## Harmonized Cognitive Assessment Protocol (HCAP) U24 Network Annual Meeting

# **Meeting Summary**

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This meeting summary was prepared by Rose Li and Associates, Inc., under contract to the University of Michigan (**U24 AG065182**). The views expressed in this document reflect both individual and collective opinions of the meeting participants and not necessarily those of the University of Michigan or the National Institute on Aging. Contributions to and review of earlier versions of this meeting summary by the following individuals are gratefully acknowledged: Martin Sabandal, Gina Castelvecchi, Dana Carluccio, Rose Li, Ken Langa, Lindsay Ryan, Emma Nichols, Alden Gross, Bernadette McGuinness, Andrew Steptoe, Salima Douhou, Minki Chatterji, David Weir, and Nancy Tuvesson.

## **Acronyms & Abbreviations**

AD	Alzheimer's disease
ADRD	Alzheimer's disease-Related dementia
AL-SEHA	A Longitudinal Study of Healthy Aging in Egypt
APOE	apolipoprotein E
BASIC-Cog	BASIC Cognitive Study
BMI	body mass index
CADAS	Caribbean American Dementia and Aging Study
CDR	clinical diagnosis rating
CHARLS	China Health and Retirement Longitudinal Study
Co-PIs	Co-Principal Investigators
COVID-19	coronavirus disease 2019
CSI-D	Community Screening Instrument for Dementia
DBS	dried blood spot
DBSR	Division of Behavioral and Social Research
DIF	differential item functioning
ELSA	English Longitudinal Study of Ageing
GFAP	glial fibrillary acidic protein
HAALSI	Health and Aging in Africa: A Longitudinal Study of an INDEPTH Community in South Africa
НСАР	Harmonized Cognitive Assessment Protocol
HMSE	Hindi Mental State Exam
HRS	Health and Retirement Study
IADL	Instrumental Activities of Daily Living
IQCODE	Informant Questionnaire on Cognitive Decline in the Elderly
ISCED	International Standard Classification of Education
ISER-N	Institute for Social and Environmental Research—Nepal
LASI-DAD	Longitudinal Aging Study in India-Diagnostic Assessment of Dementia
LSAHA	Lebanon Study on Ageing and HeAlth
MCI	mild cognitive impairment
Mex-Cog	Mexican Cognitive Aging Ancillary Study
MHAS	Mexican Health and Aging Study
MMSE	Mini Mental State Examination

MRI	magnetic resonance imaging
NfL	neurofilament light chain
NIA	National Institute on Aging
NICOLA	Northern Ireland Cohort for the Longitudinal Study of Ageing
NIH	National Institutes of Health
NIMLAS	Network for Innovative Methods in Longitudinal Aging Studies
PET	positron emission tomography
proBNP	pro-B-type natriuretic peptide
PSP	Population and Social Processes (Branch of DBSR)
pTau-181	phosphorylated tau-181
pTau-217	phosphorylated tau-217
RTI	Real Time Insights
SES	socioeconomic status
SHARE	Survey of Health, Aging and Retirement in Europe
SPS	Social Protection Survey
TICS	Telephone Interview for Cognitive Status
TILDA	The Irish Longitudinal Study on Ageing
t-Tau	total tau
WHICAP	Washington Heights/Inwood Columbia Aging Project

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## **Meeting Summary**

### Introduction

The Harmonized Cognitive Assessment Protocol (HCAP) International Network met in a hybrid in-person and virtual conference on September 19-20, 2022. The overall purpose was to discuss study progress, activities, and action items (next steps) for advancing harmonization of agingrelated cognitive research at a global scale. The presentations covered updates on HCAP Network, HCAP Studies (established and pilot), Biomarkers Core, Diagnosis and Classification Core, Protocol Core, and Statistical Harmonization Core. The meeting also included time for open discussion, questions, and planning. The meeting agenda and list of participants are included as Appendices A and B, and the substantive portions of the chat transcript are included as Appendix C.

Drs. Ken Langa and David Weir, Co-Principal Investigators (Co-PIs) of the HCAP Network, welcomed attendees and introduced National Institute on Aging (NIA) representatives: Dr. Amy Kelley, Deputy Director; Dr. Lis Nielsen, Director, Division of Behavioral and Social Research (BSR); Dr. John Phillips, Chief of the Population and Social Processes Branch (PSP), BSR; and Dr. Minki Chatterji, Program Officer for Global Health and Cognitive Epidemiology, PSP, BSR. Weir provided an overview of the meeting agenda and expressed excitement for the progress updates and discussions from the HCAP Studies and HCAP Cores.

Chatterji presented on NIA research priorities, highlighting <u>NIA's Strategic Directions for</u> <u>Research (2020-2025)</u> and the <u>implementation milestones</u> for Alzheimer's disease and Alzheimer's disease-related dementia (AD/ADRD) research conducted internationally. BSR work is guided by the recommendations from the NACA 2019 BSR Review Committee Report. She also noted <u>HCAP U24 Network's</u> main objectives, emphasized cross-national harmonization in order to contribute to NIA's research priorities, and shared new funding opportunities (e.g., HCAP U24 pilot grants, <u>AD administrative supplements</u>). In addition, Chatterji expressed that NIA is strongly motivated to expand Health and Retirement Study (HRS) and HCAP Studies more robustly around the world, particularly in understudied geographic areas including West Africa, Central Africa, and Central Asia.

### The Network for Innovative Methods in Longitudinal Aging Studies

#### Brady West and Sunghee Lee

Weir invited Drs. Brady West and Sunghee Lee, Co-PIs of the Network for Innovative Methods in Longitudinal Aging Studies (NIMLAS), to provide brief updates on NIMLAS' objectives, study progress reports, and planned activities. West stated that NIMLAS aims to be the leading force in establishing and harmonizing methodological research on longitudinal studies of aging at a global scale. Furthermore, West noted that NIMLAS is forming working groups for each of its four research areas: (1) creation of data for minority populations, (2) addressing increasing attrition rates, (3) new measurement technologies, and (4) consent to additional data collection. Additional information on NIMLAS' coordinated international training program,

consulting opportunities, thematic working group meetings, and pilot research projects can be accessed on its <u>website</u>.

### **Reports from HCAP Studies Currently in the Field**

Weir invited three studies with notable recent accomplishments during the COVID-19 pandemic to provide field work updates.

#### TILDA HCAP

#### Joanne Feeney

Because of COVID-19, The Irish Longitudinal Study on Ageing (TILDA) team added a replenishment cohort for its Wave 6 study, totaling 1,831 participants. Participants were subjected to a TILDA-HCAP respondent assessment protocol or a TILDA-HCAP family/friend informant assessment protocol. As of September 2022, greater than 50 percent of the study has been analyzed. Feeney noted that female participants or participants with less than lower secondary education were statistically more likely to refuse the TILDA-HCAP assessments. Furthermore, based on the Wave 5 study conducted in 2018, participants who previously experienced a mild or moderate cognitive impairment were more likely to refuse the TILDA-HCAP HCAP assessments. Feeney noted that the TILDA team continues to face challenges in recruitment of nurses, nurse workload, and study approval delays, but it has implemented a more systematic training for nurses to conduct interviews, recruited research assistants to help the nurses, and employed a dedicated ethics officer to mitigate study approval delays.

#### NICOLA HCAP

#### Bernadette McGuinness

The Northern Ireland Cohort for the Longitudinal Study of Ageing (NICOLA) team began its HCAP study in January 2022. To date 363 participant interviews have been conducted; the team aims to conduct 1,000 interviews by June 2023. Of the 363 interviews, less than 70 percent have been analyzed. Participants who were older or had less than secondary education were statistically more likely to refuse the NICOLA-HCAP assessments. Furthermore, participants who previously scored in the mild or moderate cognitive impairment range from Wave 2 NICOLA were more likely to refuse the NICOLA-HCAP assessments. McGuinness noted that the NICOLA team continues to face numerous challenges in staffing availability, administrative burden, data harmonization, and the recruitment and retention of NICOLA participants. In addition, McGuinness discussed that the NICOLA team plans to monitor participant recruitment in terms of age, gender, education, and cognition; as well as to populate how their NICOLA-HCAP tests are performing compared to TILDA, HRS, and the English Longitudinal Study of Ageing (ELSA).

#### **HRS HCAP**

#### Ken Langa

The HRS HCAP team began its Wave 2 HCAP study on July 2022, which will be completed by August 2023. The team re-interviewed respondents from the Wave 1 study conducted on 2016, re-invited those who declined to participate from the 2016 cohort, and added 65-70 new participants. As of September 2022, HRS-HCAP data were collected from 1,318 participants, with only 236 respondent interviews analyzed so far. Furthermore, only 164 informant

interviews (in-person or by phone) were completed. Langa noted that the HRS-HCAP team is using the same respondent and informant protocols from Wave 1 but has implemented a COVID-19 symptom screener prior to an in-person interview and mask-wearing during this interview. In addition, the HCAP Neuroimaging pilot study, which started fieldwork in 2019, was halted in March 2020 due to COVID-19. Funding for this pilot study (provided by the Alzheimer's Association) was reallocated to perform blood biomarker assays for AD/ADRD in stored blood samples for HCAP participants; additional details are in the Biomarker Core update presentation by Jessica Faul and Bharat Thyagarajan.

## **Updates from Established HCAP Studies**

Langa invited 11 HCAP studies to provide brief updates; a short discussion followed each presentation.

#### ELSA HCAP

#### Andrew Steptoe

The ELSA team is collecting data for Wave 10 (2021-2022) and is planning for Wave 11 (2023-2024), which will require computer-assisted personal interviewing (CAPI) plus nurse assessment. In addition, the first ELSA-HCAP study was conducted in 2018 and involved 1,273 participants aged 65 and older, 82.5 percent of whom completed informant interviews. The ELSA team is slated to conduct a second ELSA-HCAP study (i.e., HCAP 2) in early 2023. HCAP 2 aims to recruit 2,000 participants who will participate in three types of interviews: in-person, informant, and end-of-life. The end-of-life interview will be a valuable metric for determining the physical and mental health status of the participants before death. Data are to be released to the United Kingdom Data Service before the end of 2023.

Weir, McGuinness, and Jonathan King raised questions about the recruitment of underrepresented minority groups as well as potential language barriers that may slow progress of HCAP 2. Steptoe responded that HCAP 2 will focus on collecting a robust sample size of minoritized individuals. He further noted that the participants undergo an initial screening (i.e., English test based on an initial survey from the first HCAP study), and the study team plans to include translators so that HCAP 2 will be more inclusive and representative of the community.

#### **MHAS Mex-Cog**

#### Rebeca Wong

The Mexican Health and Aging Study (MHAS) team conducted Mex-Cog Wave 1 in 2016 and Wave 2 in 2021. Mex-Cog Wave 2 had 4,066 participants with a much greater number reporting through informant interviews compared to Mex-Cog Wave 1. No large differences were observed based on socioeconomic status metrics (e.g., education, age, marital status, and community of residence) between the two Waves. Future data (e.g., classification variables) will be released in September 2022 for Meg-Cox Wave 1, while the first dataset (e.g., clean raw variables, domain scores, weights) will be released in November 2022 for Mex-Cog Wave 2.

King asked about a resource interface that correlates the information between non-genetic MHAS versus genetic data. Wong responded that data will be available to the team soon, which will then need to be harmonized.

#### LASI-DAD

#### Jinkook Lee

The Longitudinal Aging Study in India–Diagnostic Assessment of Dementia (LASI-DAD) team has completed two pilot studies: (1) feasibility study for audiometry, caregiver stress, and retinography and (2) pretest of the Wave 2 protocol in three Delhi, Jaipur, and Pondicherry and nine rounds of Real Time Insights (RTI) COVID-19 data collection as of July 2022. Participants in Wave 2 will participate in a battery of assessments (e.g., cognitive, geriatric) and interviews (e.g., respondent, informant, end-of-life). Wave 2 aims to recruit 4,500 participants and expand across greater geographic coverage in India; the fieldwork plan will be launched in Delhi on October 31, 2022. The LASI-DAD team will actively work on collecting novel information (e.g., audiometry, indoor air pollution), participate in global initiatives (e.g., Exposome, Genomics), explore innovation (e.g., positron emission tomography [PET], mobile sensors), and continue drafting manuscripts for publication.

Phillips asked for clarification regarding test duration, study timeline, and availability of LASI-DAD data for the Exposome Initiative. Lee noted that the times to complete cognitive (1 hour) and geriatric (25 minutes) assessments are standard, study timeline will be met, and data for the Exposome Initiative will be publicly available after harmonization.

#### **CHARLS HCAP**

#### Yaohui Zhao

The China Health and Retirement Longitudinal Study (CHARLS) team fielded a national baseline in 2011 and recruited 17,708 participants, and recently conducted Wave 4 and Wave 5 from 2018 through 2022, which included a CHARLS-HCAP study to evaluate AD/ADRD prevalence. CHARLS-HCAP consists of a battery of assessments (e.g., cognitive) and interviews (e.g., respondent, informant), which will become a permanent part of CHARLS in subsequent Waves that occur every 6 years. Zhao noted low literacy and dialect biases observed in CHARLS-HCAP, with a higher percentage of illiteracy from women participants. To address these issues, the CHARLS team plans to adjust CHARLS-HCAP questions prior to the 2024 Wave.

In response to a question from Alden Gross, Zhao clarified that the language barrier alluded to differences in dialect and in regional use of phrases.

#### HAALSI HCAP

#### Lisa Berkman, Meagan Farrell, Darina Bassil

The Health and Aging in Africa: A Longitudinal Study of an INDEPTH Community in South Africa (HAALSI) team completed data collection for Wave 2 (2018-2019) and Wave 3 (2021-2022); data are being analyzed and will be prepared for public release in early 2023. Wave 1 and Wave 2 of the HAALSI Dementia study were fielded from 2019 through 2021. Wave 1 had 635 respondents: 314 were diagnosed as cognitively normal, 184 experienced mild cognitive

impairment (MCI), and 137 had dementia. The HAALSI team also developed statistical analyses models, Simple Cognition and Expanded Cognition, to generate prevalence estimates for dementia grouped by age. Additional updates on neuroimaging and blood biomarkers are available on the slide deck presentation.

#### Chile-Cog

#### Irma Elo, David Bravo, and Magdalena Delaporte

The Chile Cognitive Aging Study (Chile-Cog) team began 2-months' fieldwork on September 15, 2022, by performing a telephone follow-up survey regarding the longitudinal impacts of COVID-19 on the aging population. The Chile-Cog team is slated to conduct a validation study from October through December 2022 to determine AD/ADRD prevalence from the Telephone Interview for Cognitive Status (TICS) instrument. Moreover, the team will submit the Chilean Social Protection Survey (SPS) cohort papers for publication in fall 2022. In the future, Chile-Cog will (1) incorporate English and Spanish translations of SPS and surveys on its <u>website</u>, (2) collaborate with Wong's Mex-Cog team for data comparisons, (3) continue partnership with Gateway for data harmonization, and (4) plan for Chile-Cog Wave 2.

#### SHARE HCAP

#### Salima Douhou

The Survey of Health, Aging and Retirement in Europe (SHARE) team is continuing its HCAP fieldwork in five countries: Czechia, Denmark, France, Germany, and Italy. Douhou noted a greater uptick in study participation. Furthermore, the SHARE team observed a higher female participation in both respondent and family/friend interviews across all five countries. In addition, data collected (e.g., Mini Mental State Examination [MMSE], animal fluency) for SHARE were comparable to data observed from HRS and ELSA. The SHARE team plans to reanalyze data for each country independently, which may provide insight about differences in cross-country variation.

King requested clarification on the response rates between healthy individuals and those who had mild or severe MCI. Douhou clarified that cognitive health-based groupings were based on cognitive measures from earlier SHARE waves; the next step would be to validate the groupings by harmonizing with the MMSE scores. Gross and Weir asked how documentation will be reported when data are analyzed for individual countries rather than pooled; Steptoe indicated that differences in languages could contribute to the data variability. Douhou acknowledged the questions and noted that the SHARE team will need to be mindful of how to publicly disseminate the data and looks forward to additional feedback during the Day 2 discussion.

#### LSAHA

#### Carlos Mendes de Leon, Martine El Bejjani, Monique Shaya

The Lebanon Study on Ageing and HeAlth (LSAHA) team plans to start collecting data in April 2023. The LSAHA team aims to (1) recruit 3,000 participants aged 60 and older across three regions of Lebanon, (2) administer comprehensive health survey plus a battery of cognitive tests (e.g., symbol digits modalities test), and (3) collect blood samples from all participants for blood biomarker analyses. This study focuses on exposure to political unrest and violence.

Furthermore, the LSAHA team welcomes feedback for its planned study as it tries to harmonize with HCAP, leading to a future LSAHA-HCAP study. Weir recommended the use of the symbol cancellation task as a good substitute for the letter cancellation test when letters do not work well.

#### Nepal, ISER-N

#### Carlos Mendes de Leon

The Institute for Social and Environmental Research—Nepal (ISER-N) team is waiting for a final award from NIA. The ISER-N team aims to (1) recruit 4,000 participants from the Chitwan Valley Family Study, (2) conduct a pilot study to translate surveys in Nepalese, (3) validate the battery of cognitive tests, (4) collaborate with members of the HCAP Network to facilitate the ISER-N future studies, and (5) conduct 2 Waves of data after funding has been awarded by NIA. This study also focuses on exposure to political unrest and violence. Mendes de Leon mentioned that the team will use geocoding to measure proximity to violent events. Steptoe wondered whether it will be possible to separate out effects of violence versus other confounders related to geographical location.

#### CADAS

#### Will Dow

The Caribbean American Dementia and Aging Study (CADAS) team aims to build on the 10/66 Dementia Research from Martin Prince at King's College London, by studying life-course determinants and social consequences of AD/ADRD in Caribbean-origin populations. The CADAS team is finalizing a pilot study; a full launch for data collection will begin in fall 2022. In addition, the CADAS team plans to (1) recruit 1,500 new nationally representative participants; (2) conduct detailed cutting-edge surveys that are cross harmonized with 10/66, HCAP, and HRS; and (3) develop a 10/66 Adam algorithm to predict dementia.

#### Kenya

#### Will Dow

The Kenya team seeks to determine a "dementia baseline" by administering longitudinal HCAPtype surveys to Kenyan participants who are around age 30; the study will be fielded beginning spring 2023.

### **Biomarker Core Update**

#### Neuro Biomarkers – HRS/HCAP Pilot Results

#### Jessica Faul and Bharat Thyagarajan

Faul and Thyagarajan presented preliminary results from their neurological biomarker analyses of venous blood from the HRS 2016 samples. The results of this study are meant to replicate existing neurological biomarker data for A $\beta$ 42/40, phosphorylated tau-181 (pTau-181), neurofilament light chain (NfL), glial fibrillary acidic protein (GFAP), and the <u>Olink Proteomics</u>

<u>Neurology Panel</u>, in a replication study in representative population-based samples of older adults including people from diverse racial and ethnic minority populations.<sup>1</sup>

Because the HRS venous blood collection protocol includes a 24- to 48-hour delay in sample processing, Thyagarajan performed a pre-pilot study using samples from 30 people to determine whether these biomarkers were stable enough for analysis after this delay as well as after freeze-thaw cycles. Overall, analyte levels were much lower but more stable in serum compared to plasma. Faul and Thyagarajan decided to use plasma for Aβ42/40, GFAP, and NfL, while noting that Aβ42/40 remains relatively stable and GFAP and NfL levels are reduced by 10-15 percent. Because plasma pTau-181 levels increased due to artifactual phosphorylation of Tau, Faul and Thyagarajan opted to use serum for pTau-181. Freeze-thaw cycle results suggested that analyses of these biomarkers should minimize the number of freeze-thaw cycles and remain consistent across samples. This pre-pilot study also determined that all analyte levels were stable across a 2-week window of sample collection.

Pilot results of approximately 1,000 HRS-HCAP samples showed that while A $\beta$ 42/40 decreased and NfL and GFAP increased with age, only GFAP was most predictive of cognition across White, Black, and Hispanic HRS-HCAP participants. However, GFAP still did not perform as well for Hispanic participants compared to White and Black participants. Moving forward, Faul and Thyagarajan will assay all of the selected biomarkers in the entire HCAP 2016 sample (approximately 2,400) and may include additional samples up to a total of 4,200 for some analytes. They will also test these biomarkers in dried blood spots (DBSs) and anticipate that, given its stability, NfL could be reliably assayed in this sample type.

#### Discussion

Weir noted that although DBS analysis has not been popular for biomarker analysis, some regions that lack access to venous blood may find DBS analysis useful. King expressed interest in following HRS-HCAP participants over time to correlate biomarker levels if and when participants are diagnosed with MCI or AD/ADRD.

King and Weir also discussed with Thyagarajan the cost of running these assays. The commercial Quanterix machine costs approximately \$270,000. The pTau-181 singlicate assay costs \$35 to \$40, and the fourplex run costs are approximately \$60. The Olink panel costs more than the other analytes. Thyagarajan noted that running samples at higher numbers reduces per sample costs.

Steptoe inquired about longer-term sample stability. He indicated plans to analyze samples collected 15-20 years ago for the Whitehall longitudinal study. Thyagarajan explained that some samples used in the pilot study were collected 5-6 years ago, and he did not see differences between samples collected 6 years ago versus those collected within the past year.

<sup>&</sup>lt;sup>1</sup> Notably, these analytes are measured using Quanterix assays run on an HD-X Automated Immunoassay Analyzer.

## Blood Based and Neuroimaging Biomarkers for the Harmonized Diagnosed Assessment for LASI-DAD

#### Perry Hu

Hu outlined the LASI-DAD blood collection protocol, as well as some Wave 1 study results and Wave 2 progress. Local study sites send whole blood stored at below 4°C and plasma samples stored at below -20°C to Metropolis Laboratory, the leading independent pathology laboratory in India; typical shipping duration to Delhi is no more than24 hours. For Wave 1, whole blood and serum assays focused on vascular and more reversible etiologies of cognitive decline. After adjusting for age, sex, and education level, pro-B-type natriuretic peptide (proBNP), homocysteine, and body mass index were inversely correlated with cognitive scores in LASI-DAD and HRS-HCAP.

For Wave 2, samples will be analyzed using all markers from Wave 1 plus additional markers more directly associated with AD/ADRD (e.g., Aβ42/40, total tau [t-Tau], pTau-181, NfL, GFAP). Thyagarajan will train Metropolis Laboratory staff at the University of Minnesota during October 2022 and will perform a site visit at Metropolis Laboratory. After training, Metropolis Laboratory will validate its methods by re-analyzing 88 samples for comparison against University of Minnesota's results.

Researchers analyzing LASI-DAD neurological biomarkers will collaborate with the main LASI study researchers to measure NfL on DBSs. In addition, the LASI-DAD neurological biomarkers study is planning a neuroimaging initiative to study differences between people at risk for AD/ADRD based on blood biomarker levels and MCI participants stratified by literacy and urbanicity using T1-weighted, T2, and diffusion imaging magnetic resonance imaging (MRI) data. Four sites in India are ready to begin MRI data collection.

#### Discussion

King asked whether apolipoprotein E (APOE) status was collected for this study and recommended that the neuroimaging study contain enough APOE patients for sufficient study power. Jinkook Lee affirmed that APOE status was collected for this study.

Steptoe, King, and Lee discussed adequate statistical powering for the study. King explained that neuroimaging studies usually require thousands of individuals, but because this study is longitudinal, thousands of individuals may not be needed for adequate power. In addition, the required sample size depends on the types of analyses. Lee explained that for the proposed neuroimaging study, their sample size enables 80 percent power.

## Plasma Biomarkers in Community-Based Intergeneration Studies in Washington Heights

#### Jennifer Manly

Manly presented recent biomarker data from Washington Heights/Inwood Columbia Aging Project (WHICAP) samples. These analyses and subsequent findings will enable clearer definitions of AD/ADRD phenotypes, examination of AD and non-AD pathology interactions, and examination of structural and social determinants of disease. In a recent study from the Brickman laboratory, researchers assessed correlations between biomarker levels in plasma obtained 3 years prior to death and neuropathology findings from autopsies of study participants. Plasma phosphorylated tau-217 (pTau-217) and pTau-181 levels increased monotonically across neuropathological diagnostic groups. The combination of A $\beta$ 42/40, t-Tau, pTau-181, pTau-217, and NfL had much higher predictive value for AD neuropathology than clinical AD diagnosis (area under the curve [AUC] of 0.925 versus 0.668). The best distinguisher between clinical diagnosis of AD and non-AD participants was pTau-217, although this biomarker performed better in non-Hispanic participants compared to Hispanic participants.

Manly outlined the Offspring Study that aims to identify educational, economic, social, and biological predictors of cognitive trajectory in midlife across race, ethnicity, language, and sex/gender as well as the biological and neuroanatomical mediators of parental risk for AD by studying offspring of WHICAP participants. As of September 2022, the study has 2,000 enrolled participants. Preliminary results indicate that plasma pTau-181 levels do not differ across APOE status, race, ethnicity, or language groups. However, plasma pTau-181 levels are associated with age and are higher in men than women. Notably, higher pTau-181 levels were associated with reduced memory scores. Using a childhood socioeconomic status (SES) composite score based on parent education, occupation, and income, researchers found that pTau-181 had a weaker relationship with memory scores in participants with higher SES compared to those with lower SES. Therefore, SES may promote cognitive reserve against AD neuropathology.

## **Diagnosis and Classification Core Update**

#### **IQCODE** Performance in LASI-DAD

#### Emma Nichols

Nichols described her current study to assess the performance of the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) in India. The IQCODE assessment asks informants about the improvement or worsening of the participant's ability to perform daily activities from the perspective of an informant. To identify IQCODE items that may perform poorly in LASI-DAD, Nichols examined the magnitude of missing data (including a high rate of "never did" answers) and interrogated patterns of missingness by characteristics of study participants and informants. To further assess the performance of the measurement tool, Nichols used factor analysis, assessed criterion validity with the Hindi Mental State Exam (HMSE), and evaluated a partial IQCODE assessment.

The following IQCODE items had a high rate of missing data: ability to remember address and phone number, ability to work with familiar machines, ability to learn a new gadget or machine, ability to learn new things in general, ability to understand a story in a book or television show, and ability to handle financial matters. The rate of data missingness for each of these items was related to urbanicity, participant gender, informant generation, and/or informant type. Based on these findings, Nichols opted to remove the following items: ability to remember address and phone number, ability to work with familiar machines, and ability to learn a new gadget or

machine. Notably, both the full and new partial IQCODE scores associated strongly with HMSE scores; this association was stronger in urban compared to rural settings.

Overall, Nichols's research raises questions about the inclusion of items with high levels of missingness; certain items may lack validity in other cultures. Notably, the partial IQCODE retained information normally acquired from the full IQCODE assessment, but the effect of urbanicity still remains for the partial score. Moving forward, Nichols will assess how the relationship between informant and participant can affect reporting.

#### Discussion

One meeting participant asked whether both IQCODE assessments were compared to HRS or another data source, but these comparisons were only performed with LASI-DAD. If these removed items from IQCODE are not necessary, then other research groups may be interested in using the partial IQCODE as well. However, Gross indicated that the same items may not have high levels of missingness in other cohorts. Instead, researchers could use the same procedures as Nichols to identify problematic items with high rates of missingness in their respective cohorts. Steptoe questioned whether removal of items from IQCODE would render previous thresholds unusable, but King noted that because factor loadings for each item were very similar, adjusting those thresholds may not be too difficult. However, new thresholds would still require validation.

Feeney asked for further elaboration on the meaning of "never did" responses; a respondent may choose not to perform a task or may not have the opportunity to perform that task. Lee noted that interviewers were trained to probe further to distinguish between both of these options.

Langa and Nichols discussed the importance of the relationship between informant and participant. Nichols noted that even within generation groupings, there was variability in the nature of the informant-participant relationships.

## **Comparing Informant Measures of Functioning and Cognitive Decline in International HCAP Data**

#### Yuan Zhang

Zhang explained that recognizing social and cultural contexts for informant reporting is essential for interpreting informant data across countries. To better understand differences in informant reporting, Zhang will compare informant data from HRS-HCAP, Mex-Cog, and CHARLS. Informant ratings were obtained from IQCODE, Blessed Dementia Scale (Blessed), and the Community Screening Instrument for Dementia (CSI-D) scores, and cognition was directly measured using MMSE and the harmonized global cognition scores. Additional factors Zhang considered were the age, gender, and years of education for informants and participants, as well as the nature of the informant-participant relationship.

Comparisons between the HRS-HCAP and Mex-Cog cohorts indicated that while informant ratings were similar, direct cognitive results were lower in Mex-Cog compared to HRS-HCAP. Zhang performed multivariate analysis to predict CSI-D from harmonized global function scores.

For HRS-HCAP and Mex-Cog, increased age was associated with more reported impairment. For HRS-HCAP but not Mex-Cog, participant education was positively associated with reported cognitive impairment; in these instances, informants may have higher expectations for participants with higher education levels. HRS-HCAP female informants reported more impairment overall than males, and this difference was not detectable in Mex-Cog. In Mex-Cog informants who resided with participants reported more impairment, and spouse informants report more impairment than all other types of informants. However, for HRS-HCAP spouse informants only report more impairment than non-family informants.

Moving forward, Zhang will add another informant interview assessment and include the CHARLS cohort in her comparisons. In addition, adding more HCAP studies to these comparisons will improve the understanding of informant data and offer insights valuable for the development of diagnostic algorithms in different countries.

#### Discussion

Gross noted that there is likely cultural variability that complicates standardization of this type of information across all HCAP studies. However, Weir noted that further comparisons may provide information about ways to at least partially standardize informant data.

#### **HRS-HCAP Manly-Jones Diagnostic Algorithm**

#### **Rich Jones**

Jones outlined the procedure for implementing versions of the Manly-Jones diagnostic algorithm, which are as follows:

- 1. Assess and score participants on multiple domains of cognitive performance
- 2. Apply factor analysis in the whole cohort to identify domains of cognition
- 3. Identify robust norms sample for use as a standardization sample for the entire cohort
- 4. Standardize and normalize factor score estimates with respect to major sociodemographics
- 5. Identify the cutting point of standardized and normalized scores compared to the reference sample
- 6. Determine whether functional impairment is present using IQCODE, Blessed, and selfrated memory complaints
- 7. Use diagnostic algorithm to determine MCI and dementia status

Jones <u>published study design and methods</u>, which align with step 1 listed above. He also has a <u>preprint on factor analysis</u>, relevant to step 2, as well as an accepted manuscript that discusses the generation of a robust norms sample.

Based on the algorithm, Jones defined impairment as a score of 35 or less on a standardized and normalized domain score. Determination of MCI and dementia status also uses responses from IQCODE and Blessed as well as self-rated memory concerns. All relevant code for the Manly-Jones algorithm is <u>available on GitHub</u>.

## Facilitating Export and Adjustment of Algorithm for Other Network Studies

#### Jennifer Manly

Manly further detailed how the Manly-Jones algorithm can be adjusted for use in other network studies. She provided important considerations for each step outlined by Jones. When assessing and scoring participants on multiple domains of cognitive performance (step 1), researchers need to consider the local administration and scoring rules being applied, whether different or additional measures are included in the test battery, and whether all items are linguistically and culturally relevant. When performing factor analysis (step 2), researchers should try to keep the same number of factors used in the original algorithm (i.e., impairment in two or more of five factors equating dementia) to preserve comparability. A robust norms sample (step 3) is critical for identifying and assessing impairment severity, ruling out premorbid factors that are not due to brain injury, and enabling diagnostic use of neuropsychological tests. Creating a robust norms sample should include retrospective and prospective data and an attempt to address limitations of traditional cross-sectional norms. When standardizing and normalizing factor score estimates (step 4), researchers should truly consider whether their regression equations are appropriate for defining general expectations. Any selected cut point (step 5) should balance sensitivity and specificity, and the original Manly-Jones algorithm uses 1.5 standard deviations. When determining whether functional impairment is present (step 6), researchers need to consider potential cultural differences in informant interviews and self-reports that may in turn impact MCI and dementia status determination (step 7).

#### Discussion

Meagan Farrell asked whether the factor analyses in the Manly-Jones algorithm are exploratory or confirmatory. Jones explained that the distinction between exploratory and confirmatory factor analyses is not very clear in practice. Manly added that four of the five domains are defined from multiple scores, which enables more information across each domain due to inclusion of high and low difficulty questions.

In response to a question by Weir, Manly indicated that a less sensitive robust normative sample would result in a lower reported rate of dementia.

#### **Export of Manly-Jones Algorithm to BASIC-Cog**

#### Steven Heeringa

Heeringa described how he adapted and used the Manly-Jones algorithm for the BASIC Cognitive Study (BASIC-Cog). BASIC-Cog aims to use community-based case ascertainment and longitudinal follow-up to determine the prevalence and trajectory of cognitive impairment and dementia among Mexican Americans and non-Hispanic whites. Heeringa noted that due to the COVID-19 pandemic, the HCAP assessments required adjustment to enable phone administration. He opted to use a fixed four factor model for HRS HCAP, and the parameters from HRS HCAP are retained and used to score BASIC-Cog subjects. He also performed regression adjustments for age, sex, ethnicity, and education. Moving forward, Heeringa plans to complete the computations based on the export of HRS HCAP models and diagnostic algorithm and publish the results. He will also apply all steps of the Manly-Jones HCAP diagnostic algorithm independently and directly to the BASIC-Cog HCAP data. Lastly, he will compare results of the Manly-Jones diagnostic algorithm for BASIC-Cog to other simple and more complex approaches that use HCAP measures to directly model diagnosis.

#### Discussion

Steptoe asked about the suitability of multiple imputations for missing informant data in BASIC-Cog. Heeringa noted that the missing data were not random. Weir also noted that characteristics of the study participant may affect identification of an informant; if a participant will not provide an informant at the beginning of the study, the interviewer should ask some questions to obtain data normally provided by the informant. Jones reminded meeting participants that the term "missing at random" does not mean missing haphazardly, rather it is conditionally missing at random. Confirming the likelihood of conditional missing at random status requires very complex analyses. In addition, Jones explained that imputation is used to fill missing cognitive data based on informant data and to fill missing informant data based on cognitive data in order to estimate population level prevalence, not to classify and make treatment decisions for individuals.

Elo asked how Heeringa was handling differences in informant ratings across different cultures. Heeringa acknowledged that these cultural differences do complicate interpretation of informant ratings, and Langa indicated that future results from both Nichols's and Zhang's studies will provide more information about how to address these cultural differences.

#### Update on Diagnostic Algorithm in Mex-Cog-1

#### Silvia Mejia-Arango

Mejia-Arango discussed two issues that arose during the 2021 presentation of Mex-Cog diagnostic classifications: handling of missing informant or missing cognitive assessment data and how to improve the diagnostic algorithm to more accurately detect MCI. For missing cognitive assessment information, Mejia-Arango proposed two options: (1) use both long informant information and CSI-D data or (2) use both CSI-D and Mexican Health and Aging Study (MHAS) data. Moving forward, she will evaluate both partial algorithms with an artificial sample with missing data. She will also contrast algorithm classification in Mex-Cog Wave 1 with Mex-Cog Wave 2. The current diagnostic algorithm does not perform well for detecting MCI, even in a clinical sample with informant and cognitive assessment data. Mejia-Arango will perform exploratory analyses to identify strategies to improve classification of MCI.

#### Discussion

Mejia-Arango confirmed that this algorithm was built using a robust norms approach with retrospective data from 2015 that fits criteria for the Manly-Jones algorithm. She hypothesized that the current algorithm may not perform well for MCI due to diagnostic criteria for MCI.

## **Protocol Core Update**

#### **HRS-HCAP Missing Data Treatment**

#### Lindsay Ryan and Ryan McCammon

Ryan's team prioritized a systematic, two-step data cleaning process for missing data items (i.e., a comprehensive analysis of survey responses that were missing answers or that participants had refused to answer)—to distinguish between a missing answer versus an item that received a zero score. The first step in this process was the intensive investigation of items with missing answers, answers that respondents selected "I don't know," and refusal scores to find possible data entry or idiosyncratic errors that could be fixed after survey administration. The second step was to develop guidelines for final scoring of missing items and test scores.

For an answer to be considered missing on a test score, the interviewer must show that the respondent did not attempt to answer that question. These instances include items where respondents refused every test item or refused to answer before being presented with the test stimuli. Test scores with a zero value are then only assigned when there is evidence that the respondent attempted to complete the tests or was presented with the test stimuli and had a chance to attempt it. For sections with discrete items, a zero (incorrect) score was assigned in cases where the respondent answer "yes," "no," or "I don't know" on one item, the remaining refused items are scored. Ryan's team scored items as zero if respondents had a valid score (including zero) on the immediate task. If the respondent refused the immediate task, the delayed task is scored as missing. All data collected after the interview stopped are scored as missing, and the respondent must at least complete the MMSE to be considered a partial interview.

The proposed guidelines were devised to minimize missing data among those who were presented and attempted the tasks, while reducing the assignment of low scores for test refusals that may not be related to cognitive ability. Collectively, the Rich Jones Factor Models were not meaningfully different from the originally released data.

#### **HCAP Protocol Training Materials**

#### Lindsay Ryan

The Protocol Core, in collaboration with the University of Michigan's Survey Research Operations staff, has developed a modular set of standardized training videos on 14 cognitive tests used by HCAP (e.g., letter cancellation, backward counting, trail making). Each training video consists of (1) a narrated PowerPoint presentation explaining the test and its administration and (2) a video demonstration of the test's administration. The videos were tested during the TILDA and NICOLA HCAP in 2021 and successfully used during the HRS July 2022 HCAP interviewer training. Because of test-related copyright restrictions, the videos can be shared only with studies with approved test licenses; studies can contact Ryan or Maureen O'Brien to arrange access. The TILDA team noted that in addition to being useful for initial training, the videos can help researchers check instructions or scoring details more quickly than is possible using documentation.

## **Statistical Harmonization Core Update**

## Update on International Comparisons of Psychometric and Other Data; Gateway to Global Aging Data Resources for HCAP Studies

Alden Gross, Lindsay Kobayashi, Emma Nichols, Emily Briceño, Miguel Arce-Rentería The Gateway to Global Aging provides four key services to HCAP studies: variable construction, imputation, statistical harmonization, and algorithmic classification of dementia. The Statistical Harmonization Core has made progress on several HCAP studies:

- For Mex-Cog, LASI-DAD, and ELSA-HCAP, release of harmonized data is in process.
- For HRS-HCAP, results of coding, imputation, and statistical harmonization have been shared with the study team.
- For Chile-Cog and CHARLS-HCAP, imputation is under way.

Future data analysis is also planned for SHARE Europe, TILDA, CADAS, and Nicola HCAP. The Core plans to develop collaborative papers that leverage cross-country data, including a 12-article special issue of the *American Journal of Epidemiology* in fall 2025, and to convene an HCAP data workshop in May 2023 and a data hackathon at the University of Southern California during summer 2023.

Gross described procedures for each Gateway main service. For variable construction, the Core follows the same naming and coding convention across studies. For imputation, the Core intends to replicate for other studies the procedures it developed for ELSA-HCAP, HRS-HCAP, LASI-DAD, and MexCog and to develop adaptations for studies' second waves. For statistical harmonization, the Core performs work for overall and domain-specific cognitive scores, both study-specific and through co-calibration. Harmonization activities include pre-statistical and statistical components, which involve data management/review and study-level differential item functioning (DIF) testing, respectively. The Core plans to conduct statistical harmonization for HCAPs and to link HCAPs to core surveys using available cognitive information. For harmonization, the Core uses an item banking approach, which enables addition of studies and waves as they become available without affecting scores on previous studies. Algorithmic classifications use a neuropsychological norms approach; its approach is very similar to LASI-DAD's DSM-5 algorithm.

#### Analysis of Pooled HCAP Data: Considerations and Best Practices

#### Lindsay Kobayashi

Kobayashi presented best practices for harmonizing HCAP data to enable cross-national comparisons of risk factor associations. When harmonizing, analysts should first ensure that the exposure variable can be harmonized by fully understanding the nature of the construct. For example, education can be harmonized using the International Standard Classification of

Education (ISCED), and harmonized data for many other exposures of interest are available through the <u>Gateway to Global Aging</u>. After harmonization of the exposure variable, analysts should identify any distributional problems across countries and coarsen categories into fewer overall categories when necessary. Model covariates also need to be harmonized in a similar fashion to exposure variables.

Analysts then must select the most appropriate modeling strategy, which depends on the purpose of the analysis. Parallel analysis uses separate models per country, providing flexibility of having different model covariate sets at the potential cost of loss in comparability. For pooled analysis, analysts must choose to use either fixed or random effects for country. Fixed effects strategies control for country differences. Random effect strategies enable clustering of outcomes at the country level, but the currently small number of countries with HCAP data places limitations on weighting. HCAP sampling weights were calculated using different methodologies in each country. Standardized and unstandardized sampling weights cannot be combined. Kobayashi provided a table with HCAP sample weights for HRS-HCAP, ELSA-HCAP, Mex-Cog, LASI-DAD, and HAALSI-HCAP, and provided three approaches to harmonize these weights: (1) use unstandardized weights that sum to the size of the underlying general population of each country, (2) standardize weights so that each HCAP sample is weighted equally in analysis regardless of sample size, and (3) standardize weights so that the contribution of each HCAP is proportionate to its sample size. Kobayashi noted that she is strongly considering option 3 for her analysis, but the most appropriate harmonization method depends on the purpose of the analysis.

#### **Discussion**

Weir agreed that for many HCAP research purposes, standardizing weights so that the contribution of each HCAP is proportionate to its sample size is the most suitable sampling weight harmonization method. Manly asked whether effect modification by country can be analyzed with random effects models. Kobayashi acknowledged that analyzing effect modification by country using a random effects model is possible, but in the case of HCAP, this multilevel modeling would be difficult with only five countries. King suggested that splitting LASI-DAD data by specific regions within India may enable this type of multilevel modeling.

## Differences in the Measurement of Cognition and Functional Limitations for the Assessment of Dementia across Geographic Contexts

#### Emma Nichols

Nichols presented analyses of the performance of cognitive test items and items on functional limitations across different HCAP countries using data from HRS-HCAP, Mex-Cog, ELSA, LASI-DAD, and HAALSI. While no gold-standard measure of dementia in HCAP studies exists, this study used an actuarial neuropsychological norms approach to classifying cognitive impairment across settings. Nichols first assessed the magnitude of data missingness across different countries. Higher levels of data missingness in HCAP cognition tests were detected for executive functioning items in settings with low literacy and numeracy. For informant functional limitation data, 20 percent of ELSA-HCAP participants did not have informant data, and there was a high rate of missing Blessed data for India and South Africa.

To assess the strength of associations between HCAP cognition test items with cognitive impairment across different countries, Nichols performed weighted logistic regression models that controlled for age and sex, and she <u>published the resulting data</u> earlier this year. The HCAP cognition test association with cognitive impairment was strongest for HRS-HCAP and ELSA-HCAP compared to South Africa, India, and Mexico. This strength differential is likely because HCAP items were developed and validated in the United States or similar contexts. Some of the strongest and most consistent associations between HCAP test items and cognitive impairment across all five countries were for memory items measured on a continuous scale. The most consistent observed association across countries for language items and cognitive impairment was for the animal fluency item.

Nichols used the same logistic regression model strategy to assess the strength of associations between functional limitation informant data and cognitive impairment. Of the most common informant questionnaires (i.e., IQCODE, Blessed, and CSI-D), IQCODE and Blessed had stronger associations with cognitive impairment but higher variability in the strength of associations across countries compared to CSI-D. CSI-D likely had a lower level of variability compared to other informant questionnaires because CSI-D was designed specifically for cross-cultural comparisons. Notably, informants had a much lower rate of endorsement of functional limitations in South Africa, which could be due to a specific but unknown cultural reason. The Instrumental Activities of Daily Living (IADL) assessment had particularly high variability across countries, and therefore Nichols suggested that IADL items may require tailoring to individual settings.

#### **Discussion**

King expressed interest in further understanding the relatively low endorsement of functional limitations by informants in South Africa. He further asked whether any conclusions changed after performing a subset analysis of participants who were aged 65 or older. Nichols noted that none of her conclusions changed as a result of that subset analysis.

Farrell noted that Blessed and Jorm were actually highly correlated with cognitive measures across countries in the 2018-2019 reports compared to what Nichols reported for 2016-2017 data. Nichols commented that performing this same analysis on the more recent cohorts will be important in future research. Farrell further suggested that Nichols could analyze the differences in informant characteristics from both reports.

Steptoe initiated a discussion about retrospective lookback years for informant questionnaires, such as Jorm and Blessed. All of the HCAP studies in this presentation used the standard 10-year lookback. Weir added that while the 10-year lookback is encouraged, researchers may need guidance on what lookback period to use in longitudinal studies that test more frequently than every 10 years. One meeting participant indicated that some informants, especially non-family members, may not have known the study participant for 10 years. In those instances, Weir explained, interviewers will deliver the questionnaire with a lookback for as long as the informant-participant relationship has existed and note the length of time.

#### Harmonization of HCAP Memory and Language Domains across HRS-HCAP and Mex-Cog: Implications for Future HCAP Development

#### Emily Briceño, Miguel Arce-Rentería

The Statistical Harmonization Core has worked to derive harmonized cognitive domain scores for memory and language across HRS-HCAP and Mex-Cog. Using a cultural neuropsychology approach that considers administrative and scoring procedures as well as linguistic and cultural equivalents, the Core conducted pre-statistical harmonization of each item on the two studies to identify confident, tentative, or no links. It assessed these linking decisions through a DIF analysis that tests whether information about study membership affects performance on an item after accounting for individual ability in a domain.

For the memory domain, the DIF showed evidence of measurement differences for five of seven linking items; three of these five items favored HRS-HCAP, with linked items more difficult or measurement less precise for Mex-Cog. For the language domain, only 1 of 12 linking items showed evidence of measurement differences. The impact of these differences was also stronger for the memory domain: about 75 percent of the Mex-Cog sample and 45 percent of the HRS-HCAP sample showed evidence of meaningful or salient DIF, which (if not accounted for) results in systematic underestimation of Mex-Cog memory scores; for language, by comparison, only five observations in each sample were affected.

Information curves across the spectrum of ability level also revealed differences between the studies. The memory domain showed high reliability across ability level on HRS-HCAP; reliability was slightly lower at the lower end of the ability level range for Mex-Cog but increased at approximately 1 standard deviation above the mean. For the language domain, reliability was lost at the upper end of the ability level range for both studies and at the lower end was slightly higher for HRS-HCAP than for Mex-Cog. Importantly, the area of the ability level with better reliability is also an area with fewer observations in each study.

One hypothesis for the cross-study differences identified in this analysis are undocumented, nuanced differences in survey administration or scoring. The results thus underline the need to optimize consistent administration/scoring of items, potentially through inter-rater reliability norming, use of HCAP's recently developed training videos, or better balance of within- and across-study needs in item use. The language results also suggest a need for additional items to measure the upper end of the ability level range (e.g., more difficult naming items).

#### **Discussion**

Jones noted that Mex-Cog's lower reliability on the memory domain affects an ability level relevant to classifying dementia (1.5 standard deviations below mean) and asked what itemlevel differences might lead to this result. Gross noted that for the *language* domain, the primary driver of results is the animal naming item, a continuous item that does not correlate with and has lower factor loading than other (and more difficult) confrontation naming tasks.

Lee suggested that HCAP might add more tasks similar to the animal naming task, in part because the choice of word family can impact performance on confrontation naming, and this impact may differ across cultural settings. Manly agreed that adding more tests would capture more psychometric properties, but she also noted that the animal naming task is really a measure of *semantic fluency*, which is a different sub-set of cognitive ability than confrontation naming of any items is designed to measure; thus, adding more versions of that test may not help HCAP capture the construct of overall language ability.

Arce-Rentería added that Mex-Cog may do better at capturing abilities of people at the lower ability range because its sample has overall lower literacy levels and it thus uses more simple items designed for people with severe language deficits (e.g., aphasia).

### **Pilot Study Updates**

Langa highlighted five HCAP-funded pilot studies described below and noted that HCAP funding is available for up to two additional pilots.

- Harmonization of cognitive performance and informant-rated decline across older adults living in the United States, Mexico, and Chile (Arce Rentería and Briceño)
- Expanding cognitive measurement in the Longitudinal Study of Health and Ageing in Kenya (Ehrlich and Ngugi)
- Comparing informant measures of functioning and cognitive decline in HCAP studies in the United States, China, and Mexico (Zhang and Phillip Cantu)
- Cross-national harmonization of cognitive measures and cognitive impairment in 10/66 sister studies, MHAS, and ELSA (Jorge Llibre-Guerra)
- Supporting the development of A Longitudinal Study of Healthy Aging in Egypt (AL-SEHA) (Mohamed Salama and Axel Boersch-Supan)

Two larger-scale efforts, which aim to expand HCAP to Malawi (Hans-Peter Kohler and Iliana Kohler) and to Brazil (Cleusa Ferri and Maria Fernanda Lima-Costa), will be seeking supplemental funding.

## **Group Discussion and Next Steps**

Langa moderated the group discussion that covered five general themes: (1) Implementing Consensus Diagnosis, (2) Challenges in Identifying MCI in Population Studies, (3) Interviewing Multiple Respondents in the Same Household, (4) Combating the COVID-19 Pandemic, and (5) Fostering Harmonization of Key Variables. These themes might benefit from small group calls for further discussion. Additional ideas for small group calls included imputations for missing respondent data, and extrapolation of HCAP algorithmic diagnoses back to the HRS.

#### **Implementing Consensus Diagnosis**

Developing and implementing a gold standard for clinical dementia diagnosis will bolster the impact of the HRS-HCAP studies. The clinical dementia rating (CDR) process has been routinely used in clinical studies, but the HCAP Network must invest resources in validation studies to assess the reliability of the CDR in population-based studies, including their performance in the setting of a consensus diagnosis conference. (LASI-DAD has already performed this type of validation study.) In addition, the HCAP Network studies have developed diagnostic algorithms

using cross-sectional HCAP data. More work comparing diagnostic outcomes between consensus diagnosis and diagnostic algorithms will be important in the next few years.

## Challenges in Identifying MCI and "Preclinical Alzheimer's Disease" in Population Studies

Accurate identification of MCI in population studies is challenging because MCI is a state in between normal cognition and dementia (characterized by measurable impairment in cognitive testing and/or self- or proxy-reported cognitive concerns, without disability in daily function). Up to 20 percent of individuals identified with MCI will revert to normal cognition over the next 1 to 2 years. "Preclinical Alzheimer's Disease" is defined as biomarker evidence of amyloid, tau, and neurodegeneration (i.e., the ATN classification scheme) without any evidence of cognitive decline. Preclinical AD is a focus of significant interest and current research, and the HCAP network studies that are collecting biomarkers could make important contributions to this field of study, especially regarding whether the relationships between ATN biomarkers and future cognitive outcomes is similar or different in population-based studies compared to clinical studies.

#### Interviewing Multiple Respondents in the Same Household

Using video interviews could provide long-term benefit for assessing dementia in HCAP Network studies, particular for groups launching pilot studies or those recently fielding work. Interviewing households with multiple respondents could increase the sample size, but in these situations, respondents must be assessed separately and independently in order to prevent "contamination" and biased responses. The HCAP Network should consider establishing a small working group to determine the effectiveness and best practices for interviewing multiple respondents in the same household.

#### **Combating the COVID-19 Pandemic**

The pervasive and lingering effects of the COVID-19 pandemic on the HCAP Network studies may resurface during the winter, particularly in the Northern Hemisphere, requiring virtual rather than in-person interviewing. The HCAP Network needs to discuss (1) the ongoing effects of the COVID-19 pandemic on recruitment and interview strategies and (2) whether to implement computer-assisted video interviews instead of in-person interviews. Study leaders need to consider how to adjust for or retain comparability when survey procedures or modes of interview change over time in the same study.

#### **Fostering Harmonization of Key Variables**

Key variables (e.g., education, socioeconomic status, geography) need to be harmonized across countries in order to compare the impact of these variables on cognition and dementia. The Gateway to Global Aging Program provides an excellent platform to facilitate this type of data harmonization. Future work in should include harmonizing education variables using the ISCED, and stress and wellbeing measures.

### Appendix A: Meeting Agenda 4th Annual Meeting of the Harmonized Cognitive Assessment Protocol (HCAP) International Network September 19 -20, 2022 The Bethesdan Hotel • Bethesda, MD MEETING AGENDA Rev. 9-20-22 \*Attended In-Person

#### Monday, September 19

- 8:00 a.m. BREAKFAST
- 9:00 Welcome and Introductions \*Ken Langa and \*David Weir

#### NIA Welcome

\*Minki Chatterji

9:15 HCAP R24 Network Updates \*David Weir and \*Ken Langa

> The Network for Innovative Methods in Longitudinal Aging Studies (NIMLAS) Brady West and Sunghee Lee

#### 9:30 Reports from HCAP Studies Currently in the Field

- TILDA (\*Joanne Feeney)
- NICOLA (\*Bernadette McGuinness)
- HRS (\*Ken Langa)

#### 10:15 BREAK

#### 10:30 Updates from Established HCAP Studies

- ELSA (\*Andrew Steptoe)
- MHAS (Rebeca Wong)
- LASI (\*Jinkook Lee)
- CHARLS (Yaohui Zhao)
- HAALSI (Lisa Berkman)
- Chile-COG (\*Irma Elo, David Bravo, and \*Magdalena Delaporte)

#### 11:50 **LUNCH**

#### 1:00 p.m. Updates, Continued

- SHARE (\*Salima Douhou)
- LSAHA (Carlos Mendes de Leon)
- Nepal (Carlos Mendes de Leon)
- CADAS (Will Dow)
- Kenya (Will Dow)

#### 2:00 Biomarker Core Update

- HRS-HCAP preliminary blood biomarker results Jessica Faul and \*Bharat Thyagarajan
- LASI-DAD blood biomarker and neuroimaging activities and plans Perry Hu
- WHICAP biomarker results Jennifer Manly

#### 3:00 BREAK

#### 3:15 Diagnosis and Classification Core Update

- IQCODE performance in LASI-DAD / Harmonization of informant reports across studies
   \*Emma Nichols (LASI-DAD) and Yuan Zhang (Harmonization)
- HRS-HCAP Manly-Jones diagnostic algorithm / Facilitating export and adjustment of algorithm for other network studies Jennifer Manly and \*Rich Jones
- Export of Manly-Jones algorithm to BASIC-Cog Steven Heeringa
- Update on diagnostic classification in Mex-Cog Rebeca Wong

#### 5:00 ADJOURN

6:00 **GROUP DINNER** 

Tuesday, September 20		
8:00 a.m.	BREAKFAST	
9:00	<ul> <li>Protocol Core Update Bethesdan         <ul> <li>Classification of "missing" vs "incorrect" in HRS-HCAP and other studies *Lindsay Ryan and Ryan McCammon</li> <li>HCAP protocol training materials *Lindsay Ryan</li> </ul> </li> </ul>	
9:30	<ul> <li>Statistical Harmonization Core Update</li> <li>Update on international comparisons of psychometric and other data; Gateway to Global Aging Data resources for HCAP studies *Alden Gross, *Lindsay Kobayashi, *Emma Nichols, *Emily Briceño, Miguel Arce-Renteria</li> </ul>	
10:30	BREAK	
10:45	<ul> <li>Pilot Study Updates</li> <li>Discussion of pilot projects and exchanges</li> </ul>	
11:00	<ul> <li>Group Discussion and Next Steps</li> <li>Current concerns and roadblocks?</li> <li>Plans for joint analyses and publications?</li> <li>Solicitation of ideas for small-group follow-up sessions</li> <li>Implementing consensus diagnosis process</li> <li>Future priorities and directions from NIA's perspective (*Minki Chatterji, *Jon King)</li> </ul>	
12:30 p.m.	ADJOURN	

## Appendix B: Meeting Attendees \*In-person Participants

*	Dallas Anderson, Director, Epidemiology of Dementia Program, Division of Neuroscience, NIA
	Miguel Arce-Rentería, MHAS, Mex-Cog, HCAP Network Pilot Awardee; Gateway to Global
	Aging Data, HRS; Columbia University
	Sarah Assaad, ELSA, Research Fellow, University College London
	Frank Bandiera, Program Official, BSR, NIA
	Darina T. Bassil, Co-I, HAALSI; Harvard University
	Jere Behrman, Co-PI, Chile-Cog; University of Pennsylvania
	Lisa Berkman, PI, HAALSI; Harvard University (Day 1 only)
	David Bravo, Co-PI, Chile-Cog; Catholic University of Chile (Day 1 only)
*	Emily Briceño, Co-I, BASIC-Cog; University of Michigan
	Phillip Cantu, Team Member, Mex-Cog; University of Texas Medical Branch
	<b>Monique Chaaya</b> , Professor and Chair, Department of Epidemiology and Population Health, American University of Beirut
	Minki Chatterji, Program Officer, Population and Social Processes Branch, DBSR, NIA
*	Magdalena Delaporte, Team Member, Chile-Cog; Catholic University of Chile
	Céline De Looze, Lead of Cognitive Neuroscience and MRI research groups, TILDA; Trinity
	College Dublin
	Elaine Douglas, Co-Researcher, HAGIS
	Salima Douhou, Coordinator, SHARE; Max Planck Institute
	Will Dow, PI, CADAS; University of California, Berkeley
	Martine El Bejjani, Team Member, LSAHA; American University of Beirut (Day 1 only)
*	Irma Elo, Co-PI, Chile-Cog; University of Pennsylvania
	Meagan T. Farrell, Co-I, HAALSI; Harvard University
	Madeline Farron, Team Member, HRS-HCAP; University of Michigan
	Jessica Faul, HCAP Network Biomarker Core Leader; Co-I, HRS-HCAP; Co-I, HRS; University of Michigan (Day 1 only)
	Elena Fazio, Program Official, BSR (Day 1 only)
	Joanne Feeney, Senior Researcher, TILDA; Trinity College Dublin
	Cleusa Ferri, Contributor, ELSI
	Elizabeth Frankenberg, Co-PI, Study of the Tsunami Aftermath and Recovery (STAR);
	University of North Carolina, Chapel Hill (Day 1 only)
	Sarah Gao, Research Assistant, HAALSI; Havard Center for Population and Development Studies
	Brian Gray, Health Science Policy Analyst, Office of the Director, NIA (Day 1 only)
*	Alden Gross, Co-I, LASI-DAD, and MPI, Gateway to Global Aging Data; John Hopkins Bloomberg School of Public Health
	Shabina Hayat, Senior Research Fellow, ELSA; University College London
	Steven Heeringa, co-I, HRS-HCAP, BASIC-Cog; University of Michigan
	Richard Hodes, Director, NIA
	Perry Hu, Co-I, LASI-DAD; University of California, Los Angeles (Day 1 only)

- **Elyse Jennings**, Research Scientist, HAALSI; Harvard Center for Population and Development Studies (Day 1 only)
- \* Richard Jones, HCAP Network Statistical Harmonization Core Leader; Co-I, HRS-HCAP; Co-I, HRS; Brown University
  - Kathleen Kahn, Senior Scientist, HAALSI; University of Witwatersrand (Day 1 only)
  - Arie Kapteyn, PI, Understanding America Study; Director, Center for Economic and Social Research (CESR), and Professor of Economics, University of Southern California
     Amelia Karraker, Program Official, BSR, NIA (Day 1 only)
- \* Amy Kelley, Deputy Director, NIA (Day 1 only)
- Melinda Kelley, Senior Advisor, Office of the Director (Day 1 only)
- \* Jon King, HRS Project Scientist; Program Director, BSR, NIA Matthias Klee, PhD Student, SHARE; University of Luxembourg
- \* Lindsay Kobayashi, Team Member, HRS; University of Michigan
- \* Iliana Kohler, Malawi Longitudinal Study of Families and Health; University of Pennsylvania
- \* Kenneth Langa, Co-PI and Diagnosis and Validation Core Leader, HCAP Network, PI HRS-HCAP; Co-I, HRS; University of Michigan
- \* Jinkook Lee, PI, LASI-DAD; University of Southern California
   Sunghee Lee, MPI, NIMLAS; University of Michigan (Day 1 only)
   Mao-Mei Liu, Team Member, CADAS; University of California, Berkeley
   Ying Liu, Co-I, Gateway to Global Aging Data; University of Southern California
   Jorge Llibre-Guerra, Team Member, CADAS; Washington University in St. Louis
   Sneha Mani, Research Team, Chile-Cog; University of Pennsylvania
   Jennifer Manly, Co-I, HRS-HCAP; Co-I, HRS; Columbia University
   Ryan McCammon, Collaborator, HRS-HCAP; University of Michigan
   Christine McGarrigle, Senior Research Fellow Epidemiology, TILDA; Trinity College Dublin
- \* Bernadette McGuinness, Co-PI, NICOLA; Queen's University Belfast
   Silvia Mejia-Arango, Expert Collaborator, Mex-Cog; El Colegio de la Frontera Norte
   Carlos Mendes de Leon, PI, LSAHA and Nepal ISER-N; Georgetown University (Day 1 only)
   Marilyn Miller, Program Director, Division of Neuroscience, NIA
   Lewis Morgenstern, PI, BASIC-Cog; University of Michigan (Day 1 only)
   Sara Moustafa, Research Assistant, AL-SEHA; The American University in Cairo (Day 1 only)
- \* Emma Nichols, LASI-DAD; PhD student, Johns Hopkins University
- \* Lisbeth Nielsen, Director, BSR, NIA
  - Leeanne O'Hara, Research Fellow, School of Medicine, Dentistry and Biomedical Sciences, Centre for Public Health, Queen's University Belfast (Day 2 only)
  - Marcela Otero, Research Scientist, SHARE; Munich Center for the Economics of Aging Sarah Petrosyan, Research Programmer, The Program for Global Health, Aging & Policy, CESR,
    - USC (Day 1 only)
- \* John Phillips, Program Officer, HRS; Chief, Population and Social Processes Branch, BSR, NIA (Day 1 only)
  - Ana Rodriguez-Salgado, Neuropsychologist, TILDA; Trinity College Dublin (Day 1 only) Julia Katherine Rohr, Project Director, HAALSI; Harvard Center for Population & Development Studies

- \* Lindsay Ryan, HCAP Network Protocol Content and Administration Core Leader; co-I, HRS-HCAP; University of Michigan
  - **Nina Silverberg**, Director, Alzheimer's Disease Centers Program, Division of Neuroscience, NIA (Day 1 only)

Janine Simmons, Chief, Individual Behavioral Processes Branch, BSR, NIA (Day 1 only)
 Amanda Sonnega, HCAP Network Outreach and Dissemination Core Leader; University of Michigan

- \* Andrew Steptoe, PI, ELSA; University College London Luke Stoeckel, Program Official, BSR, NIA
   Duncan Thomas, co-PI, STAR; Duke University
- \* Bharat Thyagarajan, Co-I, HRS; Professor, University of Minnesota
   Stephen Tollman, Team Member, HAALSI; University of the Witwatersrand, South Africa (Day 1 only)
- **Ryan G. Wagner**, Research Fellow, HAALSI; University of the Witwatersrand (Day 1 only)
- \* **David Weir**, co-PI and Sampling Core Leader, HCAP Network; Co-PI, HRS-HCAP; PI, Irish HCAP R01; PI, HRS; University of Michigan
  - Brady Thomas West, MPI, NIMLAS; University of Michigan (Day 1 only)
  - Rebecca Wong, PI, MHAS Mex-Cog; University of Texas Medical Branch
  - **Codi Young**, Research Programmer, The Program for Global Health, Aging & Policy, CESR, USC
  - Yuan Zhang, Carolina Population Center, University of North Carolina Yaohui Zhao, PI, CHARLS; Peking University

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- \* Rose Maria Li, Senior Project Director
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## **Appendix C: Substantive Chat Transcript**

#### September 19, 2022

01:35:56	Brady Thomas West: NIMLAS website: nimlas.isr.umich.edu		
01:36:10	Brady Thomas West: NIMLAS inquiries: nimlas-inquiry@umich.edu		
02:13:02 Mao-Mei Liu (she/her): I wonder whether the TILDA, NICOLA teams			
	done community outreach previous or alongside fieldwork and if so, how it has		
	gone. Do older adults know about the study previously?		
02:13:46	Monique Chaaya: how long is the interview on average?		
02:14:17	Mao-Mei Liu (she/her): yes bolster recruitment		
02:15:12	Mao-Mei Liu (she/her): (I'm trying to think about how to boost		
	participation, decrease refusal)		
02:15:32	Ryan McCammon: Do either TILDA or NICOLA HCAPs conduct friends & family		
	interviews in the absence of a respondent interview?		
02:16:17	Mao-Mei Liu (she/her): thank you		
02:19:18	Rebeca Wong, Mex-Cog (MHAS): In Mexico they know ahead of time. The		
	supervisors visit the household ahead of time to confirm the respondent still		
	lives there. They leave a flier behind.		
02:23:20	Elizabeth Frankenberg: what was the reason for not repeating the		
	olfactory assessment?		
02:23:54	Monique Chaaya: we can't hear the question		
02:25:07	Dr Meagan T. Farrell: This may be a question for statistical harmonization core,		
	but have there been any analyses to look at differences in test performance due		
	to different modalities (paper, tablet, computer)		
02:25:30	Dr Meagan T. Farrell: within and across studies		
02:26:31	Sarah Assaad (UCL): Were there some interviewer's bias checks due to		
02.26.54	differences in administering tests?		
02:26:54	Rebeca Wong, Mex-Cog (MHAS): Mex-Cog distributed masks and plastic		
	shields for interviewers. And gift masks to respondents. Many interviewers		
02:27:34	preferred the plastic shield.		
02:27:34	Mao-Mei Liu (she/her): Yes In school settings Rebeca Wong, Mex-Cog (MHAS): To our colleagues from the new Network		
02.31.29	NIMLAS We are going to need a working group on how to take into account		
	heterogeneity in modes of application. From one wave to the next, and across		
	studies. COVID really forced us to make changes that will need to be considered.		
02:43:42	Shabina Hayat: How can we get access to the HRS training videos for the		
02.43.42	ELSA-HCAP 2 wave (pilot in Nove 2022)		
02:52:13	Mao-Mei Liu (she/her): Would it be possible to receive that set of		
02:02:120	questions about End of Life? sounds very interesting - and probably pretty		
	different in different country contexts (even within country contexts)		
02:53:39	Jennifer Manly: Are there questions about first language and language		
	proficiency?		
02:54:40	Mao-Mei Liu (she/her): Who is doing that language research?		

03:00:38	Jennifer Manly: Emily Briceno and Miguel Arce are doing the bilingualism research in HCAP/HRS and have also been working in Mex-COG		
03:02:08	Jennifer Manly: Jinkook Lee, Miguel Arce, and Leon Aksman just got a very good score on an RO1 that responded to the Bilingualism and reserve RFA that Jon King just mentioned		
03:30:56	Mao-Mei Liu (she/her): we (on zoom) can't here jon very well		
03:31:32	Elena Fazio (NIA-BSR):@Liu - I could not hear John Phillips either.		
03:31:35	David R Weir: John Phillips asked how long the protocol was with additions		
03:31:49	David R Weir: And he asked where the refresher was coming from		
03:31:53	Elena Fazio (NIA-BSR):thanks @Weir		
03:32:08	David R Weir: and he asked if the pollution measures could be shared across the network. i'm not sure what he means by that one		
03:35:18	Mao-Mei Liu (she/her): we can see it!		
03:36:14	David R Weir: @yaohui we skipped ahead to HAALSi and will come back to you after		
03:37:36	Yaohui Zhao: apologies! had a black out.		
04:21:49	Rebeca Wong, Mex-Cog (MHAS): @Jon King question on Biomarkers available for Mex-Cog participants. Attached is slide. Please ask if questions.		
04:23:50	Rebeca Wong, Mex-Cog (MHAS): @HAALSI. Interesting work. Can we have access to the HAALSI prediction equation when you are ready to share? Thanks.		
05:18:02	Lisa Berkman: we would love to share thiswe were going to finalize shortly after the meeting both Manly and glamour have been helping with this. David suggested we find a time to discuss everyone's strategy. As you can imagine it's complex.		
05:24:16	Jennifer Manly: Caracterials in Spanish and English on the website!		
05:30:02	Rebeca Wong, Mex-Cog (MHAS): Mex-Cog and MHAS materials are online - in English and Spanish as well.		
05:43:52	Mao-Mei Liu (she/her): Sorry if I missed this - is there an effort to expand SHARE across other countries (e.g. differing welfare regimes)?		
05:45:03	dweir: SHARE itself covers all countries in Europe. The plan is to generate dementia classifications for all SHARE from the HCAP subsample. The HCAP subsample is just 5 countries		
05:46:07	Jennifer Manly: Apples and oranges!		
05:46:13	Jennifer Manly: Perfect example		
05:46:39	Mao-Mei Liu (she/her): thank you @davidweir		
05:54:02	dweir: @carlos and martine: why not the symbol cancellation task?		
05:54:18	Darina T Bassil: So excited to see this work in Lebanon! Will you be doing		
	the battery on tablet or paper?		
05:54:50	Monique Chaaya: will use tablets		
05:55:07	Dr Meagan T. Farrell: We have done symbol cancel on tablet for HAALSI HCAP		
05:55:20	Darina T Bassil: Symbol cancellation worked for us		
05:55:24	Darina T Bassil: and we did it on tablet		
05:55:25	Darina T Bassil: For haalsi		

05:55:34	Jennifer Manly:	Not too late to add this!
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- 05:55:53 Dr Meagan T. Farrell: Yes we have a shapes trails tablet
- 05:56:32 Mao-Mei Liu (she/her): Which projects have done SDMT electronically (on tablets)?
- 05:56:57 Darina T Bassil: we did it on paper as pilot , but had dropped it as it did not work in our haalsi cohort
- 05:57:18 Mao-Mei Liu (she/her): Thanks @darina I remember that.
- 06:04:42 Mao-Mei Liu (she/her): Here's one of the articles that have come out https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3365856/
- 06:23:21 Monique Chaaya: @ Jessica do you have the protocol published or documented. can you please share
- 06:23:54 Darina T Bassil: we have also begun our pilot work for HAALSI in terms of biomarkers in collaboration with Zetterberg: amyloid, GFAP, Tau and NFL using venous blood and actually for NFL, we are using DBS too! Would be exciting to compare results when done!
- 06:39:38 Rebeca Wong, Mex-Cog (MHAS): Very interested in DBS for poor settings. As we know, very difficult to guarantee the quality of venous-blood samples from remote rural areas.
- 06:42:13 Dr Meagan T. Farrell: Yes, exactly. We hope that we will have promising results for DBS. Henrik Zetterberg's lab is among the first to try this. We are comparing NFL in DBS to the plasma samples.
- 06:48:15 Bharat Thyagarajan: That will be great. It will exciting to see if NfL is stable in DBS
- 06:49:08 Jessica Danielle Faul: @ Monica the HRS VBS collection protocol is included in the data description here:
- 06:49:10 Jessica Danielle Faul: <u>https://hrsdata.isr.umich.edu/data-products/2016-</u>venous-blood-study-vbs
- 06:49:21 Jessica Danielle Faul: Bharat has a paper under review on his validation work
- 07:17:18 Martine: interesting results !
- 07:17:37 Jennifer Manly: thanks!
- 07:43:24 Rebeca Wong, Mex-Cog (MHAS): RE: your conclusion on "Informant matters." Did you look at the informants (spouse versus other) within those of the same generation? In Mex-Cog we find that the Spouse response is different (more impairment) than other type of informant.
- 07:58:53 Jennifer Manly: IMHO: I don't think it is practical for there to be any standardization of who serves as a friend or family member for the HCAP network studies.
- 08:00:14 Rebeca Wong, Mex-Cog (MHAS): For INFORMANTS: Is there information on -- freq of contact (hours spent together in a typical day/week)?
- 08:00:47 Mao-Mei Liu (she/her): @jenmanly I agree @rebecawong, what do you think is behind that finding? it is a more accurate perspective; hardship re: caretaking; or something else?
- 08:02:49 Rebeca Wong, Mex-Cog (MHAS): Perhaps several: Accuracy of perspective; Some fatigue; But also what is acceptable 'old age' performance in the culture?

- 08:07:11 Martine: :)
- 08:35:55 Dr Meagan T. Farrell: were these factor analyses completely exploratory, or did you test a factor structure that best recreates the domains from the DSM V
- 08:37:30 Rebeca Wong, Mex-Cog (MHAS): Are we going to have the slides (including the ones with recipes)?
- 08:38:01 Darina T Bassil: Wow amazing work , thank you both for sharing!!!!
- 08:38:27 Dr Meagan T. Farrell: Yes, that makes sense to start with HRS factors
- 08:39:04 Dr Meagan T. Farrell: thank you
- 08:42:25 Rebeca Wong, Mex-Cog (MHAS): Jenn --Glad to hear that you suggest -- to add ORIENTATION back even if the items do not load in the factors.
- 09:29:01 Matthias Klee: Thank you very much for the interesting talks!

#### September 20, 2022

- 00:55:33 Marcela Otero SHARE: Thanks Lindsay, helpful presentation Suppose a Res. is shown a CERAD shape (copy trial) but does not want to attempt to draw it. Would they be given a 0 because they were shown the stim or a missing because they did not attempt to draw it?
- 00:59:07 Marcela Otero SHARE: Yes, indeed! Ok thanks.
- 01:00:58 Dr Meagan T. Farrell: how much of this do you handle in the data cleaning process vs. ask the interviewers to document
- 01:01:25 Jennifer Manly: I agree that there is no "one size fits all" solution. You have done a great job providing guidance! @Meagan I think it NEEDS to be iterative to some extent.
- 01:02:49 Dr Meagan T. Farrell: @Jennifer thank you. The more checks the better.
- 01:05:37 Jennifer Manly: There are some things that just can't be inferred from a data cleaning process like the difference between "refused" and "unable to understand task". Both are missing but the interviewer should be making that call. And making that call is sometimes tough interviewers should be able to read and see examples of borderline examples, and the administration manual should be built up to help interviewers make the call moving forward as new examples arise.
- 01:11:38 Rebeca Wong: Lindsay and Team: Great work, thank you for sharing! If we don' use these specific videos, we get good ideas to implement your strategies.
- 01:12:36 Jennifer Manly: These are great!
- 01:12:41 Mao-Mei Liu (she/her): yes I agree with @rebecawong. apologies if I missed this are there plans to translate to other languages, (like Spanish)?
- 01:13:40 Lindsay H Ryan: We don't have plans for translations yet, but it's something we can look into. Spanish would certainly be a good one to prioritize.
- 01:14:34 Jennifer Manly: Would it make sense to swap out the narration for other languages, keeping the videos the same? Are there resources to pay for dubbing (like in Money Heist!)
- 01:14:49 dweir: Maybe we could interest Silvia to work with a translation team.
- 01:25:31 Mao-Mei Liu (she/her): Or simply subtitles at first

01:26:11	Mao-Mei Liu (she/her): (so far, we at cadas have found YouTube caption translation helpful)
01:29:02	dweir: To use for training we want to be sure they are training people to do the
	tests as comparably (neuropsychologically speaking) as possible, which is why I
01.21.22	think it needs a bilingual neuropsychologist and not just a translation tool
01:31:33	Jennifer Manly: AGreed
01:33:24	Jennifer Manly: Lindsay (for later) why can't RE do interactions (effect modification)?
01:43:04	Jennifer Manly: So the "returns to education" is the same across countries,
	and that is relative within country?
01:49:40	Jennifer Manly: Please someone present quick!
02:04:42	Dr Meagan T. Farrell: The 2016 HAALSI HCAP wave was a bit before my time, but
	we see higher endorsement of limitations by informants in the 2018-2019 wave,
	mean jorm around 3.3
02:04:57	Dr Meagan T. Farrell: and strong correlations with cognitive tests
02:23:28	Jennifer Manly: And there are more people with low literacy in MexCog
02:26:29	Jennifer Manly: Animal fluency is a different aspect of the "language"
	domain than confrontation naming
02:58:57	Rebeca Wong, Mex-Cog (MHAS): Mex-Cog would appreciate a Discussion
	Group on Cross-Walking. The idea is to inform/improve our Core Surveys. It can
	be just 2 hours to review evidence/approaches/work completed, ongoing.
03:03:25	Dr Meagan T. Farrell: HAALSI would like to participate in this discussion. We
	have developed prediction models using measures from the core survey to
	predict consensus diagnoses within HAALSI HCAP to generate dementia
	probability scores on the parent cohort. Is there a plan to extrapolate HCAP
	algorithmic diagnoses back to HRS?
03:08:46	Rebeca Wong, Mex-Cog (MHAS): Is there support for the MCI Discussion? A
	special Discussion group meeting to assess how algorithms are performing for
	MCI?
03:08:48	Dr Meagan T. Farrell: How have others considered very high depression scores
	into their diagnostic definitions?
03:09:26	Dr Meagan T. Farrell: as potential confounder
03:09:52	Jennifer Manly: I would be happy to take part in within and/or cross-study
	MCI discussions.
03:12:45	Rebeca Wong, Mex-Cog (MHAS): Perhaps with the New Network on
	Longitudinal Studies we can have a Discussion group on how to adjust for
	/retain comparability when survey procedures or modes of interview change
	over time (like for COVID) in the same study?
03:19:20	Darina T Bassil: In HAALSI-HCAP, we also try to avoid this and exclude
	people within the same household
03:20:22	Mao-Mei Liu (she/her): Thank you, this is all very helpful. We are planning
	to interview multiple older adults in households for CADAS

- 03:21:15 Rebeca Wong, Mex-Cog (MHAS): Mex-Cog did have 2 spouses in households in Wave-1. There may be good people interested in analyzing the couples data within/across studies too.
- 03:34:18 Mao-Mei Liu (she/her): Can someone explain why you would exclude people who report depressive symptoms?
- 03:34:24 Mao-Mei Liu (she/her): please
- 03:37:34 Dr Meagan T. Farrell: My question relates to the possibly that depression may affect (lower) cognitive performance, independent from neurodegenerative processes
- 03:43:23 Rebeca Wong, Mex-Cog (MHAS): Another opportunity to interact with the LONGITUDINAL STUDIES network -- is the learning/re-test issue for longitudinal surveys.
- 03:45:08 Rebeca Wong, Mex-Cog (MHAS): THANK YOU to Rose Li and the TEAM for managing the virtual attendants and presentations!!