging and impairment with international HCAP studies is great. Attendees included investigators from all of the HCAP participating studies (see **Table 1**). See Appendix A for the meeting agenda and Appendix B for a list of meeting participants.

### NIA Perspectives on Harmonization

*John Phillips, Chief, Population and Social Processes Branch, Division of Behavioral and Social Research (BSR), NIA*

The HCAP Network is an important initiative for NIA. Although NIA has numerous priorities surrounding AD, it has set specific milestones toward better understanding of the international prevalence of AD. Many HCAP study investigators have received NIA awards to study this topic. The HCAP Network, focused largely on harmonization across studies, helps to facilitate discussion about protocols, survey questions, analysis, and algorithms focused on the international prevalence of AD. Harmonization is critical for meeting both NIA and Network objectives. Phillips is the NIA program official responsible for most of the international HCAP projects, as well as both the HCAP and International HRS Harmonization Networks. He will seek to facilitate harmonization across all HCAP studies in these roles. He is joined by several other NIA representatives in supporting the goals of the HCAP Network, including Jonathan King (BSR) and Dallas Anderson (Division of Neuroscience), who provide valuable guidance to HCAP investigators.

### HCAP Network Overview

*David Weir, University of Michigan*

The HCAP Network, funded by NIA to harmonize HCAP studies, consists of two co-principal investigators (i.e., Kenneth Langa [publications] and Weir [contact]), six cores (i.e., Outreach [Amanda Sonnega], Protocols [Lindsay Ryan], Biomarkers [Jessica Faul], Sampling [Weir], Diagnosis [Langa], and Statistical Harmonization [Rich Jones]), and international participating studies (see **Table 1**).

**Table 1.** HCAP Participating Studies

<b>Country</b>	<b>Study Name</b>	<b>Acronym</b>
<b>Mexico</b>	Mexican Health and Aging Study	MHAS
<b>United States</b>	Health and Retirement Study	HRS
<b>England</b>	English Longitudinal Study of Ageing	ELSA
<b>China</b>	China Health and Retirement Longitudinal Study	CHARLS
<b>India</b>	Longitudinal Aging Study in India	LASI
<b>South Africa</b>	The Health and Aging Study in Africa: A Longitudinal Study of an INDEPTH Community in South Africa	HAALSI
<b>Chile</b>	Social Protection Survey	SPS
<b>Europe</b>	Survey of Health, Ageing and Retirement in Europe	SHARE
<b>Ireland</b>	The Irish Longitudinal Study on Ageing	TILDA
<b>Northern Ireland</b>	Northern Ireland Cohort for the Longitudinal Study of Ageing	NICOLA
<b>South Korea</b>	Korean Longitudinal Study of Aging	KLoSA
<b>Caribbean</b>	Caribbean American Dementia and Aging Study	CADAS

The HCAP Network has funding for 5 years, during which it will continue to (1) support harmonized study design, implementation, and data release across countries; (2) encourage comparative research across international studies; (3) inform NIA and HCAP study investigators of developments and opportunities at the annual plenary and satellite meetings; and (4) maintain and strengthen the six core labs, pilot projects, focused data analysis (e.g., 10/66 Dementia Research Group [10/66] and HCAP data), and extended lab visits. Researchers from HCAP studies often attend the Alzheimer’s Association International Conference (AAIC). However, the 2020 AAIC meeting in the Netherlands will likely coincide with other AD meetings.

## **HCAP Network Cores: Resources and Plans**

### **Outreach Core**

*Amanda Sonnega, University of Michigan*

The 2020 Gerontological Society of America (GSA) meeting provides various instructional opportunities (e.g., pre- and post-conference workshops) that will likely coincide with other relevant conferences. Therefore, proper coordination and communication will be key to maximizing the benefits of all the conferences relevant to HCAP study investigators.

The Outreach Core drafted an HCAP website template, which includes four main tabs: (1) the “About” section includes information about the HCAP Network, the investigators involved, links to all HCAP studies, and Network meetings; (2) the “Opportunities” section includes details about HCAP pilot projects, junior faculty exchanges, and instructional activities (e.g., pre-conference workshops, recorded and archived webinars); (3) the “Publications” section includes a database of all HCAP publications; and (4) the “Resources” section provides useful HCAP study tools.

The Outreach Core also developed HCAP logos for use in various forms of communication (e.g., PowerPoint presentations) and a style guide, which can be circulated to HCAP study investigators.

### **Discussion**

HCAP branding is useful. However, HCAP must consider whether the HCAP website is intended to be an outward-facing site or an internal communication tool, especially because the HCAP Network does not have funding to provide resources for additional HCAP studies. HCAP study investigators must consider how to protect sensitive HCAP Network information.

Because some HCAP studies do not use the HCAP name, part of the current HCAP logo can be used to brand those studies independently (i.e., the logo is not copyrighted). Further, because the main HCAP website may not provide pages for each independent study, investigators can provide links to their studies for posting on the main HCAP website. Sonnega can aid in developing personalized webpages for HCAP studies, and the HCAP main site will likely include a library of publications and general references in the future.

The Outreach Core will contact the Cohort Studies of Memory in an International Consortium (COSMIC) to discuss methods of harmonization.

### **Biomarker Core**

*Jessica Faul, University of Michigan*

The Biomarker Core disseminates information and data to all users and harmonizes biomarker, genetics, epigenetics, and neuroimaging data. It also performs measurements, including periodicity, eligibility, sample size assessment, data organization, and sample weights as necessary for the HCAP Network.

Because cross-study comparisons using biomarkers have been hindered by protocol and sample collection differences, the Biomarker Core collects information from each study cohort about existing biomarkers, planned collections, calibrations, and validations. The Biomarker Core then shares this detailed information with the HCAP Network on its intranet. The University of Southern California (USC)/University of California Los Angeles Center on Biodemography and Population Health, led by Eileen Crimmins, is assessing how to facilitate harmonization of biomarkers across studies. Some information from the intranet has generated publications, including dried blood spot (DBS) protocols and testing.<sup>1</sup>

Many HRS-HCAP data files contain biomarkers, including physical measures (e.g., blood pressure, grip strength, height and weight, waist circumference) and DBS analyses (e.g., hemoglobin A1c [HbA1c], cholesterol, C-reactive protein [CRP]), which the Biomarker Core routinely assesses. Further, the Biomarkers Core analyzes venous blood, genetic and epigenetic, and neuroimaging data.

### **Genetic Data in HRS**

The Biomarker Core regularly assesses genotype and sequencing data and aids in developing imputations with investigators. The Biomarker Core is working with the genome-wide association studies (GWAS) consortia and data repositories (e.g., database of Genotypes and Phenotypes [dbGaP] and NIA Genetics of Alzheimer's Disease Data Storage Site [NIAGADS]) to create user-friendly products (e.g., candidate gene/single nucleotide polymorphisms, polygenic scores [PGS]).

### **Polygenic Scores in HRS**

Because genome-wide data have many variables and issues around multiple testing, and methods and software are not compatible across disciplines, simplification and reduction are needed. As a result, the Biomarker Core is working to expand access to genetic data for behavioral research with the use of PGS.

HRS conducted a methodological analysis comparing 217 methods of PGS construction across several phenotypes<sup>2</sup> and found that using data across the entire genome is a better method to identify PGS compared with using only the “top hits.” HRS released a public PGS data file based on large, published GWAS (e.g., Social Science Genetics Association Consortium (SSGAC), UK Biobank, and 23andMe samples) and established phenotypes (e.g., Educational Attainment (EA3), Depression, Neuroticism, and Subjective Wellbeing). HRS is preparing Version 4 PGS, which will also include scores for Hispanics and the mixed ancestry (admix) population, as well as an expanded set of cognition/AD scores carefully considering Apolipoprotein E (APOE).

The current versions of HRS PGS include the relationships of patient PGS and APOE-ε4 allele status, using GWAS data from various studies. In the next HRS PGS iteration, investigators will

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<sup>1</sup> Crimmins, E., Kim, J.K., McCreath, H., Faul, J., Weir, D., Seeman, T. Validation of blood-based assays using dried blood spots for use in large population studies. *Biodemography Soc Biol*, 2014, 60(1):38-48.

<sup>2</sup> Ware, E.B., Schmitz L.L., Faul, J.D., Gard, A.M., Mitchell, C.M., Smith, J.A., Zhao, W., Weir, D., Kardina, S.L.R. Heterogeneous effects of polygenic scores for common human traits. *BioRxiv*, 2017.

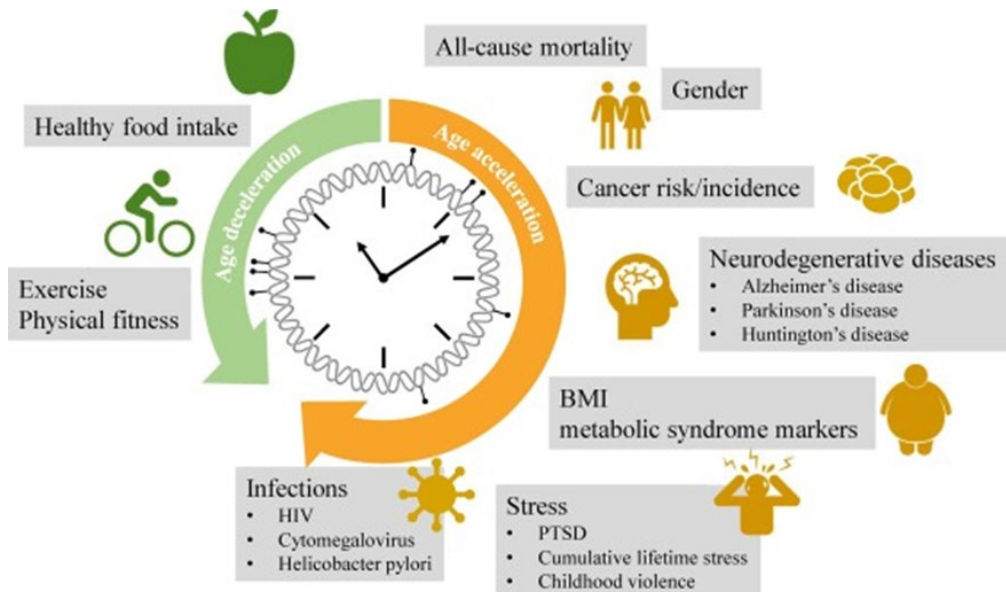
assess four scores from Brian Kunkle and colleagues' 2019 study with 21,982 total cases and 41,944 controls from four cohorts: Alzheimer's Disease Genetics Consortium; Cohorts for Heart and Aging Research in Genomic Epidemiology consortium; European Alzheimer's Disease Initiative consortium; and Genetic and Environmental Risk in AD/Defining Genetic, Polygenic and Environmental Risk for Alzheimer's Disease Consortium. This new assessment will enable HRS to determine whether the APOE risk is generalizable across populations.

### ***Genomics for Social Scientists (GeSS) Workshop***

HRS has 4 years of NIA funding (PIs: Faul, Sharon Kardia, Colter Mitchell; R25AG053227) to hold a summer training workshop at the University of Michigan, Ann Arbor, aimed at providing an overview of collection, analysis, and reporting of genetic methods for studying human complex traits (e.g., downloading data from dbGaP, computing hardware, concepts of a command line, introduction to R Programming). A subset of the workshop topics includes practical lab sessions using simulated data. HRS is developing several online modules related to biological data collection strategies, use of key statistical packages and computing resources (e.g., Linux, PLINK), and PGS creation. Faul will notify the HCAP Network when the call for applications for the June 2020 workshop opens in November 2019.

### ***Epigenetic Data***

The Biomarker Network Meeting on Epigenetics (Methylation and RNA Profiles) in Population Studies was held September 24, 2018, at NIA. HCAP Biomarker Core attendees and representatives of other population studies (including Midlife in the United States [MIDUS], the National Longitudinal Study of Adolescent to Adult Health [Add Health], Fragile Families and Child Wellbeing Study, the Dunedin Study) discussed DNA methylation and RNA profiling, quality control, data harmonization, development of public use files, and repositories for distribution (e.g., dbGaP, NIAGADS) and considered ways in which the Biomarker Core could help develop and share public files effectively. Recent work suggests that cellular aging (i.e., epigenetic clocks) may play a role in AD as well (**Figure 1**).



**Figure 1.** Declerck and Vanden Berghe’s work on epigenetic clocks.<sup>3</sup>

### **HRS DNA Methylation Data**

The HCAP Biomarker Core has completed DNA methylation analysis using the Infinium Methylation EPIC BeadChip (N=4,018), and data are ready for release (19GB HRS sensitive and restricted health data and NIAGADS). Further, 11 epigenetic clocks have been constructed by Morgan Levine at Yale University, including Horvath, Hanum, PhenoAge, and GrimAge. The full iDAT files will be released in NIAGADS only (500GB).

### **Neuroimaging**

Neuroimaging data (e.g., structural magnetic resonance imaging [MRI], amyloid imaging, and tau imaging) are increasingly used to identify individuals with AD and AD-related dementias (AD/ADRD); therefore, the Biomarker Core plans to consolidate info about best neuroimaging practices. Several HCAP projects have performed neuroimaging on subsamples of their participants (e.g., LASI, HAALSI, TILDA), while others plan to do so (e.g., KLoSA). The ongoing HRS-HCAP neuroimaging project is a collaboration with the Alzheimer’s Disease Neuroimaging Initiative (ADNI) co-investigators (including Michael Weiner, Clifford Jack, and Arthur Toga). HCAP will use the experience gained from this project to facilitate harmonization and comparisons of neuroimaging data across the HCAP studies, as well as to the ADNI data.

### **Discussion**

Brayne suggested focusing more broadly on dementia and cognitive changes, as well as risk factors across the lifespan (e.g., education), rather than on AD only. However, Weir commented that genetic analysis is often specific to AD.

<sup>3</sup> Declerck, K., Vanden Berghe, W. Back to the future: Epigenetic clock plasticity towards healthy aging. *Mech Ageing Dev*, 2018, 174:18-29.

## **Protocol Core**

*Lindsay Ryan, University of Michigan*

The Protocol Core supports two primary areas: licensing and protocol procedures, with the goal of ensuring that information is accessible and useful.

### ***Licensing***

The majority of cognitive tests included in the HRS-HCAP protocol are copyrighted and require a license to use. Adapting a test from paper to electronic versions requires additional permission. The logical memory test from Pearson requires an appropriately trained PhD-level psychologist on the research team; and the official HCAP Mini-Mental State Exam (MMSE) can now be licensed by request from Psychological Assessment Resources. The HCAP Protocol Core can assist with licensing, including providing information on how to order necessary items, as well as coordinating contracts with various licensing companies. The Protocol Core will review license request forms and will share HCAP-approved request form examples. In some cases, the University of Michigan may be able to order hardcopy materials for studies or add additional studies to existing licenses, though for others, subcontracts may be required.

### ***Discussion***

Attendees discussed test complexity across countries. Ryan confirmed that HCAP study investigators can request permission to adapt the HCAP MMSE to languages other than English. The Protocol Core's goal is to catalogue harmonized details and find current deviations.

When HCAP began, it did not have the resources to create its own assessment. However, Weir suggested that HRS-HCAP and sister studies consider developing and validating their own test, which would enable the HCAP Network to move forward without dependence on external licensing. Brayne suggested discussing MMSE licensing issues with ELSA investigators because they have successfully avoided licensing issues.

### ***Protocol Procedures and Scoring***

Copyright restrictions prevent sharing of the complete HCAP Protocol and the Blaise Program; therefore, the Protocol Core helps to facilitate communication across HCAP studies (e.g., phone/video calls to discuss questions, observational visits, interviewer training materials and certification criteria sharing, protocol/scoring discussion and documentation). The Protocol Core aims to help identify and understand differences seen across studies to develop alternate scoring methods. Ryan will provide further details on an upcoming multi-language, multi-culture protocol and scoring training session.

## **International HCAP Studies**

### **HAALSI-HCAP**

*Darina Bassil, Harvard University*

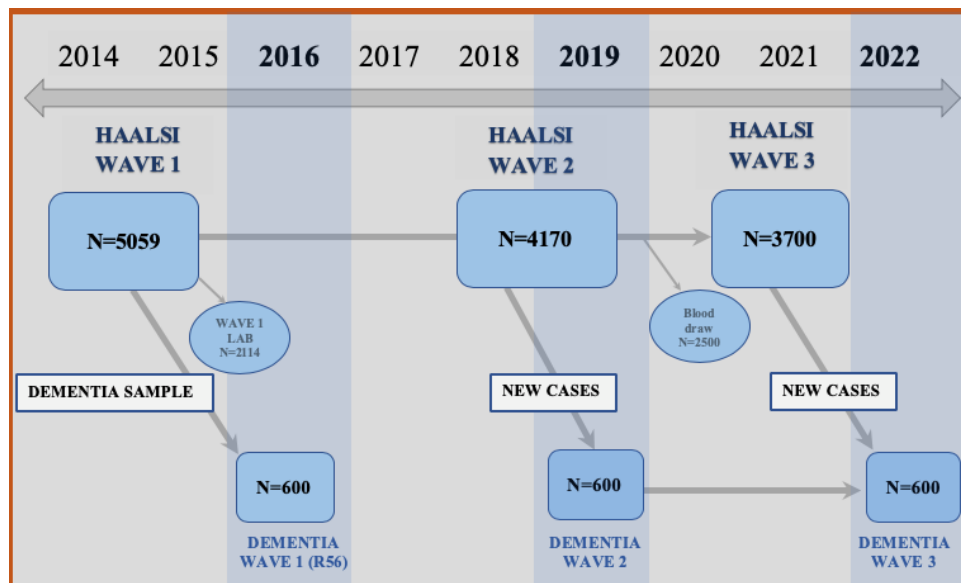
The HAALSI Baseline Cognitive Screening assessment included random sampling of individuals ages 40 and older in 27 villages in the Agincourt sub-district (N=6,281 selected; N=5,059 completed). Wave 1 ran from November 2014 to November 2015. The HAALSI Baseline



Cognitive Screening was modeled after HRS and included a questionnaire, biomarkers, and performance measures (e.g., self-reported memory, immediate and delayed recall, numeracy, number series, and orientation).

HAALSI's first project focused on dementia and cognitive function, specifically assessing the prevalence and onset of dementia, risk factors, resilience, and cognitive reserves. This assessment also identified social, economic, psychological, and biological risk factors for dementia. Investigators observed trajectories of cognitive function using novel, low literacy assessments, and they have harmonized HAALSI assessments with international assessments. HAALSI investigators are currently completing wave 2 of this assessment (**Figure 2**).

HCAP was administered to two HAALSI subsamples funded through different sources: (1) a harmonization sample funded through an NIA regular research grant (R01), including 344 participants selected via stratified random sampling based on cognitive screen scores on HAALSI Baseline Cognitive Screening; and (2) a short-term AD sample funded through an NIA high-priority, short-term project award (R56), including 263 participants who tested in the normal range during the HAALSI Baseline Cognitive Screening, stratified by age decade. Impaired participants ages 50 and older were prioritized for the harmonization R01, and respondents over age 80 were prioritized for the R56 sample. A total of 607 participants completed the HAALSI Dementia Sample wave 1.



**Figure 2.** Integration of HAALSI studies.

The average time between Baseline Cognitive Screening and Dementia Sample assessments was 20 months. However, the Dementia Sample (N=607) was not representative of HAALSI Baseline Cognitive Screening (i.e., Dementia subsample was older and less educated, with lower cognitive scores than the general population of HAALSI Baseline Cognitive Screening respondents).



From September 2016 to July 2017, HAALSI Dementia Sample respondents (N=201) were given neurological examinations, and three U.S. neurologists reviewed the summary data to assign diagnostic categories for each participant (i.e., summary cognitive scores, findings from informant questionnaires, neurological exams, diagnosis of dementia based on DSM-IV criteria, impairment in memory plus another domain, evidence of impairment in everyday function, evidence of decline from a previous state, lack of delirium or other transient condition). Investigators found that baseline impairment was 65 percent sensitive in predicting true dementia.

HAALSI has very high missing data rates for written tests, due to low literacy levels of respondents, including 45 percent missing Trails A assessments and 66 percent missing Trails B assessments; and respondents who completed Trails assessments had low accuracy rates. Therefore, timing-scores were invalid. HAALSI investigators are adjusting the HCAP assessment to address the missing data issue by removing tests with low accuracy (e.g., Trails, simple digit).

The HAALSI Dementia Sample R01 assessment (**Table 2**) includes a detailed tablet-based neuropsychological assessment (i.e., Computer-Assisted Personal Interviews [CAPI]), informant interview, neurological examination, MRIs to characterize brain atrophy (in a subsample), and a consensus diagnosis. A total of 335 participants have completed visits (i.e., respondent cognitive battery, informant interview, and neurological examination).

**Table 2.** HAALSI-HCAP Dementia Sample R01 Assessments

<b>R01 Assessments</b>
<b>(1) Informant Interview</b>
<b>(2) Respondent Interview</b>
(a) <b>General Cognitive Status: mini mental status, clock drawing, HRS telephone interview cognitive status, community screening inventory for dementia</b>
(b) <b>Verbal Memory: CERAD word recall, word recognition, Wechsler Logical Memory, Brave man story, CDR-recent memory, CDR-autobiographical memory</b>
(c) <b>Language: semantic and phoneme fluency, picture naming test, token test (LASI)</b>
(d) <b>Executive Function: go/no go (LASI), motor sequence</b>
(e) <b>Visuospatial/Visual Memory: constructional praxis/recall, spatial working memory</b>
(f) <b>Judgement/Reasoning: Ravens matrices, similarities/differences</b>
(g) <b>Attention: symbol cancellation</b>
(h) <b>Numeracy: calculations (CDR)</b>
(i) <b>Mood: CES-D 20 item</b>
(j) <b>Literacy: brief reading assessment</b>
(k) <b>Head injury: traumatic brain injury history</b>

HAALSI's wave 1 survey data were released in fall 2016 (i.e., 1 year after close of wave 1), with additional wave 1 data released in 2017 (e.g., lab visit data, HIV biomarkers). Cognition data (i.e., harmonizing dementia screening) were released in September 2019, and wave 2 survey data release is anticipated in 2020.

HAALSI investigators' future work will include the integration of waves 2 and 3 and Dementia waves 1 through 3, as well as maintenance of cohort participation.

**Discussion**

Will Dow voiced concern about the inability to assess educational differences among individuals with the removal of low-quality tests (e.g., Trails, simple digit) and those that require literacy to complete. Weir commented that interviewers may be asked to evaluate too much during the interview process (e.g., judgments about what are considered low- versus high-quality answers), and HCAP is attempting to find assessments that work well for a range of literacy levels.

**ELSA-HCAP**

*Dorina Cadar, University College London*

ELSA, the longest running cohort study in Europe and part of the Global Aging Initiative, is comparable to other aging studies across the world (e.g., HRS, SHARE, TILDA, NICOLA). ELSA-HCAP is funded by NIA and led by Andrew Steptoe at the University College London, with research support from Cadar and Jessica Abell. ELSA investigators have completed eight waves of data collection, including data from several cognitive function tests (e.g., memory, orientation, attention, language). ELSA completed one wave of HCAP from January 2018 to April 2018, including a stratified subsample of 1,273 adults ages 65 and older. ELSA-HCAP is the first England-wide dementia study completed, including extensive neuropsychology and clinical assessments and an international algorithmic dementia diagnosis. ELSA-HCAP wave 1 data were released in August 2019.

ELSA-HCAP required only minor language adaptation from HRS-HCAP. Participants were selected for ELSA-HCAP if they were an ELSA core member age 65 or older at the start of fieldwork in January 2018 (i.e., born before January 1, 1953) and completed an in-person ELSA interview in either wave 7 (2014 to 2015) or wave 8 (2016 to 2017).

ELSA-HCAP was administered to participants across all cognitive abilities, but participants identified as having low cognitive scores on prior modified Telephone Interview Cognitive Screening (mTICS) were oversampled. ELSA-HCAP recruited 5,715 participants and separated participants into groups based on their cognitive assessment (i.e., low, moderate, and normal cognition; **Figure 3**).

The ELSA-HCAP sample had few individuals with comorbidities. From 1,050 informant interviews, 194 (18.5 percent) were completed by telephone and 856 (81.5 percent) via self-completion questionnaires. However, because response rates were often linked to cognition level, investigators chose to use a weighting procedure to adjust for bias within the three cognition groups. The final weight for the study represents a combination of the design and non-response weights and will ensure that results are comparable with the general population. ELSA-HCAP's data are available from UK Data Services.<sup>4</sup>

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<sup>4</sup> See <https://ukdataservice.ac.uk>, ELSA-HCAP study number 8502, DOI: 10.5255/UKDA-SN-8502-1.

Limitations of the ELSA-HCAP assessment include its (1) cross-sectional study design, (2) lack of population diversity (i.e., only 3.2 percent of the older population sampled were ethnic minorities), and (3) lack of neuroimaging data.

ELSA-HCAP facilitated the development of an international HCAP diagnostic algorithm for dementia and data linkages (e.g., National Health Service Central Register; Hospital Episode Statistics; and tax records, savings, and private pensions). ELSA-HCAP is comparable to other prominent studies of cognitive aging and dementia (e.g., Cognitive Function and Ageing Studies and Aging, Demographics and Memory Study) providing a rich source of international data that will likely form the foundation for dementia assessments in an English nationally representative sample of people ages 65 and older.

ELSA-HCAP has a study design and methods paper under review, and Cadar and Jessica Abell will present this work at the GSA meeting in Austin, Texas, in November 2019. Several analyses and publications are also in progress. Applications for ELSA-HCAP wave 2 are currently being considered for 2022.

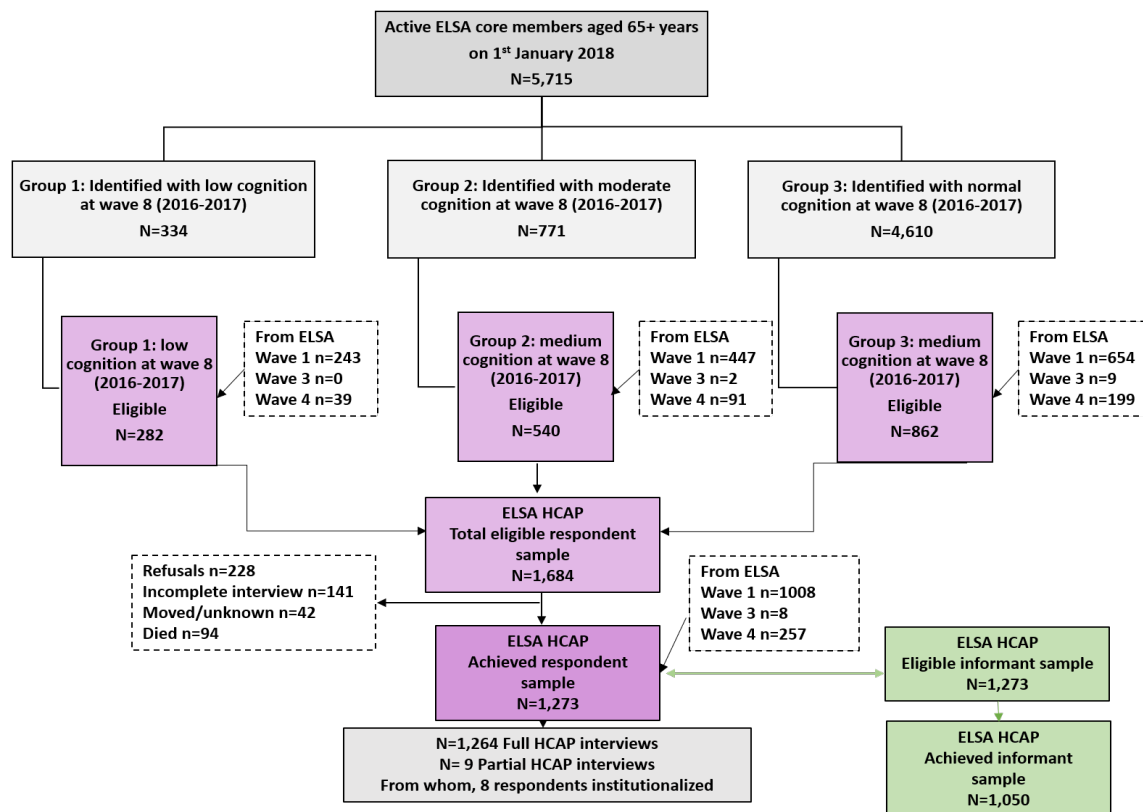


Figure 3. ELSA-HCAP sampling procedure.

**Discussion**

Brayne requested information about how ELSA-HCAP's population relates to that recruited for HRS-HCAP. She also suggested creating a flow diagram to illustrate how ELSA-HCAP and HRS-HCAP protocols compare.

**Mexican Health & Aging Study (MHAS) and MHAS Cognitive Aging Ancillary Study**

*Rebeca Wong, University of Texas Medical Branch*

The MHAS core panel wave was conducted from October to November 2015, followed by the MHAS Cognitive Aging Ancillary Study (Mex-Cog) pilot study in January 2016. Mex-Cog fieldwork occurred in two phases in 2016: March to April and September to October. The Mex-Cog sample included 70 percent of the 3,250 MHAS respondents from 2015 ages 55 and older, resulting in an effective sample size of 2,265 respondents (N=1,849 both cognitive and informant, N=193 cognitive assessment only, N=223 informant only). MHAS investigators asked HCAP investigators how to harmonize MHAS with HCAP sister studies for cases in which only cognitive or informant assessments were completed. Investigators are considering how to proceed with participants without both measures, if both measures are needed to classify cognitive status. Early data were released in December 2018, and an updated data release is expected in November 2019.

The use of CAPI often inhibits respondents unfamiliar with computers from providing accurate responses. Therefore, MHAS investigators used paper versions of the tasks that required drawing (e.g., drawing figures, writing, marking objects). However, scoring paper tasks is time-consuming. Further, many respondents have missing values in specific items due to (1) refusal, (2) previous question skips, (3) motor or visual impairment, or (4) short interviews. Because accurate scoring of missing values is challenging, MHAS investigators developed flow charts to minimize programming errors and to maximize the likelihood of harmonization with other studies.

MHAS investigators have the option to score assessments (1) based on the number of correct questions out of the maximum completed by that individual (i.e., attempted points), or (2) based on the number of correct questions out of the total possible questions (i.e., including those that the individual did not attempt). Regardless of the scoring scheme, proper data collection and documentation is necessary to maintain accuracy. Mex-Cog data users will be provided (1) cognitive assessments with raw answers and constructed scores (by task and domains), (2) informant interviews with raw and constructed variables, (3) anthropometric measures and biomarkers (on a subsample), (4) master follow-up files, (5) methods and questionnaires, including flow charts with scoring rules by task and domain, and (6) codebooks with raw and constructed variables. Detailed classification variables are expected to be released in November 2019.

In addition to measurements taken in prior waves (e.g., blood pressure, height, weight, HbA1c, Vitamin D, cholesterol), 81 percent of the Mex-Cog participants provided blood samples collected with EDTA in 2012 or 2016 and will also be evaluated for GWAS and APOE-ε4. About

60 percent of Mex-Cog participants provided saliva samples in 2018 as well. Mex-Cog is currently developing a clinical validation exercise, and fieldwork for Mex-Cog wave 2 is scheduled for spring 2020. Wave 2 will include follow-up with survivors of Mex-Cog wave 1, new participants aged 60 and older, and an oversample of mild cognitive impairment (MCI) and dementia participants.

### **Discussion**

King suggested grouping together individuals with literacy issues for analysis. Jennifer Manly proposed creating alternative items to replace original HCAP items that may be difficult to measure in communities with low literacy levels, similar to the methods used in LASI-Diagnostic Assessment of Dementia [DAD].

### **HRS-HCAP**

*Ken Langa, University of Michigan*

HRS pilot studies were conducted in August 2014, May 2015, and February 2016, followed by the HRS core panel from March 2016 to August 2017 and HRS fieldwork from June 2016 to October 2017. One-half of HRS2016 participants ages 65 and older were randomly selected for HRS-HCAP, with a response rate of 79 percent, resulting in an effective sample size of 3,496 participants (N=3,034 both testing and informant, N=313 testing only, N=149 informant only). Age, race, ethnicity, and proxy response rates were similar across groups in the 2016 HRS-HCAP cohort, with 80, 79, and 73 percent response rates in the normal cognition, MCI, and dementia groups, respectively. Early data were released in January 2019, and the final data release, including diagnostic classifications, is expected in mid-2020. The HRS-HCAP webpage has about 1,110 views and 225 data requests to date. HRS-HCAP wave 2 is planned for March 2020.

HRS-HCAP methods, including basic information and details on response rates, were recently published.<sup>5</sup> HRS-HCAP also incorporates epidemiological data, including (1) prior waves of HRS, (2) linked medical records, (3) cardiovascular risk factors, (4) GWAS (e.g., PGS for AD, cognition, and education), (5) DNA methylation (e.g., “epigenetic clocks”), and (6) whole blood assays.

In addition, HRS-HCAP is conducting an imaging pilot study (~100 patients) at Columbia University, University of Michigan, and USC using the ADNI 3 protocol (i.e., structural MRI and amyloid positron emission tomography [PET]).

### **LASI-DAD**

*Jinkook Lee, USC*

LASI is an in-depth study of late-life cognition and dementia in India using hospitals as phenotyping centers. The study includes 72,000 adults ages 45 and older, representative of the

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<sup>5</sup> Langa, K.M., Ryan, L.H., McCammon, R.J., Jones, R.N., Manly, J.J., Levine, D.A., Sonnega, A., Farron, M., Weir, D.R. The Health and Retirement Study Harmonized Cognitive Assessment Protocol Project: Study design and methods, *Neuroepidemiology*, 2019, doi: 10.1159/000503004

nation and its 30 states and 6 union territories. Individuals ages 65 and older, and those in four metropolitan cities (i.e., New Delhi, Mumbai, Chennai, Kolkata) are oversampled. LASI sampling consists of a two-stage stratified random sampling with oversampling of those at high risk of cognitive impairment.

LASI aims to (1) collect high-quality, late-life cognition and dementia data; (2) enrich geriatric and biomarker data through geriatric assessments, venous blood specimen assays, neuroimaging, and genotyping; (3) obtain clinical diagnoses; (4) estimate dementia prevalence; (5) investigate determinants of late-life cognition and dementia; (6) study the impact of dementia on families and society; and (7) disseminate anonymized data to the larger research community.

A subsample of 4,000 LASI respondents ages 60 and older were administered an enriched HCAP assessment for LASI-DAD. Fieldwork was done in three phases: October 2017 to June 2018, October 2018 to May 2019, and October 2019 to March 2020. Investigators plan to complete wave 2 from October 2021 to March 2024, and they will likely submit a renewal application in April 2020 for a subsequent LASI-DAD wave.

LASI-DAD oversampled respondents from the older population, particularly those at risk for AD, and approximately 35–40 percent were urban respondents, providing a 92 percent representative sampling of the country. LASI-DAD investigators adapted some tests because of literacy issues.

LASI-DAD includes robust geriatric and biological markers: geriatric assessments (e.g., anthropometry, blood pressure, diet); cardiovascular risk factors (e.g., self-report of stroke, heart disease, diabetes, hypertension, triglycerides); venous blood assessments (e.g., complete blood cell counts, HbA1c, lipid and metabolic panels); genomics whole genome sequencing; and whole blood analyses. The assessment also matches respondent data with air pollution exposures (e.g., aerosol, meteorological) and neighborhood conditions (e.g., density, litter, noise). LASI-DAD is collaborating on neuroimaging with National Institute of Mental Health and Neurosciences (N=54, completed); NM Medical Center, Mumbai (N=34, in progress); Institute of Neurosciences, Kolkata (N=44, in progress); and Mahajan Imaging, Delhi (at contract stage) to assess MRI and PET imaging with the ADNI 3 protocols. In addition, LASI-DAD developed and validated an online clinical consensus diagnostic tool, modeled after the Monongahela-Youghiogheny Healthy Aging Team (MYHAT) project,<sup>6</sup> as an effective alternative to in-person clinical conferences.

LASI-DAD investigators are currently generating online clinical diagnoses for the phase 2 sample, and they are developing an algorithmic model for dementia diagnoses. LASI-DAD phase 1 and 2 data were released through Gateway to Global Aging Data in December 2019. Further, investigators recently published a LASI-DAD methodology paper to illustrate the challenges they

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<sup>6</sup> Weir, D.R., et al. Reducing case ascertainment costs in U.S. population studies of Alzheimer's disease, dementia, and cognitive impairment-Part 1, *Alzheimers Dement*, 2011, 7.1:94–109, doi:10.1016/j.jalz.2010.11.004



faced<sup>7</sup> and are preparing publications for a special issue in the *Journal of American Geriatrics Society*.

### **Discussion**

Attendees discussed the process by which clinicians change their diagnostic decisions. Lee confirmed that during consensus meetings, clinicians may decide to change their initial diagnosis based on the discussion about a disagreement (e.g., subjective decisions about what an individual can successfully do). Lee also confirmed that LASI-DAD will make disagreement data and disciplinary or geographical differences in diagnosis data available to other HCAP investigators.

### **CHARLS-HCAP**

*John Strauss, USC*

A CHARLS-HCAP validation survey was conducted from July to August 2017 to select a subset of the HCAP assessments to administer. The validation survey consisted of individuals ages 65 and older selected from CHARLS respondents and hospital neuropsychiatric patients, resulting in a remarkably high response rate (93 percent) with majority of respondents completing both the HCAP tests and informant test (1,473 out of 1,591 in the recruited sample).

The first CHARLS-HCAP national survey was conducted from July to October 2018. It consisted of all CHARLS subjects ages 60 and older and had a 99 percent response rate. Of the total 11,056 participants recruited, 10,955 participants completed HCAP assessments (N=824 HCAP tests only, N=9,164 HCAP tests and informant, N=967 informant only). CHARLS-HCAP investigators published a paper providing information on the subsample of HCAP questions included in the CHARLS-HCAP assessment, as well as details about decreasing the assessment age from 65 to 60 and older to capture the largest sample of potential dementia cases over time.<sup>8</sup> Full data release is anticipated in April 2020.

Full HCAP assessments will be included in future CHARLS waves, beginning in 2024. However, in 2021, CHARLS-HCAP will conduct additional HCAP assessments on one-fourth randomly selected respondents who received HCAP in 2018 (~2,500 respondents), resulting in a subsample with HCAP completed every 3 years, rather than waiting for the next regularly scheduled full HCAP in 2024 (i.e., 6 years post initial CHARLS-HCAP assessment).

### **Discussion**

CHARLS-HCAP investigators considered respondents' negative reactions to blood collection, the interval between CHARLS-HCAP assessments (i.e., 2018 to 2024), and the necessary staff training for such a large number of respondents all at one time in 2024. CHARLS-HCAP

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<sup>7</sup> Lee, J., Banerjee, J., Khobragade, P.Y., Angrisani, M., Dey, A.B. LASI-DAD Study: a protocol for a prospective cohort study of late-life cognition and dementia in India, *BMJ*, 2019, doi:10.1136/bmjopen-2019-030300

<sup>8</sup> Meng, Q., Wang, H., Strauss, J., Langa, K., Chen, X., Wang, M., et al. Validation of neuropsychological tests for the China Health and Retirement Longitudinal Study Harmonized Cognitive Assessment Protocol. *Int Psychogeriatr*, 2019, 31(12):1709-1719, doi:10.1017/S1041610219000693

investigators discussed an interim CHARLS-HCAP assessment (with a subsample of CHARLS-HCAP respondents in 2021) to mitigate some of the potential issues with a complete CHARLS-HCAP assessment in 2024. Weir expressed concern about inconsistencies between CHARLS-HCAP and other international studies. Strauss and King commented that determining how to address the issues surrounding the extremely high response rate in CHARLS-HCAP was challenging, and an interim CHARLS-HCAP was considered the best potential solution.

## Future International HCAP Studies

### Chilean SPS

*David Bravo, Universidad Católica de Chile, and Irma Elo, University of Pennsylvania*

SPS, based largely on MHAS and HRS, was developed in 2002 by Bravo, with guidance from Jere Behrman, Olivia Mitchell, Beth Soldo, and Petra Todd from the University of Pennsylvania. SPS is a national, stratified, random, longitudinal, public use sample of about 20,000 adults ages 18 and older with seven follow-ups, with some sample replenishment over time. The latest wave is scheduled for late 2019.

The SPS Quality of Life Survey for 60+ (i.e., SPS60+) is a supplementary survey administered to 2,523 SPS participants ages 60 and older from 2017 to 2018. The survey included mental and physical health assessments, wellbeing and sociodemographic characteristics (e.g., chronic diseases associated with aging), and an abridged version of the MMSE. Data from SPS60+ can be inked to previous SPS data, providing opportunity to study predictors of physical and cognitive health. Data collected thus far support the idea that women live longer than men, and parental and personal education in women, but not men, is influential on quality of life. The Chilean government intends to proceed with future rounds of the SPS60+.

SPS-HCAP is funded by an administrative supplement to the University of Pennsylvania's P30 Population Aging Research Center (PARC) grant with supplemental funding from internal University of Pennsylvania sources. SPS investigators worked closely with Rebeca Wong and Silvia Mejia-Arango to establish the protocol with an anticipated sample size of 2,000 SPS60+ respondents, and Mejia-Arango conducted interviewer training. SPS-HCAP includes minor adjustments to Mex-Cog, and extra memory, depression, and loneliness measures were added to the end of the assessment. Fieldwork was conducted from August to November 2019 (N= 1,847 as of October 27, 2019). However, Chilean riots prohibited the continuation of fieldwork. SPS investigators hope to return to the field soon to collect the year's remaining samples.

SPS-HCAP investigators plan to prepare the database (e.g., weights, scoring) from December 2019 to January 2020, followed by data analysis from February to June 2020. They will likely compare results with other HCAP international studies and will examine predictors of cognitive change. From March to April 2020, SPS-HCAP investigators plan to conduct a validation study and anticipate validation data release in fall 2020. Because scoring may be challenging, SPS-HCAP investigators requested input from Wong and Mejia-Arango to ensure appropriate assessments. SPS-HCAP investigators will contact Manly regarding HCAP validation.



**SHARE**

*Salima Douhou, Max Planck Institute for Social Law and Social Policy, Munich Center for the Economics of Aging*

SHARE is a cross-national study on health, socioeconomic status, and social and family networks spanning 28 countries (27 across continental Europe, plus Israel). SHARE conducted a module with measures of cognitive functioning (e.g., word recall) beginning with data collected in wave 1. In wave 8, additional cognitive measures were included in SHARE to harmonize with existing HCAP studies, and SHARE's first official HCAP assessments will be conducted in wave 9.

SHARE investigators are considering potential countries to include in SHARE-HCAP: Denmark, Germany, Poland, France, Italy, Czech Republic, and Sweden. However, regulations surrounding the collection of human tissue in Czech Republic and Poland may limit collection of biomarkers there but does not endanger the collection of HCAP data in either location. SHARE investigators aim to collect data from approximately 500 respondents per country, oversampled for cognitive impairment, and harmonize the data across SHARE-HCAP countries. No clinical validation is planned for SHARE-HCAP, but investigators would be interested in adding this validation in the future.

Because restrictions regarding how to collect DBS samples differ in each country (e.g., nurses versus self-collection), SHARE conducted a DBS condition validation experiment (e.g., fieldwork temperatures), suggesting DBS are relatively stable.

The aim of SHARE is to use data from different countries to identify international aging patterns in a more cost-effective way than conducting separate HCAP studies in 28 countries. SHARE-HCAP investigators have examined the accuracy and relevance of imputing information across countries; and SHARE-HCAP investigators are considering the needs and requirements of all countries (e.g., medical and ethical approval, consent) and are aiming to complete the ethics review process by mid-2020.

HCAP translation quality across countries may be a challenge. Therefore, SHARE-HCAP might seek experts in each country to provide appropriate translations of tests, as most tests in HCAP do not have readily available translations in the relevant languages (or are of poor quality). SHARE will complete a pre-test by the end of 2020, with the main data collection in fall 2021 (i.e., end of wave 9). Participant interviews and DBS collection will be completed at the same visit.

**Discussion**

Attendees discussed challenges surrounding HCAP harmonization across cultures and acknowledged the complexity for SHARE herein. Weir confirmed that harmonization of word recall is conducted in all studies across HCAP, even when repetition is needed to successfully complete the assessment. For example, some HCAP studies conduct word recall assessments multiple times with different word lists. Generally, attendees agreed that HCAP harmonization is most important as it pertains to how investigators assess a particular domain, but no strict

harmonization of every question is needed. It is clear that SHARE needs to balance harmonization among its countries with harmonization among its sister studies. Weir and Douhou planned to discuss aspects of SHARE-HCAP that may need harmonization with HCAP studies (e.g., word recall).

## **TILDA**

*Christine McGarrigle, Trinity College Dublin*

TILDA is a nationally representative prospective cohort study of the social, economic, and health circumstances of a randomly selected, representative sample of individuals ages 50 and older in the Republic of Ireland (N=8,504). TILDA consists of (1) an in-home CAPI conducted by trained social interviewers (i.e., cognitive, socio-demographics, health, wealth, lifestyle and social support assessments); (2) a self-completion questionnaire assessing sensitive information (e.g., alcohol use, relationships); and (3) a comprehensive health assessment conducted by trained nurses. TILDA has harmonized its CAPI across international HCAP studies, though TILDA includes greater detail than many other studies. TILDA received external funding to conduct genotyping, blood-based biomarker assessment, blood pressure, sensory function, and physical performance during its health assessment as well (included in TILDA waves 1 and 3).

TILDA plans to perform HCAP assessments in community-dwelling and nursing home participants ages 65 and older (N=1,800). A number of other cognitive measures are conducted as a part of TILDA's health assessment, including the Montreal Cognitive Assessment (MOCA), Color Trails, National Adult Reading Test (NART), Choice Reaction Time, and the Sustained Attention to Response Task (SART). The TILDA-HCAP sample will be recruited from participants who complete the TILDA wave 6 CAPI (scheduled from 2020 to 2021).

## **NICOLA**

*Bernadette McGuinness, Queen's University Belfast*

NICOLA began in 2016 as a study of evidence-based research on aging in Northern Ireland with implications for public policy and national and international comparative analysis. NICOLA's HCAP principal investigator and funding have not yet been confirmed; however, McGuinness will likely lead the project. Wave 1 was completed, and wave 2 completion (~6,500 interviews thus far with an additional 800 respondents ages 50–54) is anticipated in 2019. Data linkages are established for death reporting, and NICOLA investigators are working toward other linkages as well.

Within the next 12 months, NICOLA plans to curate wave 2 data and link them to wave 1; complete wave 1's health assessment report (April 2020); provide key findings from wave 2 (mid-2020); prepare for wave 3, including CAPI and the health assessment; and provide additional reports with focus on the unique aspects of NICOLA.

NICOLA-HCAP aims to recruit 1,000 participants over age 65 for ELSA- and HRS-HCAP harmonization, with dementia and MCI as primary outcomes. NICOLA-HCAP will also use cross-

country analyses to investigate how stress and long-term exposure to conflict (i.e., adults in Ireland from the 1960s to mid-1990s) affects cognitive aging and epigenetic patterns. Future NICOLA work will include collaborations with Northern Ireland government and policy makers (e.g., Northern Ireland Frailty Network, Gaelic Athletic Association Healthy Clubs).

## **CADAS**

*William Dow, University of California, Berkeley*

Investigators from the 10/66 Dementia Research Group conducted baseline assessments on individuals ages 65 and older in 12 countries from 2004 to 2006 (i.e., Caribbean: Cuba, Dominican Republic, Puerto Rico; Latin America: Argentina, Brazil, Mexico, Peru, Venezuela; Others: China, India, Nigeria, South Africa; about 2,000 participants per country in urban catchment areas). Incident follow-ups were completed in most countries from 2007 to 2009. Investigators are currently in the field collecting wave 3 samples (i.e., “Life2Years”) in Cuba, Dominican Republic, Puerto Rico, Venezuela, Mexico, Peru, and China.

Because 10/66 assessed participants from urban catchment areas, it did not include a random, representative sample. Moreover, 10/66 began prior to HCAP and therefore was not designed to harmonize its data with HCAP; thus investigators are currently comparing 10/66 and HRS-HCAP data. CADAS has identified missing executive functioning assessments; and CADAS investigators are concerned about how some measures (e.g., number and letter cancellation) will accurately assess illiterate populations.

Additionally, CADAS plans to evaluate 10/66 data (e.g., Geriatric Mental State, Community Screening Instrument for Dementia) to harmonize with HCAP international studies. The CADAS project will draw nationally representative refresher samples (N=1,500 each) to supplement the original 10/66 collection (i.e., Dominican Republic [Daisy Acosta], Puerto Rico [Ivonne Jimenez-Velazquez]).

## **Discussion**

Weir suggested waiting to use 2020 U.S. census data to assess Puerto Rico, rather than reweighting 2010 U.S. census data. He also commented that investigators from China have used Google mapping to identify new areas/settlements in remote locations (i.e., those outside of urban catchments), but Weir and Dow agree that this method may become challenging because many populations resettle often. It may be useful to contact the U.S. Census Bureau to help address these issues.

King emphasized the importance of updating the CADAS sample to include more diversity, especially in Cuba, and Dow confirmed that CADAS investigators will explore ways to increase diversity. Manly suggested oversampling participants younger than age 65 to reach diversity goals, but attendees expressed concern over the value of data from such participants. Dow confirmed that CADAS will oversample rural areas because the current study population is largely urban. Dow also commented that performance on assessments appears to be very strongly related to education (even when controlling for age) in CADAS populations.

Attendees discussed issues surrounding assessments for illiterate populations (e.g., executive function tests). Weir suggested using the Ravens test because more participants can complete the assessment, regardless of literacy. Dow will follow up with attendees to discuss how to proceed with appropriate assessments for illiterate populations.

## **Sampling Design in Current and Future Studies**

*David Weir, University of Michigan*

Proper documentation of all HCAP study design choices (e.g., geographic or age exclusions, differential sampling, cognitive ability measurements) is critical for harmonizing sample weights and calculating accurate national prevalence estimates. HCAP study investigators must also be aware of the main study design outcomes in their respective countries: (1) response rate by elements of design, stratification, cognitive ability, education, and location; and (2) sampling weights that combine study weights, non-response, and adjusted weights.

HCAP's goals for year 1 include (1) constructing a network of study sampling leads who can work together on harmonization, (2) compiling documentation on current HCAP study sampling design, (3) considering harmonized analysis of non-response rates from international aging studies to all HCAP studies, and (4) considering implementation of revised sampling weights.

Studies that have not yet started fieldwork can speak directly with HRS-HCAP investigators for guidance and resources. The HCAP Intranet will likely be an important resource for harmonizing study designs.

### ***Discussion***

King expressed concern over the wide variety of stratified HCAP samples (e.g., Mex-Cog and HRS-HCAP stratified by geographic region). He suggested that HCAP investigators consider how to draw more participants in and how to cut costs, rather than stratifying current populations.

Brayne suggested gathering data on the consent processes at each study site and identifying patterns of parallel issues (e.g., attrition, item nonresponse) to help fill existing gaps in population evidence.

## **Statistical Harmonization**

*Richard Jones, Brown University*

### **Friday Harbor Workshop**

The advanced psychometrics in cognitive aging research Friday Harbor Workshop has been funded through an NIA R13 scientific conference grant since 2004. The weeklong, remotely located workshop focuses on different themes associated with cognitive aging, AD, measurement, and complex data analysis. Programmed activities include didactic lectures and small group activities, with three main workgroups: applied harmonization (e.g., LASI-DAD

versus HRS-HCAP), measurement bias (e.g., anchor items), and simulation studies. The workshop results in subject matter expertise, measurement expertise, and publications.

### **Missing Data**

Missing data in cognitive assessment performance is not a problem if the data are missing at random (MAR). However, investigators should apply the same principles of missing data from other areas of epidemiological inference when analyzing cognitive performance assessments.

Missing data can be handled in several ways: (1) multiple imputation, maximum likelihood (good choices); (2) mean imputation, single imputation, listwise complete analysis, Last Observation Carried Forward, missing data indicators (bad choices); or (3) stochastic single or hotdeck imputation (not enough known).<sup>9</sup> If investigators assess cognitive assessment performance by calculating the proportion correct out of only those attempted (i.e., correct/attempted), the overall score represents a mean imputation, rather than an individual's true score. Further, correct/attempted provides an unbiased assessment of cognitive ability *only* if all items are of equal difficulty. Advanced statistical technology allows for more refined measurements of complicated data than correct/attempted.

### **Non-Equivalent Anchor Test Linking**

Scales across studies can be linked as long as some questions are the same (i.e., Non-Equivalent Anchor Test Linking [NEAT] linking). In NEAT linking, groups do not require the same distribution of ability, as long as assumptions are met: (1) items are MAR; and (2) anchor test items have the same measurement properties in all groups (i.e., items are exactly the same in content and context).

In cross-national harmonization, it is difficult to maintain consistency in the anchor items. However, when assessing cognitive assessment performance data across countries, investigators must consider how *severely* the assumptions of NEAT linking are broken, not *if* they are broken. The language domain in HCAP has no anchors; however, investigators can use thresholds for non-language items to serve as anchors for the language domains based on relationships between the items. Even the addition of a couple extra questions could facilitate anchoring for the purposes of harmonization.

### **Discussion**

Attendees discussed how to differentiate between questions that *could not* versus those that *would not* be answered, suggesting adding auxiliary variables to determine why a person did not answer a question or including why a person did not answer directly in the assessment. Variables can also be added to statistical models to account for home interview interruptions (e.g., grandchild running into room). Attendees emphasized it is best to choose assessments that work well in all populations (i.e., illiterate and literate), the importance of a consistent approach to address MAR, and transparency.

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<sup>9</sup> National Research Council. *The Prevention and Treatment of Missing Data in Clinical Trials*. Panel on Handling Missing Data in Clinical Trials. Committee on National Statistics, Division of Behavioral and Social Sciences and Education. Washington, DC: The National Academies Press, 2010.

Attendees discussed the possibility of adding a variable to represent a person's abilities. However, Weir stated that investigators cannot characterize a person's abilities unless there is clinical justification (e.g., missing limb). Attendees discussed training interviewers to assess cognitive impairment with standardized questions (e.g., adaptive testing and benchmarks). However, Weir also expressed concern about the amount of supervision, training, and retraining needed to maintain consistency. Jones noted that stochastic regression imputation adds a random error term to the predicted value within the imputation model, which could address this issue. Dow commented that investigators often evaluate patterns of cognition as they relate to literacy. Therefore, it is important to keep all questions included in the assessments. Literacy could be added into a statistical model if and when it is important to an investigator's particular research question.

Order effects are important in assessment validity. However, order effects cannot be tested in simulations. Therefore, it is difficult to determine the precise effect order might have on the results. Dow suggested conducting a random re-ordering assessment to determine the effects of participant exhaustion. Weir emphasized that all HCAP studies should conduct HCAP in the same order to prevent possible order effects. Attendees raised the possibility of using HCAP data for analysis at a Friday Harbor Workshop to determine potential issues when working directly with the data.

Weir confirmed HCAP investigators will create a working group to address issues surrounding patient refusal to answer questions and how best to handle missing data. HCAP investigators should identify potential individuals to participate in the working group.

## **Diagnosis and Validation**

*Ken Langa, University of Michigan*

Several methodologies have been used previously for dementia diagnosis in clinical and population-based research, including consensus conferences, algorithmic diagnoses, and probabilistic models. Consensus conferences, such as those used in Aging, Demographics, and Memory Study (ADAMS), aim to re-create typical clinical decision-making among expert clinicians to arrive at a gold-standard diagnosis based on established diagnostic criteria. Algorithmic diagnoses are pre-specified algorithms for diagnosis, such as those used in Washington Heights/Inwood Columbia Aging Project (WHICAP), defined based on cognitive impairments domains or informant reports and established diagnostic criteria. Probabilistic models estimate regression models that classify individuals using data containing common tests or domains with gold-standard diagnoses.

Although each method can be useful for HCAP data harmonization, each has disadvantages. Consensus conferences are idiosyncratic and difficult to replicate across time and location. Algorithmic diagnoses must have pre-specified data element weighting (e.g., self versus informant), and they must develop or identify valid norms to define impairment. Probabilistic



models require data with gold-standard diagnoses and are often considered “black-boxes,” reducing their clinical validity.

### **HRS-HCAP Approach and Update**

HRS investigators are developing a diagnostic algorithm based on the 2011 NIA-Alzheimer’s Association Diagnostic Criteria,<sup>10</sup> which defines impairment across five cognitive domains: orientation, memory, executive function, language/fluency, and visuospatial activity. Impairment classification domains will be identified using a robust, normative sample, excluding respondents (1) with diagnosis of dementia, stroke, or Parkinson’s disease; (2) who died, live in nursing homes, or were represented by a proxy in the 2018 core survey; or (3) exhibited activities of daily living (ADL) limitations in the 2016 or 2018 core survey.

HRS assessments inquire not only about whether individuals can perform ADL, but also why individuals do not perform the behaviors (e.g., an individual does not shop because of memory impairment). Comparisons of functional assessments in the different HCAP countries may require adjustments in order to maximize comparability. These kinds of cross-country analyses will be an important part of the harmonization work of the R24 Network in the years ahead.

### **Validation of HRS-HCAP in Clinical Populations**

HRS-HCAP conducted pilot validation studies using the Seattle Adult Changes in Thought (N=64) and Michigan Alzheimer’s Disease Research Center (N=89) populations, in which HCAP-trained interviewers conducted HCAP testing and informant interviews. Diagnoses in both samples were derived by clinical case conferences.

The HCAP renewal application proposed developing a clinical case conference to compare HCAP algorithmic diagnoses to those derived from a consensus conference of clinicians. Relevant data from the HCAP assessment and HRS core survey (e.g., ADL impairment) would be presented to a panel of five clinicians during an in-person meeting, where they would review and discuss data and make diagnostic designations blind to the HCAP algorithmic diagnoses. Investigators could possibly compare outcomes from HRS in-person conferences with the LASI-DAD online consensus process.

HRS-HCAP pilot validation research determined that Medicare records are far from perfect, though they do offer a completely independent clinical perspective; health-related anxiety seems to increase chances of a positive diagnosis; and some patients remain undiagnosed by the health care system.

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<sup>10</sup> McKhann, G.M., Knopman, D.S., Chertkow, H., Hyman, B.T., Jack, C.R. Jr., Kawas, C.H., Klunk, W.E., Koroshetz, W.J., Manly, J.J., Mayeux, R., Mohs, R.C., Morris, J.C., Rossor, M.N., Scheltens, P., Carrillo, M.C., Thies, B., Weintraub, S., and Phelps, C.H. The diagnosis of dementia due to Alzheimer’s disease: recommendations from the National Institute on Aging-Alzheimer’s Association workgroups on diagnostic guidelines for Alzheimer’s disease. *Alzheimers Dement.* 2011, 7(3):263-269.

HRS-HCAP 2020 will provide longitudinal data to identify incident cases of dementia in the HCAP sample, though death, attrition, and nursing home entry pose potential issues to HRS-HCAP 2020 completion. Exit interviews or Medicare data may provide solutions to these issues.

### ***Discussion***

Manly noted that investigators and clinicians may disagree whether an individual who performs poorly or refuses to do a test on the functional battery is in cognitive decline because the definition of dementia and AD has not been identified. If HCAP investigators only include participants who can complete all tests, the assessment is likely to have large amounts of missing data.

### **MHAS Harmonization and Validation**

*Silvia Mejia-Arango, Colegio de la Frontera Norte*

MHAS diagnostic validation is using clinical sample from Mexico City previously classified by clinicians as dementia, MCI, or normal. The MHAS validation study applied the Mex-Cog informant and cognitive assessment to a sample of approximately 150 participants. Respondents were classified into cognitive domains based on the following criteria: orientation, immediate memory, delayed memory, attention, language, constructional praxis, and executive functions. Clinicians were trained to score patients according to the cognitive domain grouping. Results suggest that MCI, dementia, and normal patients scored differently in the Mex-Cog instruments. However, the classification of MCI cases using the algorithmic diagnostic criteria was inconsistent.

### ***Discussion***

Attendees discussed that the informant questionnaire may not be necessary for diagnosing participants and suggested contacting the 10/66 Dementia Research Group to determine whether 10/66 uses the informant questionnaire to aid in participant diagnosis.

Attendees agreed that more information on how domains are grouped and classification algorithms are used to diagnose participants is needed, in order to harmonize studies. The issues surrounding MCI misclassification are being assessed by Columbia University, although Mejia-Arango requested input from other HCAP investigators to address this issue. Mejia-Arango confirmed that measures of education were used to create the normative sample for classification; hence illiteracy likely did not play a role in misclassifying patients.

Manly suggested using the robust norms approach to mitigate issues in cross-sectional sampling. However, this method may be difficult in the Mex-Cog and the other HCAP studies because there are currently no follow-up sessions.

Attendees discussed the importance of choosing a clinical sample that is representative of the population (e.g., age range, education). A representative sample could be taken from participants who previously had an HCAP assessment completed. However, the extensive geographical distribution of the national samples makes clinical assessment of the subjects



infeasible, especially among participants with the lowest cognition, composing a majority of the clinical sample for dementia. In addition, because diagnoses would be completed at different times, the clinical diagnosis from the original HCAP assessment and the validation assessment might not be the same. Further, many physicians are not trained to perform community-based cognitive testing; therefore, clinical diagnoses in the clinic and in the home may differ.

### **NICOLA Harmonization and Validation**

*Bernadette McGuinness, Queen's University Belfast*

NICOLA diagnostic validation will include participants (n=80) recruited from Belfast Health and Social Trust Memory Clinics. Standardized cognitive assessments will be conducted by consultants and senior trainees, and consenting participants will undergo in-home HCAP assessments. Patient cognitive grouping has not yet been determined, though it will likely include subjects entering the clinic with self-reported cognitive impairment.

#### **Discussion**

Weir expressed concern about consultants and senior trainees administering the HCAP assessment. He indicated that highly trained individuals could introduce variability into the diagnoses, because most HCAP studies do not have highly trained clinician interviewers. Attendees discussed inconsistencies in interview personnel and the need to address this issue moving forward.

Weir confirmed that NICOLA will need to recruit cognitively normal patients (i.e., controls) to conduct HCAP assessments in the clinic (e.g., hospital staff, family members).

### **Classification Algorithms for Cognitive Impairment in LASI-DAD**

*Alden Gross, John Hopkins Bloomberg School of Public Health*

To classify cognitive impairment in LASI-DAD, 12 clinician raters across India scored LASI-DAD participants on an online Clinical Dementia Rating (CDR) scale, with the goal of reproducing clinical decision-making processes. Consensus was derived within three to four initial raters, with additional raters included if agreement was not met. Because more than half of the LASI-DAD sample is illiterate, investigators are concerned that the online CDR may not accurately classify individuals in this population.

Participants received slightly different batteries of tests at each wave and phase: LASI wave 1 (about 72,000 participants); LASI-DAD phase 1 (about 1,587 participants); LASI-DAD phase 2 (1,637 participants); and LASI-DAD phase 2 online adjudication subsample (N=829). In main LASI waves, informants were only interviewed when a battery was not done. LASI-DAD phase 3 will likely be used as a complete validation subset.

LASI-DAD assessments include questions related to demographics (e.g., age, sex, education, married, literacy); cognition (e.g., orientation, memory, language/fluency); self-rated factors (e.g., memory, ADL); informant reports (e.g., informant questionnaire on cognitive decline in the elderly, 10/66 items); and lifestyle/social activities (e.g., religious, political, movies).

Responses were analyzed using probabilistic models for LASI wave 1, LASI-DAD phases 1 and 2, and the LASI-DAD phase 2 online adjudication subsample, rather than grouped into domains. Specifically, area under the curve (AUC) was calculated using univariate or multivariate logistic regressions for each variable independently, combinations of variables, and variable interactions.

Preliminary analysis on LASI-DAD phase 2 suggests that age and education are most predictive of cognitive status, and summed orientation scores predict cognition better than memory scores in literate and illiterate individuals. Some variables include combined factor scores (e.g., memory, ADL); therefore, it may be useful to break these variables into separate factors to gain further information about the relationships. Informant reports appear to provide useful, accurate data. However, not all LASI-DAD participants have an informant interview conducted.

Both informant and cognitive testing can be used to classify dementia in LASI-DAD based on the Phase 2 online adjudicated CDRs. Gross plans to assess the ability to perform cross-national classification with LASI algorithms. However, the purpose of this preliminary analysis was to estimate prevalence and correlates, not to evaluate causal predictors or outcomes.

## **Wrap Up Discussion**

*Moderated by David Weir, University of Michigan*

Weir confirmed the HCAP Network could potentially provide support for (1) specialized meetings, (2) exchanges for junior investigators to learn new techniques, (3) pilot projects (e.g., statistical analysis), and (4) subcontractors to aid in analytical methods. Weir asked attendees to share ideas by January 1, 2020, and to prepare to report on their progress at the next HCAP meeting.

## Appendix A: Meeting Agenda

### Second Annual Meeting of the Harmonized Cognitive Assessment Protocol (HCAP) Network

Hyatt Regency Bethesda • One Bethesda Metro Center • Bethesda, MD 20814  
and

Serendipity Labs • 4500 East West Highway • Bethesda, MD 20814

October 29-30, 2019

#### MEETING AGENDA

*Rev. 10-25-19*

Tuesday, October 29	Hyatt Regency Bethesda: The Rooftop
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- |           |  |
|-----------|--|
| 1:00 p.m. | <b>Welcome and Introductions</b><br><i>Ken Langa and David Weir</i>  |
| 1:15      | <b>NIA Perspectives on Harmonization</b><br><i>John Phillips</i>   |
| 1:25      | <b>Overview of HCAP Network R24</b><br><i>David Weir</i>   |
| 1:40      | <b>R24 Cores: Resources and Plans</b><br>Outreach – <i>Amanda Sonnega</i><br>Biomarkers – <i>Jessica Faul</i><br>Protocols – <i>Lindsay Ryan</i>   |
| 2:25      | <b>BREAK</b>   |
| 2:40      | <b>Reports from Studies with One Wave Completed</b><br>ELSA – <i>Dorina Cadar</i><br>MHAS – <i>Rebeca Wong</i><br>HRS – <i>Ken Langa</i><br>LASI – <i>Jinkook Lee</i><br>CHARLS – <i>John Strauss</i><br>HAALSI – <i>Darina Bassil</i> |
| 4:00      | <b>BREAK</b>   |

**4:15 Reports from Studies Underway or In Planning**Chile SPS – *David Bravo, Irma Elo*SHARE – *Salima Douhou*TILDA – *Christine McGarrigle*NICOLA – *Bernadette McGuinness*Caribbean – *Will Dow***5:30 ADJOURN****5:50 Meet in Hotel Lobby / Depart for Group Dinner****6:00 GROUP DINNER*****Cesco Osteria***

7401 Woodmont Avenue

2 Bethesda Metro Center

Bethesda, MD 20814

**Wednesday, October 30****Serendipity Labs Conference Room**

The goal for day 2 is to identify challenges to harmonization and decide which ones to prioritize for year 1 of the R24.

**9:00 am Sampling***David Weir*

- Sampling design issues in new studies
- Patterns of non-response in completed studies
- Weighting

**9:30 Statistical Harmonization***Rich Jones*

- Report on Friday Harbor workshop findings from HCAP analyses
- Logical memory (story recall) harmonization
- Factor-analytic approach to domains
- Imputation? -- *LASI*
  - Items within tests; tests; factors; domains
  - Designed skips, meaningful missings
  - Protocol deviations
- Harmonization to 10/66 – *MHAS*

**10:30 BREAK**

10:45      **Diagnosis (Classification) and Validation**

*Ken Langa*

- HRS approach and update
- Other approaches to diagnosis
- Validation evidence so far – LASI, CHARLS, MHAS?
- Planned validations – NICOLA
- Incidence considerations

11:30      **Wrap-up**

- Discussion of possible pilot projects and exchanges
- Satellite meetings
- Priorities

12:00 pm      **ADJOURN**

## **Appendix B: Meeting Participants**

### **Second Annual Meeting of the Harmonized Cognitive Assessment Protocol (HCAP) Network**

Hyatt Regency Bethesda • One Bethesda Metro Center • Bethesda, MD 20814  
and

Serendipity Labs • 4500 East West Highway • Bethesda, MD 20814

**October 29-30, 2019**

#### **EXPECTED PARTICIPANTS**

*Rev. 04-20-20*

#### **U.S. Health and Retirement Study (HRS)**

**David Weir**, Principal Investigator (PI), University of Michigan (UM)

**Ken Langa**, Co-PI, UM

**Eileen Crimmins**, Co-Investigator, University of Southern California (USC)

**Richard N. Jones**, Co-Investigator, Brown University

**Jennifer Manly**, Co-Investigator, Columbia University

**Madeline Farron**, Research Area Specialist, UM

**Jessica Faul**, Research Affiliate, UM

**Lindsay Kobayashi**, Assistant Professor, UM

**Cathy Liebowitz**, Research Process Senior Manager, UM

**Ryan McCammon**, Research Associate, UM

**Lindsay Ryan**, Associate Research Scientist, UM

**Amanda Sonnega**, Associate Research Scientist, UM (by phone 10/29 only)

#### **Caribbean American Dementia and Aging Study (CADAS)**

**William Dow**, PI, University of California, Berkeley

**Amal Harrati**, Co-Investigator, Stanford University

#### **Chilean Social Protection Survey**

**David Bravo**, PI, Universidad Católica de Chile

**Irma Elo**, HCAP Co-PI, University of Pennsylvania

#### **China Health and Retirement Longitudinal Study (CHARLS)**

**John Strauss**, Co-PI, USC (by phone 10/29 only)

#### **English Longitudinal Study of Ageing (ELSA)-The Healthy Cognitive Ageing Project (HCAP)**

**Jessica Abell**, Research Fellow, University College London (UCL)

**Carol Brayne**, Co-Investigator, University of Cambridge

**Dorina Cadar**, Senior Research Fellow, UCL

**Health and Aging Study in Africa: A Longitudinal Study of an INDEPTH Community in South Africa (HAALSI)**

**Lisa Berkman**, PI, Harvard University (by phone 10/29 only)

**Darina Bassil**, Research Associate, Harvard University

**Irish Longitudinal Study on Ageing (TILDA)**

**Christine McGarrigle**, Epidemiology Research Fellow

**Longitudinal Aging Study in India (LASI)**

**Jinkook Lee**, PI, USC

**Alden Gross**, Psychiatric Epidemiologist, Johns Hopkins Bloomberg School of Public Health

**Mexican Health and Aging Study (MHAS)**

**Rebeca Wong**, PI, University of Texas Medical Branch

**Silvia Mejia-Arango**, Co-Investigator, Colegio de la Frontera Norte

**Northern Ireland Cohort for the Longitudinal Study of Ageing (NICOLA)**

**Bernadette McGuinness**, Consultant Geriatrician NICOLA

**Survey of Health, Ageing and Retirement in Europe (SHARE)**

**Salima Douhou**, Max Planck Institute for Social Law and Social Policy, Munich Center for the Economics of Aging

**National Institute on Aging (NIA)**

**John Haaga**, Director, Division of Behavioral and Social Research (BSR)

**Dana Plude**, Deputy Director, BSR (10/29 only)

**Dallas Anderson**, Director, Epidemiology of Dementia Program, Division of Neuroscience

**Frank Bandiera**, Health Scientist Administrator, BSR

**Partha Bhattacharyya**, Program Director, BSR

**Jonathan W. King**, Program Director, BSR, and HRS Project Scientist

**Carmen Moten**, Health Scientist Administrator, Division of Extramural Activities (10/29 only)

**Lis Nielsen**, Chief, Individual Behavioral Processes Branch, BSR

**Georgeanne Patmios**, Program Director, BSR, and HRS Program Official (10/29 only)

**John W. R. Phillips**, Chief, Population and Social Processes Branch, BSR

**Rose Li and Associates, Inc. (RLA)**

**Rose Li**, Project Director

**Kristyn Sylvia**, Science Writer

**Kim Williamson**, Meeting Planner