National Institute on Aging

Harmonized Cognitive Assessment Protocol (HCAP) International Network Videoconference

Meeting Summary

February 18, 2021

Rev. April 28, 2021

Table of Abbreviations

AD	Alzheimer's disease
ADRD	Alzheimer's Disease-Related Dementias
BSR	Division of Behavioral and Social Research
CADAS	Caribbean American Dementia and Aging Study
CFA	Confirmatory Factor Analysis
CHARLS	China Health and Retirement Longitudinal Study
COVID-19	Coronavirus disease 2019
DN	Division of Neuroscience
ELSA	English Longitudinal Study of Aging
FOA	funding opportunity announcement
GCP	General Cognitive Performance
HAALSI	Health and Aging in Africa: A Longitudinal Study of an INDEPTH Community in South Africa
HCAP	Harmonized Cognitive Assessment Protocol
HRS	Health and Retirement Study
LASI-DAD	Longitudinal Aging Study in India-Diagnostic Assessment of Dementia
MCI	Mild Cognitive Impairment
MHAS	Mexican Health and Aging Study
MMSE	Mini-Mental State Exam
NIA	National Institute on Aging
NICOLA	Northern Ireland Cohort for the Longitudinal Study of Aging
NIH	National Institutes of Health
NOSI	Notice of Special Interest
SHARE	Survey of Health, Ageing and Retirement in Europe
TILDA	The Irish Longitudinal Study on Ageing

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Meeting Summary

Introduction

The Harmonized Cognitive Assessment Protocol (HCAP) International Network met by videoconference on February 18, 2021, to discuss study progress, activities, and next steps. The presentations covered new funding opportunities (internal pilots and NIA Alzheimer's Disease [AD] and Alzheimer's Disease-Related Dementias [ADRD] funding), HCAP Network study updates, and HCAP study methods updates. The meeting agenda, list of participants, and associated verbatim chat transcript are included as Appendices A, B, and C.

Ken Langa and David Weir, Co-Principal Investigators of the HCAP Network, welcomed those in attendance, and especially thanked participants joining during nonbusiness hours. Langa noted that the data collected by members of the HCAP Network have grown in value due to the Coronavirus disease 2019 (COVID-19) pandemic and will make an important contribution for understanding its world-wide impact on cognitive aging and dementia. Weir commented that, as a plenary session, this meeting provides only a high-level overview of the status of selected projects within the HCAP Network. An intended outcome of the plenary meeting is to develop plans for smaller follow-on meetings focused on covering specific studies or topics of special interest in more depth. He encouraged participants to enter general questions in the chat function to be answered during discussion and to follow-up with other participants by email with specific questions; this type of interaction is what the Network seeks to promote.

Jonathan W. King, Senior Scientific Advisor to the Director of the Division of Behavioral and Social Research (BSR) and Project Scientist for the Health and Retirement Study (HRS) and HCAP, and Lis Nielsen, Director, BSR, welcomed participants on behalf of the NIA. Nielsen commended the Network on its progress and efforts to build such an important harmonized resource for the research community as well as the potential of HCAP for dementia studies around the world. She also praised the [HCAP Network website](#), noting the value of promoting the work through a variety of channels, and offered the NIA as another conduit for communication to the research community.

New Funding Opportunities
David Weir and Ken Langa

Langa reminded participants that the HCAP Network has $50,000 available per year to fund pilot projects. The aim is to fund two or three projects each year at a level of $15,000 to $25,000, focused on international harmonization of measures and other key methodological issues to enhance data comparability. The amount and timing of pilot projects can be flexible, and the pilot grant application process is relatively simple:
- Applicant emails Weir and Langa outlining initial ideas and tentative budget;
- Applicant submits a short (about 3 pages) application for initial review with aims, research strategy, budget, and budget justification;
- Relevant experts (both internal and external to the Network) review the proposal;

- NIA BSR staff review to ensure fit with R24 grant mechanism; and
- Applicant receives funding decision as quickly as possible.

Funding is also available to subsidize travel and living expenses for junior faculty to participate in an extended stay with another Network team to enable more intensive cross-country collaboration and exchange. These exchanges are currently on hold due to COVID-19 restrictions.

King described broader ongoing NIA funding opportunity announcements (FOAs) and Notices of Special Interest (NOSIs) for which HCAP data might be well suited, in particular:

[PAR-19-070: Research on Current Topics in Alzheimer's Disease and Its Related Dementias (R01 Clinical Trial Optional)](). This FOA is designed to solicit AD/ADRD projects and to help the NIH Center for Scientific Review assign them to the most appropriate NIH study section. Applications through this mechanism should cite the FOA as well as a specific NOSI. Of the many NOSIs that are available, the most successful for HCAP applicants to date (including those not attached to HCAP but propose to use HCAP data) has been NOT-AG-18-053 ([NOT-AG-18-053: Notice to Specify High-Priority Research Topic for PAR-19-070 and PAR-19-071]()), which is subtitled *Major Opportunities for Research in Epidemiology of Alzheimer's Disease and Related Dementias and Cognitive Resilience*. Use of this NOSI offers several advantages. First, and in particular, the application can be submitted one month after the usual due date because reference to this NOSI targets the application for review by one of several appropriate study sections, including the Social Sciences and Population (SSP) Study Section. King also encouraged applicants who believe their grant application has been assigned to an inappropriate study section to contact BSR program officials, who can help ensure that the application is assigned to the most appropriate locus of review. King further noted that funding rates for applications that propose to use HCAP data or to collect additional HCAP data have generally been strong. If appropriate, an application could also cite a more targeted FOA or the parent FOA. King also advised that applicants spell out Alzheimer's Disease or Alzheimer's Disease-Related Dementias before using an abbreviation (i.e., AD or AD/ADRD) to ensure that the text-mining system that NIH uses to categorize research will tag the application as relevant to Alzheimer's Disease.

Weir and Nielsen underscored that the NIA is well endowed to support AD/ADRD research and encouraged interested researchers to contact BSR staff to explore initial ideas, especially to extend on HCAP accomplishments. Weir suggested tracking applications by HCAP Network members so that other study directors can learn from the successful applicants. Interested applicants seeking to propose HCAP collaborations that might require larger budgets (i.e., more than $500,000 in direct costs in any one year) or that originate from a foreign institution are encouraged to contact BSR staff early (at least 6 and ideally 10 weeks before submission) to obtain necessary clearances. Weir and Langa welcomed inquiries from investigators in the exploratory stages of undertaking a data collection to help with brainstorming or coordinating with NIA staff.

HCAP R24 Network Study Updates

Weir credited Amanda Sonnega, the HCAP Network Outreach and Dissemination Core Leader with the development and launch of the new HCAP Network website (https://hcap.isr.umich.edu). Led by Lindsay Ryan, the HCAP Network Protocol Content and Administration Core Lead, efforts are also underway to develop video training materials (in conjunction with developing Irish Study training materials) to help studies train their staff to administer the HCAP batteries in as harmonized a way as possible. Because some of these tests are copyrighted (limiting the ability to post videos to YouTube), Weir asked interested parties to contact him or Langa directly to access.

The COVID-19 pandemic has affected research activities everywhere, including the parent HRS network studies and the HCAP studies, but the impact varies considerably depending on the timing of planned activities. Ten HCAP studies provided brief updates that were shared in advance of the meeting with all participants. Weir provided an overview of the status of 11 HCAP studies and the impact on study progress from the COVID-19 pandemic.

HCAP Study	Progress update received	Delayed due to COVID-19	Not Yet Delayed	No Plans
Wave 2 Studies with Completed Baseline				
HRS	●	●		
MHAS Mex-Cog	●	●		
LASI-DAD	●		2021-2023	
HAALSI	●		Sep 2021	
CHARLS	●		●	
CHILE-COG	●		Mar 2021 phone survey	
ELSA	●			(*)
Planned Baseline for New Studies				
CADAS	●	●		
NICOLA	●	●		
TILDA	●	●		
SHARE	●		Pretests: Jul-Oct 2021 Survey: Jan-Jun 2022	

(*) In part as a consequence of this meeting, ELSA is now planning an application to conduct a second wave of HCAP.

Weir invited four studies with notable recent accomplishments during the pandemic to provide brief updates. Study progress reports and the presentation slide decks can be accessed through the HCAP Network website.

- Mexican Health and Aging Study (MHAS) Mex-Cog was conducted in 2016; all data and documentation are available at www.MHASweb.org. An additional subsample was to be added in spring 2020 but data collection was paused due to the COVID-19 pandemic.

The MHAS Mex-Cog team is fully in data analysis mode, and welcomed discussion on two topics:
  - Integrating informant data with cognitive assessments to classify participants (for those who completed both instruments, and for those who have only one source)
  - Cross-walking between sub-sample and core survey.

- Chile-Cog field work took place August through December 2019 and there are plans to conduct a phone survey in March 2021. A validation study originally scheduled for March-April 2020 has been rescheduled for April-June 2021. The team is currently collaborating with Jinkook Lee to integrate Chile-Cog to the Gateway to Global Aging Data.

- Longitudinal Aging Study in India—Diagnostic Assessment of Dementia (LASI-DAD) baseline was fielded 2018-20; Wave 2 is planned for 2021-23. Since May 2020, the team has been carrying out a bi-monthly COVID-19 phone-survey, completing 6 rounds of data collection as of April 2021 and plans to continue the panel data collection by April 2022. The team has been actively working on analyzing the Wave 1 data and carrying out whole genome sequencing, which will become the largest reference panel for South Asians in the world.

- Health and Aging in Africa: A Longitudinal Study of an INDEPTH Community in South Africa (HAALSI) HCAP pilot study was administered in 2016-2017, which revealed that modifications to the battery was needed to minimize missingness in low literacy respondents, and that quality informant data on functional decline is critical. Wave 1 of the HAALSI Dementia study was fielded September 2019 to March 2020; data are being prepared for public release in February 2021. HAALSI is still on target to field Wave 2 in Fall 2021. It received a supplement to examine bidirectional associations between COVID-19 and cognitive function/dementia, and will soon begin a phone survey to capture information on pandemic-related disruptions to social life, economic stability, and caregiving dynamics.

HCAP Study Methods Updates

The baseline HRS HCAP was fielded from June 2016 to October 2017, and data were released in January 2019. Wave 2 and the HCAP neuroimaging pilot, both initially planned for 2020, are on hold due to COVID-19 restrictions. The HCAP team expects to complete two manuscripts in 2021 on dimensions of cognitive functioning and a diagnostic algorithm.

HRS HCAP Diagnostic Algorithm Development

Richard Jones explained that the HRS HCAP general approach for the diagnostic algorithm development is to use factor analysis to characterize cognitive performance along multiple dimensions, and to identify thresholds for cognitive impairment using a robust normative group, adjusted for age, sex, education, and race/ethnicity.[1] This multi-step process that

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[1] The "robust normative group" is defined by excluding HCAP respondents: with diagnosis of stroke, Parkinson's disease (2013-2016 Medicare); who died, are in nursing home, or represented by proxy in

involves restriction, normalization, and standardization is described in more detail in the [preprint](#). For about 4 percent of the HCAP sample (149/3,496), only informant interviews are available (i.e., no cognition measures). The algorithm combines identified cognitive impairment with informant reports of functional decline, applies Bayesian imputation procedures as needed (thereby avoiding selection bias regarding study participation), and checks distributions by demographic characteristics.

The HRS HCAP approach relies on a factor model that analyzes five a priori–defined domains of performance, including **m**emory (delayed episodic and recognition), **e**xecutive functioning (set shifting and attention/speed), **l**anguage and fluency, **v**isuospatial, and **o**rientation (Mini-Mental State Exam [MMSE] 10 items, time and place).[2] It then identifies an impairment cut-point for each domain using a robust normative sample and defined impairment as a T-score 1.5 standard deviations below the mean of the normative sample, again adjusting for age, sex, race/ethnicity, and education. Impairment in daily function, the criterion that differentiates mild cognitive impairment (MCI) from dementia, is currently operationalized using published cutoffs and inspection of the distribution of scores on the IQCODE and BLESSED informant report scales. The HRS-HCAP team continues to refine the diagnostic algorithm, including the best method(s) for combining cognitive testing data with informant report data.

Jones noted that this work is still preliminary. Current activities and next steps include exploring potential racial bias in the normative sample (due to use of Medicare data), finalizing the demographic adjustment strategy for impairment cut-points, and validating the cognitive data in a subsample using an online consensus panel of experts, similar to LASI and HAALSI consensus methods.

Jennifer Manly observed that the chat comments (Appendix C) during the presentation mainly center on sensitivity and specificity of impairment measures. She explained that the HRS HCAP's robust normative approach recognizes that older individuals with fewer years of education may reach a certain age without cognitive impairment. She described taking a longitudinal view of performance over time and returning to the baseline contact to use those earlier scores as an indicator of what the individual's normal performance might have been. When looking at neuropsychological test performance and the acquired impairment, the standardization sample is the person before the impairment was acquired. Although age is a risk factor for dementia, it is important to identify those people who reach certain ages without impairment, and then treat them as a standard against which to compare others in the sample.

Jones added that by establishing a threshold for cognitive impairment using the robust normative sample that excludes people who are likely to have a clinical problem likely to experiencing cognitive decline, adjusted for many factors including age, sex, education, and

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2018 HRS core survey; with any limitation in instrumental activities of daily living in the 2016 or 2018 core survey.

[2] See Jones R, Manly J, Langa K, Ryan L, Levine D, McCammon R, and Weir D. 2020. [Factor structure of the Harmonized Cognitive Assessment Protocol Neuropsychological battery in the Health and Retirement Study](#).

race/ethnicity, that cut-point is of a very skewed sample. To the extent that age is predictive of being in the normative group, that is the degree of relationship that will be seen in the overall sample for age and whether someone is counted by the algorithm as MCI or demented. Thus, the cut-point on the cognitive test score that is determined in a robust sample that is not age-adjusted is just a raw indicator of impairment or disease. Each study will have its own data for defining a robust normative group depending on its design. Manly offered MHAS Mex-Cog as an example: this study developed a set of norms without follow-up, even though follow-up is ideal.

Langa highlighted Andrew Steptoe's question in the chat about the quality of informants' reports. He considers conflicting information—for example, when informant reports and cognitive testing conflict, or when the same informant provides conflicting information on different informant scales—to be one the greatest challenges to algorithmic diagnosis. Manly stressed the importance of collecting as much information about informant interviews and how they work in each setting. For cases when the emphasis is diagnostic prediction and classification rather than domain consistency, Langa noted David Llewellyn's suggestion (in the chat) to compare these elegant cognitive approaches involving consensus diagnosis to a crude approach (e.g., MMSE) and alternative approaches (e.g., transfer learning).[3]

HCAP Network Pilot Projects

Emily Briceño and Miguel Arce Renteria spoke about their pilot project on Harmonization of HCAP and Informant Rating Across the United States, Mexico, and Chile, which is scheduled to begin soon. Briceño reviewed the rationale for the project, observing that even though the assessments have been designed to optimize comparability across studies, each study in the HCAP Network has unique regional and methodological characteristics, which complicates direct comparison of scores across studies. Their goal is to perform careful, precise, and culturally informed harmonization work that accomplishes three specific aims:

1. Produce comprehensive **pre-statistical harmonization data** of cognition and informant ratings that will lay the foundation for future researchers to perform harmonization utilizing these cohorts. Requires understanding the scoring and coding procedures, as well as linguistic demands that can inform how similar the items might be across the different studies, across obviously different cultural contexts.

2. **Generate harmonized scores** of global cognitive performance, memory, and language, in addition to informant ratings of cognitive decline. The statistical harmonization aim is led by Alden Gross and Jones. Their strategy is to estimate a series of item response theory (IRT) models using an item-banking approach; generate co-calibrated factors for global cognitive performance, memory, and language, based on all available items in

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[3] Transfer learning is a machine learning approach that uses knowledge gained from solving one problem and then applies it to solve a different though related problem. For example, an algorithm trained to predict global cognitive decline may help to improve the prediction of Alzheimer's disease risk. Alternatively, data may be used to pretrain a model in one dataset, in order to improve predictive performance in a second dataset, that includes different though overlapping features to solve the same problem more effectively. Llewellyn has an Exeter-Turing grant to explore the application of transfer learning to dementia prediction in the National Alzheimer's Coordinating Center dataset.

these domains from HRS HCAP, Mex-Cog, and Chile-Cog; and generate a co-calibrated measure of informant-rated cognitive decline using all available informant-rated items.

3. **Validate harmonized cognitive scores** and informant ratings using demographics and medical risk factors (i.e., age, educational attainment, cardiovascular disease [hypertension, diabetes, heart disease, stroke]).

Expected outputs include comprehensive pre-statistical data to document methodological differences across cohorts; harmonized scores of global cognition, memory, and language; harmonized informant ratings; and preliminary validation of these harmonized scores. These scores are expected to lay the foundation for substantive investigations of the social, economic, and cultural determinants of cognitive health and cross-national prevalence estimates of MCI and dementia.

International Harmonization of HCAP Cognitive Measures

Gross explained that the main goal of this project is to co-calibrate general and domain-specific cognitive functions cross-nationally for five HCAP studies: HRS-HCAP, ELSA-HCAP, LASI-DAD, Mex-Cog, and HAALSI-HCAP. He reported that coordinated analyses in HRS-HCAP, Mex-Cog, and LASI-DAD have separately shown that a similar hierarchical confirmatory factor analysis (CFA) of cognitive abilities fits well. Gross has worked with Lindsay Kobayashi and neuropsychological colleagues to determine which items are comparable across the studies; decisions were then reviewed by the Gateway to Global Aging team. Most of the HCAP batteries have about 40 to 47 items; HAALSI has only 27 items. Gross also noted that one country's HCAP study might be conceptually split into separate samples. For example, LASI-DAD administered slightly different batteries depending on whether a participant is literate. Of particular interest are differences or adaptations in test versions and in administration procedures.

Gross illustrated the degree of overlap among the different studies. When constructing a harmonized battery or co-calibrated measures of general cognitive performance, researchers must ensure a sufficient number and quality of common items between the surveys based on judgements from pre-statistical harmonization. For example, HAALSI and Mex-Cog have at least 14 items in common. The overlap in common items across the studies for orientation, memory, and language appears reasonable. However, less overlap on measures of executive functioning (which Gross used to represent a mixture of attention, speed of processing, and abstract reasoning) and visuospatial orientation is concerning.

Following the pre-statistical harmonization work, Gross and colleagues undertook statistical co-calibration that entailed estimating, within each study and for each domain, CFA for overall and domain-specific cognitive functioning to estimate the degree to which the models fit the data and the degree to which modifications would be needed to improve fit to the data. An item-banking approach was used to achieve co-calibration for each domain. Diagnostics included examining the extent of missing data in items and estimating the reliability of scores by data set. Factor scores can be estimated for a person even if that person has few test items. The only difficulty has been acquiring factor scores and general cognitive performance (GCP) measures for the 150 or so HRS HCAP subjects for whom only informant data are available. The marginal

reliability of scores for some people are poor, which is often due to having few tests or tests that are of lower quality. Most domain-specific models fit in the good-to-adequate range, although orientation is highly imprecise, which is to be expected because it involves questions about, for example, today's date or one's current location. Language appears to be poorly estimated in HRS and ELSA due to binary naming questions; memory and executive functioning appear to be fine. In summary, Gross concluded that co-calibration of GCP and domains is possible, provided overlap in items is sufficient and item characteristics are good. The sparseness of items in specific domains is a problem. Next steps include empirical testing for any item differences.

Open Discussion and Next Steps

For investigators preparing to field a baseline survey, in a new context and new country, Weir suggested arranging a consultation with the HRS team and selected people from a few relevant studies to talk through the practical aspects of the HCAP administration and best practices. Weir welcomed suggestions such as substitutions and updates to improve the quality of the HCAP batteries, which should benefit all studies. Lee added that the LASI-DAD team is currently evaluating the addition of judgment questions. She suggested that new study investigators review the literature in their own country. Examining how some of the tests that were already carried out in the country compares with the HCAP batteries can be a very useful exercise.

King concluded by observing that the harmonization aspects about which this group is wrestling are fundamentally difficult and thorny. Langa agreed that this work is complicated, because the brain is complicated. Weir indicated that HCAP would propose several follow-up calls (maximum one hour) on topics of interest to participants, which might include:

- Integrating informant reports with cognitive testing measures to classify participants, and how to best adjudicate conflicting information.
- Cross-walking between sub-samples and the core survey.
- Ensuring minimal duplication of effort between the pilot studies and Gateway harmonization activities. (Lee, Gross, Briceño, Arce, and Elo plan to develop a plan.)

Appendix A: Meeting Agenda
Rev. 2-12-21

10:45 a.m.   **Socializing Time (Optional)**

11:00   **Welcome**
David Weir and Ken Langa

11:05   **NIA Welcome**
Jonathan W. King, NIA Project Scientist to HRS, and Lis Nielsen, Director, Division of Behavioral and Social Research

11:10   **New Funding Opportunities (R24 Internal Pilots and NIA ADRD funding)**
Ken Langa and Jonathan W. King

11:30   **HCAP R24 Network Study Updates**
Session Chair: David Weir

> **Mexican Health and Aging Study (MHAS), Mex-Cog** (5 min)
> *Rebeca Wong and Silvia Mejia-Arango*
>
> **Chile-Cog** (5 min)
> *Irma Elo and David Bravo*
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> **Longitudinal Aging Study in India-Diagnostic Assessment of Dementia (LASI-DAD)** (5 min)
> *Jinkook Lee*
>
> **Health and Aging in Africa: A Longitudinal Study of an INDEPTH Community in South Africa (HAALSI)** (5 min)
> *Meagan Farrell and Lisa Berkman*

12:00 p.m.   **HCAP Study Methods Updates**
Session Chair: Ken Langa

> **HRS HCAP Diagnostic Algorithm Development** (25 min)
> *Jen Manly and Rich Jones*
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> **R24 Network Pilot Projects** (10 min)
> *Miguel Arce Renteria and Emily Briceño*
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> **International Harmonization of HCAP Cognitive Measures** (10 min)
> *Alden Gross*

12:45   **Open Discussion, Questions, Plans for Future Meetings**

1:00   **ADJOURN**

Appendix B: Meeting Attendees
Rev. 2-18-21

U.S. Health and Retirement Study (HRS)
David Weir, PI, HRS; Co-PI, HCAP Network, Co-I, HRS-HCAP; University of Michigan
Ken Langa, Co-PI, HCAP Network, PI HRS-HCAP; Co-I, HRS; University of Michigan
Eileen Crimmins, Co-I, HRS; University of South California
Jessica Faul, Co-I, HRS; University of Michigan
Richard N. Jones, Co-I, HRS; Brown University
Jennifer Manly, Co-I, HRS; Columbia University
Miguel Arce-Renteria, Columbia University
Eva Giatas, University of Michigan
Lindsay Kobayashi, University of Michigan
Deb Levine, University of Michigan
Ryan McCammon, University of Michigan
Lindsay Ryan, University of Michigan
Amanda Sonnega, University of Michigan
Caroline Wixom, University of Michigan

Caribbean American Dementia and Aging Study (CADAS)
William Dow, PI, CADAS; University of California, Berkeley
Daisy Acosta, Universidad Nacional Pedro Henriquez Urena
Ivonne Jiménez-Velàzquez, University of Puerto Rico School of Medicine
Jorge Llibre-Guerra, Washington University School of Medicine in St. Louis

Chile-Cog
Jere Behrman, Co-PI, Chile-Cog; University of Pennsylvania
David Bravo, Co-PI, Chile-Cog; Catholic University of Chile
Irma Elo, Co-PI, Chile-Cog; University of Pennsylvania

China Health and Retirement Longitudinal Study (CHARLS)
Yaohui Zhao, PI, CHARLS; Peking University
John Strauss, Co-PI, CHARLS; University of Southern California
Huali Wang, Peking University

English Longitudinal Study of Ageing (ELSA)-The Healthy Cognitive Ageing Project (HCAP)
Andrew Steptoe, PI, HCAP; University College London
David Llewellyn, Co-I, HCAP; University of Exeter
Carol Brayne, Co-I, HCAP; University of Cambridge
Dorina Cadar, University College London

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

Darina Bassil, Harvard University

Meagan Farrell, Harvard University

Julia Rohr, Harvard University

Beth Truesdale, Harvard University

The Irish Longitudinal Study on Ageing (TILDA)

Rose Anne Kenny, PI, TILDA; Trinity College Dublin

Niamh Clarke, Trinity College Dublin

Orna Donoghue, Trinity College Dublin

Joanne Feeney, Trinity College Dublin

Ann Hever, Trinity College Dublin

Christine McGarrigle, Trinity College Dublin

Longitudinal Aging Study in India-Diagnostic Assessment of Dementia (LASI-DAD)

Jinkook Lee, PI, LASI-DAD; University of Southern California

Sandy Chien, University of Southern California

Alden Gross, John Hopkins Bloomberg School of Public Health

Ying Liu, University of Southern California

Erik Meijer, University of Southern California

Sarah Petrosyan, University of Southern California

Mexican Health and Aging Study (MHAS), Mex-Cog

Rebeca Wong, PI, Mex-Cog; University of Texas Medical Branch

Silvia Mejia-Arango, Expert Collaborator, Colegio de la Frontera Norte

Alejandra Michales-Obregon, University of Texas Medical Branch

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

Bernadette McGuinness, PI, NICOLA; Queen's University Belfast

Charlotte Neville, Queen's University Belfast

Leeanne O'Hara, Queen's University Belfast

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

Nora Angleys, Max Planck Institute

Salima Douhou, Max Planck Institute

Other Interested Study Contributors

Dararatt Anantanasuwong, PI, Panel Survey on Health, Aging, and Retirement in Thailand

David Bell, PI, Healthy Aging in Scotland (HAGIS)

Fernando Bertolotto, PI, Study of Health and Aging in Uruguay (ELSE Uy)

Emily Briceño, Brain Attack Surveillance in Corpus Christi (BASIC) – Cognitive Study

Camila Esteben, Study of Health and Aging in Uruguay (ELSE Uy)

Arie Kapteyn, PI, Understanding America Study (UAS)

Hans-Peter Kohler, PI, Malawi Longitudinal Study of Families and Health (MLSFH)

Iliana Kohler, MLSFH; University of Pennsylvania

Norma Binti Mansor, PI, Malaysia Aging and Retirement Study (MARS)
Carlos Mendes de Leon, PI, Dementia and Related Health and Social Challenges in Lebanon
Lewis Morgenstern, PI, BASIC Cognitive Study
Cesar de Oliveira, Co-PI, Brazilian Longitudinal Study of Aging (ELSI)
Mohamed Salama, PI, A Longitudinal Study of Egyptian Healthy Aging (AL-SEHA)
James P. Smith, PI, HRS Around the World; RLA

National Institute on Aging (NIA)
Richard Hodes, Director
Lis Nielsen, Director, Division of Behavioral and Social Research (BSR)
Frank Bandiera, Health Scientist Administrator, BSR
Jill Beaver, Health Science Policy Analyst, Office of Legislation, Policy, and International Activities (OLPIA)
Elena Fazio, Health Scientist Administrator, BSR
Brian Gray, Health Science Policy Analyst, OLPIA
Amelia Karraker, Program Official, BSR
Melinda Kelley, Director, OLPIA
Jonathan W. King, HRS Project Scientist; Senior Scientific Advisor to the BSR Director, BSR
Marilyn Miller, Program Director, Division of Neuroscience (DN)
Carmen Moten, Health Scientist Administrator, Division of Extramural Activities
Georgeanne Patmios, **Senior Scientific Administrator**, BSR
Nina Silverberg, Director, Alzheimer's Disease Centers Program, DN
Janine Simmons, Chief, Individual Behavioral Processes Branch, BSR
Luke Stoekel, Program Director, BSR

Rose Li and Associates, Inc. (RLA)
Rose Li, Project Director
Beth Finch, Science Writer
Sabira Mohamed, Meeting Planner
Derek Smith, Meeting Assistant

Appendix C: Chat Transcript

February 18, 2021

11:13:07 From Lis Nielsen to Everyone : This is the Notice Jon is referring to:
https://grants.nih.gov/grants/guide/pa-files/par-19-070.html

11:13:48 From Lis Nielsen to Everyone : Major Opportunities for Research in Epidemiology of Alzheimer's Disease and Related Dementias and Cognitive Resilience
https://grants.nih.gov/grants/guide/notice-files/NOT-AG-18-053.html

11:20:49 From Jonathan King to Everyone :
https://www.nia.nih.gov/research/blog/2019/07/applying-dementia-research-funding-choose-your-codes-carefully

11:22:26 From Lis Nielsen to Everyone : And here is our new Notice of Special Interest related to COVID-19, in case you have ideas related to this: https://grants.nih.gov/grants/guide/notice-files/NOT-AG-21-015.html

11:22:52 From Luke Stoeckel to Everyone : and our twitter handle:
https://twitter.com/NIA_BSR

11:24:42 From Luke Stoeckel to Everyone : @NIA_BSR

12:08:20 From Jennifer Manly to Everyone : MELVA is not the name, he just made that up just now

12:12:17 From Andrew Steptoe to Everyone : Why 1.5 SD - is there a strong rationale for this?

12:12:46 From Jennifer Manly to Everyone : This cut balances sensitivity and specificity

12:13:14 From Andrew Steptoe to Everyone : thanks

12:13:37 From Carol Brayne to Everyone : Following up on this. If age and sex normed the actual increase in prevalence of impairment (and dementia) with age is potentially controlled out - flattening the actual shape...i.e. creating a certain circularity

12:14:25 From Jennifer Manly to Everyone : That circularity is balanced through the robust approach... I can say more after Carol

12:14:41 From Carol Brayne to Everyone : thanks, I'm sure we've talked about this many times!

12:18:12 From Andrew Steptoe to Everyone : The informant report is quite important in your algorithm. Are the informants pretty reliable in this respect?

12:20:10 From Meagan Farrell to Everyone : How many years of follow up are needed to develop robust norms?

12:22:07 From Carol Brayne to Everyone : Drop out is important in this. As age increases the proportion of the older old without any impairment really does dramatically decline. I still worry that these methods might lead to underestimation of impairment and dementia at the oldest ages.

12:22:31 From Huali Wang to Everyone : Did you try placing the informant report on the first level, the cog. assessment on the second level of the algorithm?

12:22:46 From David Llewellyn to Everyone : Given the concern about possible overadjustment/circularity is it possible to benchmark or compare to the consensus diagnosis cases? We've been arguing about this for years!

12:24:02 From Rebeca Wong to Everyone : In Mex-Cog we find that INFORMANTS who are spouses systematically report worse function than the other types of Informants (e.g. children). Do you observe something similar?

12:24:56 From Rich Jones to Everyone : Great questions everyone thanks for the written comments. Please keep them coming.

12:27:19 From Jennifer Manly to Everyone : Rebeca we have not looked at that yet but it is a great question. IMHO a great pilot might be to carefully examine the informant measures across setting.

12:27:38 From Bernadette McGuinness to Everyone : Spouses will notice more functional impairment as they live with the participant, children have usually grown up and moved out so may not be aware of all functional impairments so they just have a snapshot, that's what we find clinically usually

12:28:06 From Carol Brayne to Everyone : Rebecca - complex question. In one population we studied this was socially patterned - spouses tended to minimise, middle class educated children would be over sensitive to change - thus it seems we need to be careful about how we interpret informant interview (including fact that these can be care home staff who might not know individuals, or friends who have known them for years as well as cultural/stigma aspects).

12:29:08 From Rebeca Wong to Everyone : Yes. Co-residence with children is common in Mexico. We look at and control for co-residence though.

12:41:39 From Miguel Arce to Everyone : Re: the informant ratings, it will also be critical to evaluate which items may be more valid assessment of participant's functioning. For instance, from my work in using the informant report to define a robust normative sample in Mex-Cog, there was over-endorsement of certain complaints that may suggest cultural differences in responding versus true functional decline. In those cases, we selected items considered to be

more clinically relevant and only the highest frequency reported (i.e., always versus sometimes).

12:51:48 From Rich Jones to Everyone : Another pilot project could be looking if a purely exploratory approach to characterizing domains of HCAP performance come close to the *a priori* models summarized by Jones and Gross. This is brought up by Alden saying animal naming is a good language item, but many researchers consider this a measure of executive functioning.

12:53:19 From Huali Wang to Everyone : Emily, Miguel and Alden, great work!

12:54:05 From David Llewellyn to Everyone : I'd like to see these elegant cognitive approaches compared to a crude approach (e.g. MMSE) and alternative approaches (e.g. transfer learning). Particularly when the emphasis is diagnostic prediction/classification rather than domain consistency

12:55:05 From Jennifer Manly to Everyone : And I think representation from the pre-stat harmonization team in that consultation is also important

12:56:08 From Carlos F Mendes de Leon to Everyone : Thanks Jen!

12:56:12 From Meagan Farrell to Everyone : I am wondering if MHAS and HRS teams are willing to share more about imputation methods— our missing data is strongly associated with cognitive impairment, age, education.

12:56:45 From Rich Jones to Everyone : rich_jones@brown.edu

12:57:33 From Alden Gross to Everyone : Ditto what Jennifer said about the importance of prestatistical harmonization - the end product is only as good as that.

12:57:40 From Rebeca Wong to Everyone : Absolutely Meagan. Please contact me (rewong@utmb.edu) and we can send all our documentation. Scoring and Imputation was a careful and long process. We documented as much as possible -- for ourselves and others.

12:58:01 From Rich Jones to Everyone : Double ditto on pre-stat harmonization

12:58:13 From Meagan Farrell to Everyone : Thank you, Rebeca!

12:58:30 From Carol Brayne to Everyone : There's a really interesting piece on this about how those who haven't been involved in the creation of the datasets then use the data even with these amazing efforts...

12:58:47 From Andrew Steptoe to Everyone : thanks. Much food for thought...

12:58:56 From Dararatt to Everyone : Thank you for all very stimulating studies in cognition!

12:59:03 From Carlos F Mendes de Leon to Everyone : Thanks very much! I will follow up to get more documentation on pre-statistical harmonization

12:59:21 From IRMA ELO to Everyone : Thanks everyone!

12:59:24 From Cesar de Oliveira to Everyone : Thank you

12:59:41 From Rebeca Wong to Everyone : Thank you all. Stimulating.

12:59:48 From Lindsay Kobayashi to Everyone : Thank you, everyone!!

12:59:48 From Bernadette McGuinness to Everyone : Thanks everyone

12:59:54 From Dorina Cadar to Everyone : It would be essential to have a better understanding of the international algorithm of ascertaining MCI and dementia and how this can be generated given the differences in items available in all HCAP studies

12:59:54 From Niamh Clarke to Everyone : From all in TILDA thank you

13:00:00 From F.Bertolotto to Everyone : Thank you!!!